# Rheumatic heart disease in Southwestern Ethiopia: Burden, Severity and Self-Management Education Effectiveness

A PhD Dissertation

By

Hiwot Berhanu Meshesha

A PhD Dissertation Submitted to the School of Graduate Studies, Jimma University in Partial Fulfillment of the Requirements for the Award of the Degree of Doctor of Philosophy (PhD) in Medical Physiology.

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**Table of Contents**

**Contents** **Pages**

**Acknowledgments** ..... **vi**

**Table of Contents** ..... **vii**

**Glossary of Acronyms and Abbreviations** ..... **xiii**

**Summary** ..... **xv**

**Chapter One: General Introduction** ..... **1**

1.1 Overview ..... 1

1.1.1 General over view of rheumatic heart disease ..... 1

1.2 The burden of RHD (epidemiology of RHD) ..... 2

1.3 Risk factors for rheumatic heart disease ..... 3

1.3.1 Socio-demographic factors ..... 3

1.3.2 Genetics factors ..... 5

1.3.3 Nutritional factors ..... 5

1.3.4 Environmental factors ..... 6

1.3.5 Hygiene related factors ..... 7

1.3.6 Oral health related factors ..... 7

1.3.7 Health facility related factors ..... 8

1.3.8 Smoke exposure ..... 8

1.4 Pathophysiology, echocardiographic pattern, and complications related to RHD ..... 9

1.4.1 Pathophysiology of rheumatic heart disease ..... 9

1.4.2 Echocardiographic patterns among RHD ..... 12

1.4.3 Complications related to RHD ..... 13

1.5 Preventive strategies in rheumatic heart disease ..... 14

1.5.1 Importance of chronic disease self-management education for individuals living with RHD ..... 16

1.6 Significance of the study ..... 16

1.6.1 Why this PhD. dissertation research necessitated? What gap does it addressed? ..... 16

1.7 Conceptual framework ..... 19

1.8 Outline of the dissertation ..... 21

**Chapter Two: Research Questions, Hypotheses and Objectives** ..... **23**

2.1 Research questions ..... 23
2.2 Research hypotheses ..... 23
2.3 Research objectives ..... 24
2.3.1 General objective ..... 24
2.3.2 Specific objectives ..... 24
**Chapter Three: Materials and Methods ..... 25**
3.1 Study setting, and period ..... 25
3.2 Study participants and criteria ..... 25
3.2.1 Criteria ..... 25
3.3 Sample size determination and sampling procedures ..... 26
3.4 Data collection and measurements ..... 27
3.5 Data quality control ..... 28
3.6 Intervention and protocol ..... 29
3.7 Data analysis ..... 29
3.8 Ethical approval ..... 30
3.9 Dissemination of the study findings ..... 31
**Chapter Four: The Prevalence of Rheumatic Heart Disease in Ethiopia: a Systematic Review and Meta-analysis ..... 33**
4.1 Background ..... 34
4.2 Materials and methods ..... 35
4.2.1 Outcome variables ..... 35
4.2.2 Eligibility criteria ..... 35
4.2.3 Search strategy ..... 35
4.2.4 Risk of bias assessment ..... 38
4.2.5 Data extraction and outcome of interest ..... 38
4.3 Reliability of data ..... 38
4.3.1 Analysis of the Data ..... 38
4.4 Results ..... 39
4.5 Discussion ..... 49
4.6 Conclusion and recommendation ..... 51

**Chapter Five: Rheumatic Heart Disease Burden, Pathophysiology, and Determinants in Cardiac Patients: A Follow up Care Concern in Ethiopia ..... 53**
5.1 Background ..... 54
5.2 Materials and Methods ..... 55
5.3 Results ..... 59
5.4 Discussion ..... 64
5.5 Conclusion and recommendation ..... 67
**Chapter Six: Echocardiographic Parameters, Pathophysiology and Complication Profiles among Adult Patients with Rheumatic Heart Disease at Jimma Medical Center ..... 68**
6.1 Background ..... 69
6.2 Materials and Methods ..... 70
6.3 Results ..... 71
6.4 Discussion ..... 76
6.5 Conclusion and recommendation ..... 79
**Chapter Seven: Effects of Self-Management Education on Clinical Outcomes of Adults with Rheumatic Heart Disease: a Quasi-Experimental Study ..... 81**
7.1 Background ..... 82
7.2 Materials and Methods ..... 83
7.3 Results ..... 90
7.4 Discussion ..... 93
7.5 Conclusion and recommendation ..... 96
**Chapter Eight: General Discussion, Future Research Perspectives, and Conclusion ..... 97**
8.1 Introduction ..... 97
8.2 Summary of the main findings ..... 98
8.3 Implication of the findings ..... 100
8.4 Methodological considerations: strength and limitations with future research direction . 100
8.5 Conclusion ..... 101
8.6 Recommendations ..... 101
**9. Reference ..... 103**
10.1 Curriculum Vitae of the candidate ..... 123
10.2 Conference participations and Certificates ..... 129
10.3 Information sheet ..... 133

10.4 English version questionnaire for data collection ..... 135
10.5 Concise summaries of the 2012 World Heart Federation criteria for the echocardiography diagnosis of rheumatic heart disease ..... 142
10.6 Risk of bias assessment ..... 145
10.7 Declaration ..... 157

## Lists of Figures

Figure 1.1: Causal pathways from GAS exposure to ARF and RHD showing major hypothesized groups of risk and protective factor (Baker et al. 2019) ..... 9
Figure 1.2: Schematic presentation of the conceptual framework of interrelated etiologic factors of Rheumatic Heart Disease (adapted from different literature reviews) ..... 20
Figure 1.3: Schematic representation of the PhD dissertation ..... 22
Figure 4.1: PRISMA flow chart for identifications of studies included in systematic review and meta-analysis on prevalence of Rheumatic Heart Diseases in Ethiopia ..... 39
Figure 4.2: Funnel plot for assessment of publication bias across studies ..... 42
Figure 4.3: Forest plot on studies that quantitatively assessed pooled prevalence of rheumatic heart disease in Ethiopia ..... 44
Figure 4.4: Forest plot on studies that quantitatively assessed pooled prevalence of Rheumatic Heart Disease in Ethiopia ..... 45
Figure 4.5: Subgroup analyses on the prevalence of Rheumatic Heart Disease among different regions of Ethiopia ..... 46
Figure 4.6: Prevalence of Rheumatic Heart Disease among males (a) and females (b) in Ethiopia ..... 48
Figure 4.7: Trends of Rheumatic Heart Disease prevalence by year of publication in Ethiopia .. 48
Figure 5.1: A flow chart showing the recruitment of study participants ..... 58
Figure 6.1: Complications related to rheumatic heart disease ..... 76
Figure 7.1: A summary of the study time lines ..... 84
Figure 7.2: Study identification and selection flow diagram ..... 86
Figure7.3: Hospital Anxiety and Depression subscales ..... 93

## List of Tables

Table 3.1: Summary of the study methods of the dissertation, 2023-2024 ..... 32
Table 4.1: Searching strategy and information sources ..... 37
Table 4.2: Characteristics of the individual studies included in the systematic review and meta-analysis on prevalence of rheumatic heart diseases in Ethiopia ..... 41
Table 4.3: Assessment of publication bias using egger's test among studies ..... 43
Table 5.1: Socio-demographic characteristics of cardiac patients attending follow-up at JMC cardiac clinic from January 5 to April 15, 2023 (n = 340) ..... 60
Table 5.2: Echocardiographic diagnostic classifications by age in cardiac patients attending follow-up at JMC cardiac clinic from January 5 to April 15, 2023 (n = 340) ..... 61
Table 5.3**:** Bivariables and multivariable logistic regression model of factors independently associated with RHD among cardiac patients attending follow-up at JMC cardiac Clinic, 2023 (n = 340) ..... 63
Table 6.1: Socio-demographic characteristics of patients with RHD at JMC cardiac Clinic from January 5 to April 15, 2023, (n=115) ..... 72
Table 6.2: Classification of valvular lesions in adults with RHD at JMC Cardiac Clinic from January 5 to April 15, 2023 (n = 115) ..... 73
Table 6.3: Severity of valve lesion among adults with RHD attending at JMC cardiac Clinic from January 5 to April 15, 2023, (n=115) ..... 74
Table 6.4: Echocardiographic parameters severity classification among adults with RHD at JMC cardiac clinic from January 5 to April 15, 2023 (n = 115) ..... 75
Table 7.1: Components and contents of chronic disease self-management education program at JMC, southwest Ethiopia ..... 88
Table 7.2: Socio-demographic characteristics of patients with RHD at JMC Southwest Ethiopia 2023 ..... 91
Table 7.3: Effect indicators and measurement values of patients with RHD chronic disease self-management education ..... 92

## Glossary of Acronyms and Abbreviations

| | |
|---|---|
| AOR | Adjusted Odds Ratio |
| AR | Aortic Regurgitation |
| ARF | Acute Rheumatic Fever |
| AS | Aortic Stenosis |
| BMI | Body Mass Index |
| CI | Confidence Interval |
| COR | Crude Odds Ratio |
| CVD | Cardiovascular disease |
| DCMP | Dilated cardiomyopathy |
| EF | Ejection Fraction |
| ES | Effect size |
| FS | Fractional shortening |
| GAS | Group A Streptococcus |
| HCMP | Hypertrophic cardiomyopathy |
| HHD | Hypertensive heart disease |
| IHD | Ischemic heart disease |
| JMC | Jimma Medical Center |
| LV | Left Ventricle |
| LVIDd | Left ventricular internal diameter end diastole |
| LVPWd | Left ventricular posterior wall end diastole and end systole |
| LVSd | Left ventricular systolic dysfunction |
| MR | Mitral Regurgitation |
| MS | Mitral Stenosis |
| OR | Odds Ratio |
| RF | Rheumatic fever |
| RHD | Rheumatic Heart Disease |
| SD | Standard deviation |
| SNNP | Southern Nation Nationality and People |
| SPSS | Statistical package for social science |

| | |
|---|---|
| TAPSE | Tricuspid annular Plane systolic excursion |
| TR | Tricuspid regurgitation |
| US$ | United States dollar |
| WHF | World Heart Federation |
| WHO | World Health Organization |
| IRB | Institutional Review Board |
| PhD | Doctor of Philosophy |

## Summary

***Background:*** *Rheumatic heart disease (RHD) is a long-term complication that arises from a systemic, inflammatory, and autoimmune reaction triggered by Group A Streptococcus bacteria. RHD causes impairment of one or more heart valves, resulting in significant structural and hemodynamic abnormalities. According to the estimated data from the Global Burden of Disease, RHD has impacted over 40.5 million individuals and resulted in approximately 1,100,000 cases of heart failure as well as 320,000 deaths annually. Despite RHD being the leading cause of cardiovascular disease in Ethiopia, the country lacks established policies, guidelines, or programs aimed at reducing the morbidity and mortality associated with this preventable condition. Ethiopia, a nation heavily affected by RHD, experiences a significant burden from the disease. However, the full extent of this burden and its underlying determinants has not been adequately studied. In addition, there is a lack of research and evidence regarding educational interventions that could potentially improve clinical outcomes for patients with RHD in Ethiopia's existing health care system.*

***Objectives****: To determine the prevalence, severity and determinants of rheumatic heart disease, as well as to investigate the effectiveness of chronic disease self-management education among patients with RHD in Southwestern Ethiopia, Jimma Medical Centre.*

***Methods****: This study utilized systematic review and meta-analysis, cross-sectional and quasi-experimental study designs. Data collection was done using structured questionnaires containing both open- and closed-ended questions. Data were gathered through interviews and reviews of patient's medical records. Study participants were recruited from a purposively selected hospital at Jimma Medical Center in Southwest Ethiopia based on caseloads. Data collectors were trained nurses from cardiac clinics. For the systematic review and meta-analysis, various databases such as PubMed/Medline, Scopus, HINARI, and Google Scholar were searched for peer-reviewed articles. The pooled prevalence of RHD in Ethiopia was calculated using a random-effects model at a 95% confidence interval (CI), taking into account the weight of each study. Statistical meta-analysis was conducted using STATA Version 16.0 software to determine the pooled prevalence of RHD.*

*Descriptive statistics for frequency, means and standard deviations were used to summarize the dependent and independent variables. Bivariable and multivariable logistic regressions were conducted to determine the association between the dependent and independent variables. Variables with a p-value of ≤ 0.25 on bivariable analysis were then entered into multiple logistic regressions to control confounders. Finally, variables with a p-value of < 0.05 on multivariable regression were considered as determinants of RHD. Model fitness was assessed with the Hosmer-Lemeshow test. Adjusted Odds ratios with a 95% CI were used to indicate the degree of association between the dependent and independent variables.*

*For the echocardiographic study, 115 patients were recruited and evaluated by two cardiologists following the recommendations established by the American Society of Echocardiography. The data were entered into Epidata 3.1, and then transferred to SPSS Version 25.0 for analysis. The Kolmogorov-Smirnov test was used to evaluate the normality of variables and revealed that the data were normally distributed. The outputs of the analysis were then summarized by categorizing and presenting the data using counts, percentages, and standard deviations. A Chi-square test was utilized to compare the proportions of categorical variables, evaluate the statistical significance of the association, and determine the level of significance.*

*For the interventional study, 174 study participants were recruited. A one-group quasi-experimental study using a pre-test and post-test was implemented using a consecutive sample*

*technique. Clinical and laboratory measurements were taken before and after education. One-to-one nurse-led multicomponent chronic disease self-management education (CDSME) was endured for four consecutive months. Hospital Anxiety and Depression Scale (HADS) was used to detect the levels of anxiety and depressive symptoms. Data analysis was done on SPSS Version 25.0. Values are presented as means ± SD for continuous variables and percentages for categorical variables. Continuous data were considered statistically significant at p-value <0.05 with two-tailed t-tests.*

***Results:*** *For the systematic review and meta-analysis, the pooled prevalence of RHD was 3.19% (95% CI: 1.46-5.56%). The prevalence was higher among the population who visited hospitals at 5.42% (95% CI: 1.09-12.7%) compared to schoolchildren at 0.73% (95% CI: 0.30-1.34%) and community based studies at 3.83% (95% CI: 3.16-4.55%). Addis Ababa had the lowest prevalence of RHD (0.75% (95% CI: 0.38-1.25%), whereas the highest prevalence was observed in the Amhara (8.95% (95% CI: 7.21-11.06%) and Oromia (5.29% (95% CI: 0.65-13.92%) regions. In the cross-sectional study, the most frequent morbidity encounter was RHD in 27.9% of cases. Female sex [AOR=3.06: 95% CI 1.73–5.47], using wood (biomass fuel) for cooking [AOR=1.94: 95% CI 2.22-6.86], dental caries [AOR=2.09: 95% CI 1.12-3.87], and living in crowded households [AOR=2.02: 95% CI 1.15-3.52] were identified as determinants of RHD. For the echocardiographic study, it was found that the mitral valve was affected in 98.26% of cases, while abnormalities in the aortic and tricuspid valves were diagnosed in 49.5% and 21.17% of cases, respectively. The most common combinations of valve lesions were mitral regurgitation (MR) + mitral stenosis (MS) + aortic regurgitation (AR) (15.7%), followed by MR + AR + TR (8.7%). The occurrence of MR + MS + AR was higher in males (24.1%) compared to females (20.9%). Females also had a significantly lower ejection fraction compared to males (84% vs. 15.2%, p = 0.044). Additionally, nearly two-thirds (63.5%) of individuals experienced RHD-related complications the most commonly encountered complications were pulmonary hypertension (26.1%) and atrial fibrillation (19.1%). In the quasi-experimental study, systolic blood pressure decreased from 131.31 mmHg (SD±15.68) before education to 113.77 mmHg (SD±20.98) after education (t-12.25, p<0.001). The diastolic blood pressure also decreased from 94.87 mmHg (SD±19.41) pre-education to 79.28 mmHg (SD±9.33) post-education (t-12.306, p<0.001). Hemoglobin levels changed from 11.97 g/dl (SD±1.99) before the intervention to 13.84 g/dl (SD±1.37) after the intervention (t-11.96, p<0.001). Similarly, the mean score for the HADS depression subscale decreased from 11.93 (SD±3.43) at the pre-test to 9.48 (SD±3.67) at the post-test (t-8.37, p<0.001). As for the HADS anxiety subscale, the mean score before the education program was 8.59 (SD±2.91) and decreased to 7.30 (SD±1.97) after education (t-6.44, p<0.001).*

***Conclusion****: Rheumatic Heart Disease poses a major public health challenge in both Ethiopia and the study area. Female sex, biomass use, malnutrition, dental caries, and overcrowding were identified the determinants factors. The majorities of patients in the study has multiple valve lesions and have experienced RHD-related complications. Chronic disease self-management education has been shown to improve patients' clinical outcomes, including a reduction in anxiety and depression levels. These findings implicates need to strengthen RHD surveillance and improve access to early diagnosis. Addressing female healthcare, reducing biomass fuel exposure, improving nutritional status, providing regular dental care, and enhancing living conditions are all potential strategies to reduce the disease burden. The study also underscores the importance of developing policies, programs, and guidelines for RHD prevention and treatment.*

***Keywords****: rheumatic heart disease, pathophysiology, prevalence, echocardiography, chronic disease self-management education, Ethiopia*

# Chapter One: General Introduction

## 1.1 Overview

### 1.1.1 General over view of rheumatic heart disease

Rheumatic heart disease is an autoimmune disease in which an exaggerated immune response damages the heart valves. Even though the disease primarily affects the heart, it can also impact various connective tissues throughout the body, including the brain, joints, and skin (Passos et al. 2021).

The main cause of RHD is a Group A Streptococcal (GAS) bacterial infection, which leads to rheumatic fever (RF) and eventually progresses to RHD (Dougherty et al. 2017). RHD typically begins with a sore throat caused by the bacteria Streptococcus pyogenes, which can be easily transmitted from person to person, similar to other upper respiratory tract infections (Avire et al. 2021). RHD is the sequel of RF, happens when untreated recurrent upper respiratory tract infections provoke body immunity (Banday et al. 2021).

The disease begins after GAS bacteria infect the pharynx and causing neutrophils, macrophages, and dendritic cells to phagocytosis the bacteria and present to T cells (Fieber and Kovarik 2014). In response to infection caused by GAS bacteria, both B and T cells will be activated. Initially, cells produce antibodies specifically of IgM and IgG, and later on T cells, mainly $CD4^+$ cells, become activated at the latter stage to cause cross-reactivity (Tanaka et al. 2020). Several bacterial antigens are involved in valvular damage in patient with RHD (Passos et al. 2021). The concept of molecular mimicry (cross reactivity) is associated with the presence of certain epitopes that are attributed to structural similarity between the bacterial carbohydrate and the host cardiac myosin, laminin, vimentin, and tropomyosine, which share similarity and contribute to the concept of molecular mimicry (Root-Bernstein 2014; Thaper and Prabha 2022). Similarly pro-inflammatory cytokines, such as TNF α, IFN γ, IL-1 and IL-17, have been shown to be associated with disease progression (Sharma and Sharma 2024).

Rheumatic heart disease typically affects the mitral valve in the majority of cases, with other valves such as aortic and tricuspid valves potentially involved, while pulmonary is rarely affected. Valvular lesions typically begin with regurgitation and later progress to valvular

stenosis (Saxena 2013). Classic echocardiographic findings include combinations of morphological changes such as leaflet thickening, sub-valvular apparatus thickening, shortened chorda tendinea, commissural fusion, calcification, and restricted leaflet motion (Vieira et al. 2021). RHD is a leading cause of heart failure in endemic regions, responsible for about one in four cases, and is the primary cause of acquired cardiovascular disease globally. It significantly contributes to mortality, morbidity, and long-term disability (Katzenellenbogen et al. 2017).

## 1.2 The burden of RHD (epidemiology of RHD)

According to the Global Burden of Disease data, RHD impacts more than 40.5 million people worldwide. It contributes to about 1.1 million cases of heart failure and results in approximately 320,000 deaths annually (Yingying et al. 2022). This number is projected to exceed 48 million by 2030, continuing to impose a significant economic burden in the near future (Murugasen et al. 2023; Watkins and Daskalakis 2015). Similarly, RHD leads to significant financial losses for countries due to the premature deaths of young adults and those in the working age population, with an estimated annual cost of 2.2 trillion dollars (Chinonso et al. 2021). RHD is also responsible for more than 10.5 million disability-adjusted life years globally (Watkins et al. 2017).

According to 2015 data, countries with the greatest number of estimated RHD cases among population data were India (13.17 million), China (7.07 million), Pakistan (2.25 million), Indonesia (1.18 million), and Democratic Republic of Congo (805,000), which together accounted for 73% of the global prevalence for this condition. In addition, approximately 84% of cases of RHD and 80% of estimated deaths are attributed to Africa, Southeast Asia, and the Western Pacific regions (WHO 2018).

In Africa, RHD is the most common cause of heart failure and carries a poor prognosis due to the lack of specialized medical centers and limited access to cardiac surgery (Keates et al. 2017; Mayosi et al. 2014). Studies conducted across Africa have indicated that RHD accounts for up to 34% of hospital admissions related to cardiovascular disease. This makes RHD the predominant cause of morbidity among children and young people in the region (Mebrahtom et al. 2023; Sliwa and Mayosi 2013).

Sub-Sahara Africa remains the hotspot for RHD (Belay and Aliyu 2021). A systematic review and meta-analysis conducted in East African countries revealed the prevalence of RHD in four specific countries. The study found that the pooled prevalence of RHD was 22% in Ethiopia,

11% in Uganda, 9% in Tanzania, and 3% in Sudan. This data provides clear evidence that the prevalence of RHD in the region is high (Mebrahtom et al. 2023).

Ethiopia is a country that is significantly impacted by the burden of RHD. Different studies have been conducted in Ethiopia to estimate the prevalence of RHD. A community-based study carried out in rural Ethiopia, which utilized transthoracic echocardiography screening on a sample of 987 patients, estimated the overall prevalence of RHD to be 37.5 cases per 1,000 populations (Gemechu et al. 2017). Another multisite echocardiographic based study was conducted among school children in 28 randomly selected primary and secondary schools in six regions of the country. The study estimated the prevalence to be 19 cases per 1000 school children between the ages of 6 and 18 years (Yadeta et al. 2016). Similarly, a community-based study in rural Ethiopia found that the overall mortality rate in individuals related to RHD was 125.3 per 1000 people, which is the highest death rate reported so far (Günther 2005). Furthermore, a recent systemic review and meta-analysis revealed the pooled prevalence of RHD is 3.19% among the Ethiopian population, inclusive of all sexes and age groups (Berhanu et al. 2023).

## 1.3 Risk factors for rheumatic heart disease

Rheumatic heart disease is a long-term complication and sequel of RF, and not all individuals who develop RF will develop RHD. However, there are certain risk factors that predispose individuals to an increased chance of developing the disease (Baker et al. 2019). The etiology of RHD is complex, multifactorial in origin, and not clearly understood. It includes socio-demographic factors (Owusu et al. 2022) genetics (Guilherme et al. 2007; Muhamed et al. 2020), environmental (Christina et al. 2021), nutritional (Kłak et al. 2015; Zaman et al. 1998), behavioral factors (Article 2024) or a combination of these factors is often identified in literature as contributing to various risks. However, even when these risk factors are recognized, different risks may still exist within the same region of the country.

### 1.3.1 Socio-demographic factors

Studies indicate that individuals with lower socioeconomic status (SES) have a higher prevalence of RHD, and SES plays a crucial role in influencing general health outcomes and predicting cardiovascular health (William 2018). Studies conducted in Srinagar and Bikaner, India showed a relationship between RHD and SES. The study reported a reduction in RHD prevalence due to economic improvement and the expansion of health services over the last 15 years (Negi et al.

2019) . A case control study in Assam, India, found that a low monthly income is associated with an increased risk of RHD (Baro et al. 2018). In contrast, RHD patients from Uganda did not show any elevated risk of having RHD due to low income compared to healthy individuals (Okello et al. 2014). Studies have shown that RHD is more common in areas with lower socioeconomic status. However none of the studies have found a direct correlation between RHD patients and SES (Kangid et al. 2021).

Another risk factor associated with RHD is sex. In most populations, RHD is more prevalent in females compared to males. Even though the exact cause for this higher prevalence in females is not clearly identified, previous research has shown that females have a higher risk of developing the disease compared to males (Jaine et al. 2011). Existing research supports the notion that females exhibit higher levels of immunoglobulin compared to males, a difference attributed to the X chromosome carrying about 1000 genes, while the Y chromosome contains approximately 100 genes (Passos et al. 2021). Another mechanism discussed in literature as a factor is that sex hormones can directly or indirectly affect the immune response by modulating gene expression through endoplasmic reticulum stimulation. Immune cells express estrogen and androgen receptors, and engagement of these receptors affects lymphocyte responses (Moulton 2018). Additionally the other reason in literature is, women and girls may have limited access to primary and secondary measures for preventing RF compared to men and boys. This disparity could be a contributing factor to the differing rates of RHD between genders (Zühlke 2018).

Pregnancy can also lead to a hyperdynamic circulatory state, resulting in various cardiovascular changes. These changes include increased blood volume, heart rate, and cardiac output. In some cases, these pregnancy-induced circulatory alterations can unveil an undiagnosed vascular abnormality in a previously asymptomatic patient (Anthony et al. 2016). The potential reason for this could be the exacerbation of pre-existing conditions due to hemodynamic changes associated with pregnancy, rather than an increased vulnerability to RF or RHD during pregnancy (Vaughan et al. 2021). Data from developing countries show that RHD is the leading cause of indirect obstetric death, accounting for nearly 25% of all maternal-related deaths (Hossain and Shaikh 2022).

Another factor that influences the prevalence and progression of RHD is the literacy level of patients or their guardians. It is essential to increase community and patient awareness about the control and progression of disease in order to better understand the disease in advance (Okello et

al. 2014). Research conducted in Bihar, India, emphasized the importance of public awareness for successful RHD control initiatives. The study revealed that 81% of the participants had inadequate knowledge about RHD, with 75% having limited education levels (illiterate or below $10^{th}$ grade) (Kumar S 2017). These findings emphasize the need to prioritize public education and awareness-raising as key components of RHD control efforts in regions where understanding of the disease remains limited.

### 1.3.2 Genetics factors

Between 50% and 80% of individuals diagnosed with carditis during their first episode of RF are likely to develop RHD (Auala et al. 2022). Although there is a confirmed link between GAS infection and RHD, the autoimmune mechanism responsible for RHD can persist even after the triggering factor has been eliminated. This indicates that the onset of the disease is initiated through molecular mimicry. Host factors, particularly genetic factors, are believed to significantly influence the advancement of the condition in individuals who are prone to it (Abdallah and Abu-Madi 2021). This hypothesis is supported by multiple strands of evidence. A systematic review and meta-analysis of twin studies, including 175 monozygotic and 260 dizygotic twin pairs, represents the largest quantitative assessment of the heritability of RHD. The study shows that the risk of RHD in a monozygotic twin with a history of RF in the co-twin is more than six times higher compared to that of dizygotic twins (Engel et al. 2011). Similarly, another study on twins reported a rate of RHD of 44% among monozygotic twins, while it was only 12% among dizygotic twins (Woldu and Bloomfield 2016). This suggests that genetics plays a role in an individual's susceptibility to developing RHD (Gray et al. 2017; Vaitinadin et al. 2023).

### 1.3.3 Nutritional factors

The other factor associated with RHD is malnutrition. The relationship between malnutrition and RHD is bidirectional. Malnutrition can increase susceptibility to RHD by weakening the immune system, enhancing inflammation, and reducing cardiac function. Conversely, RHD can also worsen malnutrition by reducing nutrient intake and decreasing metabolic demand (Shirley et al. 2019). Studies have shown that poor nutritional status is associated with RHD (Omurzakova et al. 2009; Thorup et al. 2020).

Similarly to malnutrition, low body mass index and low birth weight are also linked to an increased risk of developing RHD (Baker et al. 2019; Saxena et al. 2011). Additionally, a study

conducted in Bangladesh found that children with lower upper arm circumferences, which are thought to be signs of protein energy malnutrition, have an increased chance of developing RF (Zaman et al. 1998 ).

### 1.3.4 Environmental factors

Environmental factors have also shown a significant association with RHD. Studies have found that poverty and economic disadvantage can increase an individual's risk of developing the disease (Brown et al. 2007). Household overcrowding is considered one of the most well-established risk factors for RHD. Improving living conditions, including reducing overcrowding, has been reported as one of the most important factors underlying the decline in RHD burden in wealthy countries during the twentieth century (Katzenellenbogen et al. 2017).

Different literature indicates that the risk of developing RHD is found to be highest in rural areas (Gemechu et al. 2017; WHO 2005; Zühlke and Steer 2013). Indigenous Australians residing in remote communities are 3.3 times more likely to develop RHD compared to indigenous Australians living in urban centers in the same region (Katzenellenbogen et al. 2019). On the contrary, some studies findings also suggest that the risk of RHD has been highest in urban populations (Bregani et al. 2021; Riaz et al. 2013).

A survey in Congo found that children from overcrowded suburban families had a higher prevalence of RHD, regardless of their parents income and social class (Longo-Mbenza et al. 1998). In Soweto, South Africa, a similar study found a higher prevalence of RHD among people living in suburban areas. These individuals typically belong to the low socioeconomic class and tend to live in overcrowded residences (Sliwa et al. 2010).

In regions where living conditions have improved, the prevalence of RHD has substantially declined. For instance, economic development, which translates into better living conditions, is related to the recent drop in China and other emerging economies. It is critical to keep in mind that the drop in RHD was also linked to comprehensive changes in infrastructure and living standards (Zühlke and Steer 2013).

Studies have also discovered a significant correlation between RHD and the size of larger households (Mulatu HA, Woldemichael M 2015; Opara et al. 2021). An echocardiographic screening study with strict methodology has revealed a multivariate association between indicators of household overcrowding and RHD (Baker et al. 2019). A cross-sectional investigation conducted in Africa revealed a notable correlation between increased household

sizes (exceeding 8 individuals per household) and the prevalence of RHD (Longo-Mbenza et al. 1998). Conversely, a separate study in India did not find an association with household crowding in multivariate analysis. Likewise, another study conducted in India found no correlation between the number of GAS-positive sore throat episodes per year and area per person (Nandi et al. 2001).

Another factor related to RHD epidemiology is access to health facilities. Results from studies indicate that the impact of overcrowding on the likelihood of developing RHD increases as the distance from the nearest health facility grows larger. In other words, the detrimental effect of being far from health facilities increases the possibility of not being treated early and protecting against further disease progression and complications (Christina et al. 2021). In the same manner, the distance to a health center would determine the availability of preventative medication such as penicillin for households at high risk of streptococcal pharyngitis (Katrachanca and Koleske 2017).

The issue of RHD patients ability to receive regular benzathine penicillin injections, a crucial part of the treatment provided to patients with RHD, is exacerbated by delays in receiving care due to longer distances from medical facilities (Katzenellenbogen et al. 2017).

### 1.3.5 Hygiene related factors

Lack of washing facilities and resources may increase the amount of bacteria on household members skin on inanimate items, which can enhance transmission and lead to pharyngeal and skin infections (Steer and Carapetis 2009). An intervention study conducted in Pakistani squatter colonies found that appropriate hand washing practices and using soap were associated with a reduction in upper respiratory infections, including RF (Luby et al. 2005). Similarly studies also indicate that regular bathing and good hygiene may also serve a preventive measure for RHD (Carapetis et al. 1995).

### 1.3.6 Oral health related factors

Studies have identified an association between dental caries and RHD. For example, a study conducted in Canada reported that advanced dental caries were present in the majority of patients with RF and bacterial endocarditis (Maharaj and Vayej 2012). High sugar consumption has been suggested as a potential cause linking poor oral health and the development of RHD (Thornley et al. 2014). A cohort study comprising 20,333 adolescents from Auckland who were RHD-free at the commencement of the research was monitored for an average duration of five years. During

the study period, 96 participants were diagnosed with RHD. The research indicated that individuals with five or more primary teeth affected by caries had a 57% higher risk of developing RHD in comparison to those with no signs of tooth decay (Thornley et al. 2017).

### 1.3.7 Health facility related factors

The availability and standard of health care services are key factors that impact the likelihood of developing RHD. Barriers that restrict access to high-quality healthcare, whether due to distance, resource limitations, or other factors, can result in delayed and inadequate treatment of streptococcal infections, which are essential precursors to RF and RHD (Vervoort et al. 2023).

Comprehensive care clinics were broadly available in Cuba and Costa Rica. These developments coincide with significant decreases in the incidence rates of RF, which were confirmed by ecological studies (Arguedas and Mohs 1992; Nordet et al. 2008).

### 1.3.8 Smoke exposure

Although there is no direct evidence linking air pollution to RHD, the known negative effect of smoke exposure on immune system health and the mucosal barriers suggest that the impacts of smoke on immune system function and mucosal defense could be important factors in streptococcal infections as precursor for RHD (Phillips et al. 2017). Pollution and poor air quality are closely linked with living conditions especially in resource-poor nations where biomass burning and the resulting pollution are prevalent. This may also explain the connection between RHD and poverty (Rentschler and Leonova 2023). In numerous households across sub-Saharan Africa, indoor air pollution is a common occurrence. Cooking, in most cases, involves the use of open fires, which results in the entire house being filled with smoke. Infants and young children may be exposed to high levels of this smoke, particularly in low-income households that often use burned crop waste or animal dung as a fuel source (Atnafu et al. 2021). Studies has revealed that both indoor and outdoor pollution are associated with higher rates of illness and death from respiratory infections such as a RF (Nicole 2017). In many regions of the world, indoor air pollution continues to be widespread and could be a contributing factor to the prevalence of RHD. Improving ventilation in households could potentially play a role in preventing the spread of this devastating disease (Phillips et al. 2017). Causal pathways from GAS exposure to ARF and RHD has been as presented on Figure 1.1

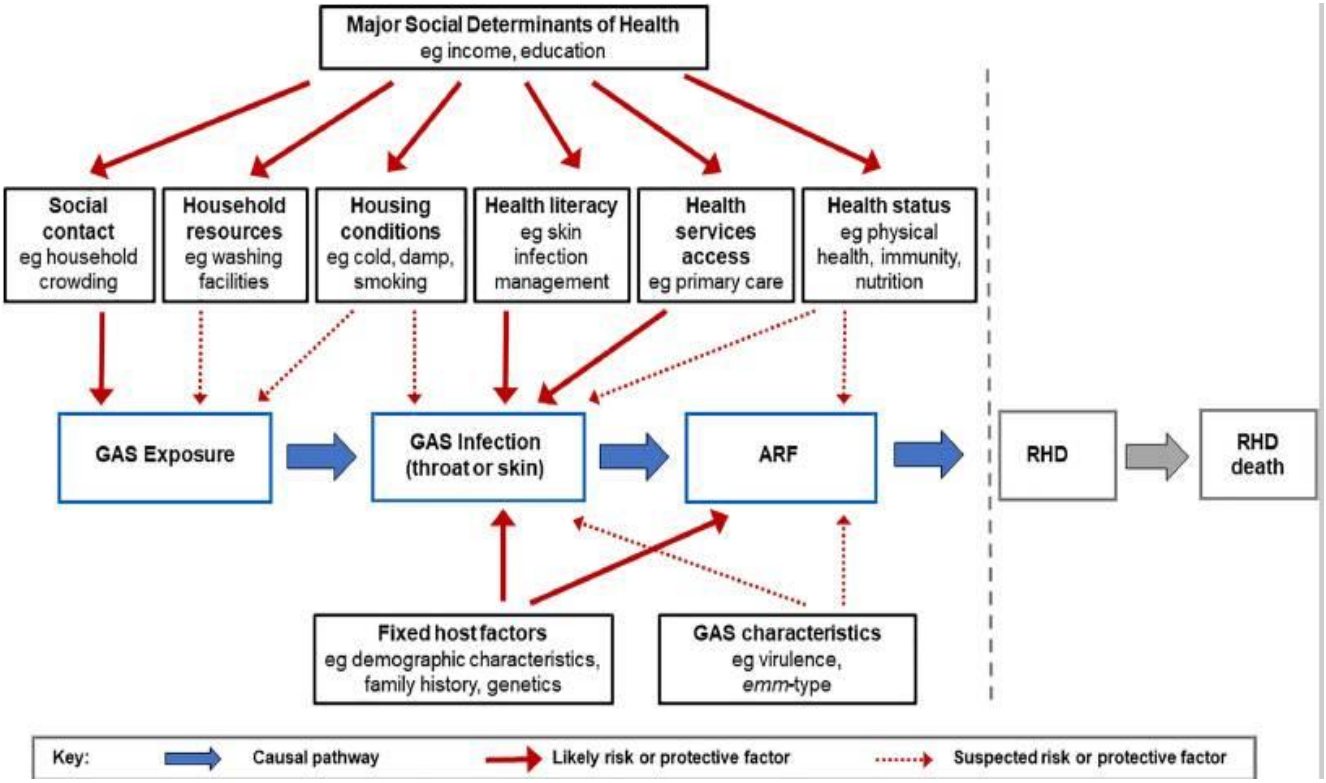



Figure 1.1: Causal pathways from GAS exposure to ARF and RHD showing major hypothesized groups of risk and protective factor (Baker et al. 2019)

## 1.4 Pathophysiology, echocardiographic pattern, and complications related to RHD

### 1.4.1 Pathophysiology of rheumatic heart disease

Rheumatic heart valve disease is a severe condition that arises following RF as a result of an abnormal immune response to streptococcal infection, causing harm to the heart valves (Passos et al. 2021). RHD typically originates in childhood; its prevalence reaches highest point in adulthood, typically occurring between the ages of 25 and 45 years. RHD primarily affects the heart valves on the left side of the heart, leading to valve regurgitation, stenosis, or a combination of both hemodynamic consequences (Peters et al. 2020). The mitral valve is composed of three layers of specialized connective tissue surrounded by two layers of endothelial cells, and its composition undergoes notable changes as rheumatic heart disease progresses (Goodwin et al. 2021). The degradation of the mitral valve initiates when autoantibodies in the bloodstream bind to the endothelial surface of the valves, leading to increased levels of vascular cell adhesion protein 1 (VCAM-1) (Mahler and Butcher 2011).

Tissue damage exposes elements of the extracellular matrix, triggering the production of anti-collagen antibodies. These antibodies can accumulate in the valve, contributing to an inflammatory setting. These modifications make the heart valves a susceptible and immune-privileged site for potential harm. In people with advanced rheumatic disease, the inflammatory response in the mitral valve is mostly made up of mononuclear cells, including helper $CD4^+$ T lymphocytes, cytotoxic $CD8^+$ T lymphocytes, macrophages, and B cells. This composition of immune cells reflects the persistent inflammatory condition observed in the rheumatic mitral valve during the later stages of the disease (Shiba et al. 2018).

Rheumatic heart disease can also affect the aortic valve, and one of the common outcomes associated with aortic valve disease is calcific degeneration (Passos et al. 2021). In the early stages of RHD, small wart-like lesions or nodules can form on the heart valves. These are caused by the presence of thrombi or blood clots along the lines where the heart valves close. Over time, the long-term inflammation resulting from one or more episodes of RF can lead to valve dysfunction in individuals who are genetically predisposed to the disease and do not receive appropriate treatment (Carapetis 2007; Vieira et al. 2021). In patients with end-stage disease, the typical pathological examination of mitral valve samples reveals thick and rigid valves characterized by extensive fibrosis (Robinson et al. 2021). The pathological progression typically unfolds slowly over several decades, during which distinct morphological features are evident at different stages of the disease's advancement. Over the course of several decades, different morphological changes predominate in each phase of this process (Romero Daza et al. 2021). Recent studies have indicated that the development of RHD may involve more complex immune responses beyond traditional hypotheses like molecular mimicry or immune system failure. Researchers are exploring alternative explanations to gain a deeper understanding of the disease. One proposed mechanism suggests that the production of autoantibodies targeting basement membrane collagen type IV on the host endothelium could be a key step in initiating the pathological process of RHD (Shiba et al. 2018). In a streptococcal infection, the M protein of the bacteria attaches to the $CB_3$ region of collagen IV, resulting in the creation of a complex that induces structural alterations in the collagen. The modified collagen structure initiates an immune response against the body's own collagen, further fueling the advancement of RHD beyond the initial RF episode. Consequently, a frequently found protein may transform into a self-antigen, disrupting the equilibrium between collagen synthesis and degradation. The

imbalance eventually results in valve fibrosis in RHD (Dinkla et al. 2009). In RHD, the inflammatory process involves several cytokines, with a notable increase in the expression of transforming growth factor-beta (TGF- β) being linked to valvular fibrosis. TGF- β plays a crucial role in activating myofibroblasts and promoting collagen production, key factors in the progression of valvular fibrosis (Kim et al. 2018).

Another key pathophysiologic mechanism in RHD is neo-angiogenesis. Chronic inflammation in RHD can lead to the increased production of vascular endothelial growth factor, which then stimulates endothelial cells to express adhesion molecules such as vascular cell adhesion molecule-1 and intercellular adhesion molecule-1. These adhesion molecules facilitate the recruitment and migration of inflammatory cells into the affected cardiac tissues, further perpetuating the inflammatory process and contributing to the development and progression of RHD (Kim et al. 2018). This facilitates the movement of monocytes and lymphocytes into the extracellular matrix, thereby adding to the continuous inflammatory activity in RHD. Numerous angiogenic factors play a crucial role in attracting inflammatory cells in the setting of RHD. Chemokines with the glutamyl-leucyl-arginine motif, along with CXC chemokines, play a role in the movement of inflammatory cells. Moreover, fibroblast growth factors stimulate the migration of inflammatory cells by prompting endothelial cells to generate plasminogen activator and collagenase, which break down the extracellular matrix (Park 2014).

In addition, several crucial angiogenic factors, including TNF-alpha, IL-1, IL-6, IL-8, and IL-18, are also associated with inflammation (Alfaddagh et al. 2020). These cytokines play a role in boosting the generation of additional inflammatory agents, cell adhesion molecules, and in amplifying cyclooxygenase activity and matrix metalloproteinase expression. The intricate interaction between angiogenic and inflammatory mechanisms is responsible for the development of RHD (Deardorff and Spinale 2009).

The diverse morphological presentations of RHD lead to various clinical manifestations. In individuals with mitral stenosis, chordal shortening is the predominant characteristic, present in approximately 90% of cases, whereas it only occurs in about 3% of patients with pure mitral regurgitation (Passos et al. 2021). On the other hand, annular dilatation is found in around 90% of individuals diagnosed with isolated mitral regurgitation, whereas it is observed in only 30% of cases with isolated mitral stenosis. In advanced stages of RHD, the valve leaflets fuse at the commissures, and erosion of the endothelial surface is frequently noted. Additionally, the

chordae tendineae may exhibit fusion and shortened length. These various morphological alterations play a role in the broad range of clinical manifestations observed in individuals with the disease (Gomes et al. 2022).

### 1.4.2 Echocardiographic patterns among RHD

Previously, RHD was frequently identified in patients with a rheumatic fever background through the detection of a heart murmur using a stethoscope during a physical examination (Asmare et al. 2021; Shub 2003). The availability of echocardiograms at affordable rates, even in remote locations, has increased the accessibility of this diagnostic tool. This progress has led to a rise in its utilization for the prompt and precise identification of RHD in previously undiagnosed individuals (Topçu and Uçar 2024). Echocardiography demonstrates superior effectiveness in detecting cases compared to relying solely on clinical examination, with the potential to identify up to ten times more cases than clinical examination alone (Marijon et al. 2007). Likewise, echocardiography is an essential instrument that offers crucial insights into physiological metrics such as valve integrity and performance, cardiac output, stroke volume, pulmonary arterial pressure, and various other parameters. Echocardiography is also crucial for assessing the degree of valve abnormalities, left ventricular chamber dimensions, left ventricular function, and pulmonary arterial pressure, all of which serve as key indicators of cardiac well-being (Gill et al. 2003; Maganti et al. 2010).

The most widely accepted method for screening and diagnosing RHD is the echocardiographic criteria outlined by the World Heart Federation in 2012. A concise summary of the World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease, which includes the four essential components, is provided as supplementary information for clinical reference. This evidence-based guideline serves as a valuable tool for screening RHD (Quarato et al. 2017). A brief overview of the 2012 World Heart Federation criteria for echocardiographic diagnosis of RHD is located in the **(Annex 10.4**).

A study conducted in Cameroon revealed that the primary reasons for referral for echocardiography were typically attributed to heart failure resulting from RHD. The research findings also indicated that mitral regurgitation was the most prevalent rheumatic valve defect, often paired with aortic regurgitation, with a higher incidence among female patients (Clovis et al. 2018). A separate study carried out in Nigeria analyzed 1499 echocardiograms from two medical facilities and identified that 129 individuals (9.8%) were diagnosed with rheumatic heart

disease. The research sample comprised 47 male and 82 female participants, with a ratio of 1:1.7, aged between 5 and 60 years. Among them, mitral regurgitation was the predominant echocardiographic finding in 49 individuals (Sani et al. 2007). Likewise, research conducted at Jimma Medical Center, based on medical records of 47 patients with RHD, revealed that 91.5% of these individuals exhibited mitral valve leaflet thickening, calcification, and restricted motion (Mulugeta et al. 2020). The research indicated that 53.2% of patients displayed thickening and calcification of the aortic valve cusps, whereas 14.9% showed thickening of the tricuspid valve. Both the mitral and aortic valves were affected in 40.4% of patients, while the mitral valve alone was impacted in another 40.4% of patients. The average left atrial diameter in a sample of 25 patients was found to be 5.61 ± 1.77 cm, exceeding the normal range of 2-4 cm.

A research conducted in Pakistan at tertiary cardiac centers revealed that the most prevalent condition among patients was mitral regurgitation, with 56% of cases (7500 patients), followed by tricuspid regurgitation with 48.2% (6449 patients), and aortic regurgitation with 41.4% (5550 patients). Out of the 2729 individuals studied, mitral stenosis was present in 20.3% of the subjects, aortic stenosis in 0.8% (102 patients), and tricuspid stenosis in 0.2% (31 patients) of the participants (Aurakzai et al. 2009).

Research conducted at a hospital in Uganda showed that mitral regurgitation was the most prevalent valvular abnormality, followed by a combination of mitral and aortic regurgitation, mitral stenosis, and mixed-valve disease. In cases of mitral regurgitation, the average left ventricular end-diastolic diameter was 65mm (normal range 35-55 mm), the average left ventricular end-systolic diameter (LVESD) was 50 mm (normal range 25-40 mm), and the average left ventricular ejection fraction (LVEF) was 56%. Additionally, 46% of these cases exhibited severe aortic regurgitation, while 49% of mitral stenosis cases were classified as severe (Okello et al. 2013).

### 1.4.3 Complications related to RHD

Rheumatic heart disease may result in a range of acute and chronic complications. Acute complications commonly occur during the first episode of rheumatic fever and may involve pericarditis, myocarditis, and valvulitis (Webb et al. 2015). Chronically, the damaged heart valves can deteriorate gradually, leading to further impairment and a reduced ability of the heart to effectively circulate blood. As a result, several severe complications can arise, such as

pulmonary hypertension, atrial fibrillation, arrhythmias, infective endocarditis, and thromboembolic events like stroke (Dougherty et al. 2020; McLeod and Pemberton 2020) .

Data from a cardiac center in Africa revealed that complications were found in 49% of the newly diagnosed RHD cases. The data reveals that the most common complication was heart failure, affecting 46.9% of the newly diagnosed RHD cases. This was followed by pulmonary hypertension, which was observed in 32.7% of the cases. Additionally, the data showed that pulmonary hypertension was present in approximately 33% of the cases, with no significant difference between male and female participants (Okello et al. 2013). A study conducted in Nigeria revealed that the primary complication associated with RHD was pulmonary hypertension, affecting the majority of patients at 72.1%. This was followed by valvular cardiomyopathy in 31.8% of cases, tricuspid regurgitation in 30.2%, atrial fibrillation in 10.1%, and left ventricular thrombus occurring in 2.3% of the cases (Sani et al. 2007). A study conducted in India documented that 7% of participants exhibited clinical complications related to RHD. Among the screened cases, only one instance of pulmonary valve stenosis was identified. The study found that mitral stenosis led to atrial fibrillation and was linked to embolic complications, occurring in 4% of the cases (McLeod and Pemberton 2020).

It is approximated that RHD is responsible for up to 7.5% of all strokes in developing nations. This accounts for 144,000 to 360,000 strokes annually, leading to 108,000 to 290,000 stroke-related fatalities each year (Wang et al. 2013). The Global Rheumatic Heart Disease Registry, a prospective study, included 3,343 patients diagnosed with RHD from 25 hospitals spanning 12 African countries, India, and Yemen. The research findings indicated that a large proportion of the patients (63.9%) had moderate to severe multivalvular disease, which was further complicated by congestive heart failure (33.4%), pulmonary hypertension (28.8%), atrial fibrillation (21.8%), stroke (7.1%), infective endocarditis (4%), and major bleeding disorder (2.7%) ( Zühlke et al 2015).

## 1.5 Preventive strategies in rheumatic heart disease

Preventive strategies for RHD consist of a comprehensive set of established measures designed to prevent the onset of the disease and minimize associated complications. Implementing these strategies is crucial for managing patients at risk of developing the disease. The effectiveness of these strategies has been demonstrated by the low rates of the disease in countries where they

have been put into practice, as well as by the overall decline in the global prevalence of the disease (Kumar et al. 2020; Shimanda et al. 2024).

The World Health Organization (WHO) has set up a global action plan with the goal of achieving a 25% decrease in premature deaths from non-communicable diseases by the year 2025. This involves managing and reducing deaths related to RHD, which will be crucial in reaching the sustainable development goal (Palafox et al. 2017; Richards 2018). Preventive measures consist of primordial, primary, secondary, and tertiary prevention, each designed for particular groups and circumstances (Karthikeyan and Mayosi 2009; Nordet et al. 2008).

Worldwide, 80% of people with RHD are located in developing nations, while the remaining 20% of the affected population live in vulnerable or indigenous communities in high-resource settings (Kangid et al. 2021). RHD stems from social, environmental, and economic factors, typically arising in impoverished settings with limited access to education, healthcare, and medical services. It has emerged as a significant contributor to illness, disability, and mortality (Myers and Myers 2008; Zühlke and Engel 2013).

In developed countries, enhanced economic circumstances and population-wide prevention efforts have led to a decline in mortality rates associated with RHD. The reduction in the occurrence of RHD throughout the 20$^{th}$ century is primarily attributed to preventive measures rather than the introduction of antibiotics (Baker et al. 2023; Remenyi et al. 2013; Rwebembera et al. 2022).

Preventing RHD requires a comprehensive approach. Primordial prevention aims to decrease fundamental risk factors like poverty, enhance living conditions, and ensure access to high-quality healthcare to prevent the illness (Baker et al. 2023). Primary prevention of RHD involves early detection and treatment of streptococcal pharyngitis to reduce the likelihood of RF (Irlam et al. 2013). Upon confirming a diagnosis of pharyngitis, it is recommended to initiate treatment within a week, as this may prevent the onset of RF in most vulnerable individuals (Mirabel et al. 2014). Secondary prevention includes administering monthly benzathine penicillin injections to patients with RHD or a history of RF to prevent the reoccurrence of streptococcal pharyngitis and RF (Belay et al. 2022; De Dassel et al. 2020). Tertiary prevention concentrates on the medical care of RHD-related heart failure, surgical management of valve lesions, and treatment of complications such as stroke, infective endocarditis, and arrhythmia (Laudari and Subramanyam 2017).

### 1.5.1 Importance of chronic disease self-management education for individuals living with RHD

Individuals affected by RHD frequently encounter substantial challenges and hardships that have far-reaching effects on multiple facets of their lives. From the responsibility of following a complicated medication schedule to navigating their everyday routines (Haynes et al. 2020; Riaz et al. 2018). Insufficient awareness about RHD among affected populations renders the condition very serious (Tellawy et al. 2021). Numerous studies have highlighted the issue of low awareness levels among the general public and patients (Boom et al. 2010; Kumar S 2017; Naz et al. 2023; Nkoke et al. 2018). The primary challenges to effectively managing RHD include inadequate patient involvement and compliance with medication and preventive measures, alongside limited knowledge about the disease and insufficient self-management abilities among individuals. These factors impede their capacity to proficiently deal with and oversee this condition (Naz et al. 2023; Read et al. 2018) .

Chronic disease self-management education involves equipping patients with the knowledge, skills, and abilities required for self-care. This approach adheres to evidence-based standards and considers the needs, goals, and life experiences of individuals with chronic illnesses (Fracso et al. 2022; Ory et al. 2013) .

The primary objective of CDSME is to enhance awareness regarding symptom monitoring, smoking cessation, preventive behaviors, self-care practices, decision-making skills, problem-solving abilities, and active engagement with the healthcare team. Ultimately, the aim is to enhance clinical outcomes, health status, and the quality of life for patients (Kerari et al. 2024). CDSME provides information by emphasizing knowledge related to nutrition, physical activity, prophylaxis, medications, and the prevention of acute and chronic complications. Additionally, CDSME has been shown to enhance clinical outcomes and reduce RHD-related distress and depression (Manji et al. 2013; Mingo et al. 2015; Oliveira et al. 2020; Robertson et al. 2006).

## 1.6 Significance of the study

### 1.6.1 Why this PhD. dissertation research necessitated? What gap does it addressed?

RHD continues to be the predominant form of acquired heart disease worldwide, affecting individuals across all age groups and accounting for up to 50% of all cardiac-related hospitalizations in low and middle-income countries (Gamble 2011). Despite being a leading cause of heart failure in children and young adults, resulting in disability and premature death,

and disproportionately impacting the workforce in emerging countries, RHD is frequently overlooked and excluded from the global agenda (Marijon et al. 2021; Marijon et al. 2012).

The increasing prevalence of RHD as a public health concern in recent decades highlights the need for adequate surveillance data for prevention and evaluation. However, there is limited data on RHD in lower-income countries (Gamble 2011; Oli K and Asmera 2004). Ethiopia is one of the countries where population estimates of the burden of RHD are not routinely collected.

In Ethiopia, the available data on the prevalence of RHD is based on a limited number of fragmented studies that have primarily been conducted in small areas of the country. Therefore, this study was intended to estimate the pooled prevalence of RHD and its pattern among all Ethiopian populations. Although risk factors for RHD have been extensively researched in various countries, there is a scarcity of studies that investigate the prevalence, geographical spread, and causes of cardiovascular diseases, including RHD, in resource-constrained nations (Edwards et al. 2021; Kumar and Tandon 2013; Rizvi et al. 2004). Therefore, this study aimed to determine the burden of RHD and its determinants among cardiac patients.

Understanding the echocardiographic patterns observed in patients with RHD is essential for several important reasons. Echocardiography serves as the primary diagnostic tool for RHD, enabling clinicians to precisely identify and measure valve abnormalities, assess the disease's progression and severity, and make informed decisions regarding treatment strategies (Beaton et al. 2015; Tani 2014). It guides the selection of the best therapeutic approaches, including medication options and the timing for valve repair or replacement. It helps in assessing the effectiveness of treatments through evaluating changes in valve function post-intervention. Furthermore, it facilitates risk stratification by identifying specific echocardiographic patterns linked to various prognoses and risks of complications. This enables a more personalized approach to monitoring and follow-up care for patients with RHD (Nascimento et al. 2021; Nunes et al. 2019). In general through understanding of the echocardiographic characteristics of RHD essential for providing comprehensive and effective care to individuals affected by this condition (Negi et al. 2018; Zühlke et al. 2015).

Some studies have been carried out in Ethiopia on the echocardiography patterns and diseases, with the majority being of retrospective nature (Engida et al. 2022; Mulugeta et al. 2020). This study differs from previous studies by directly intervening with the patient and having senior cardiologists analyze echocardiographic patterns to diagnose RHD using the WHF

echocardiographic imaging criteria (Baumgartner et al. 2009;Heidenreich et al. 2022). Furthermore, the degree of valvular dysfunction was classified as mild, moderate, or severe. Therefore, the other objective of this study was to evaluate the echocardiographic parameters in patients diagnosed with RHD.

Knowing about the complications of RHD is crucial, as this condition can have significant and far-reaching consequences if not properly treated (Ong 2020; Parks et al. 2023). Rheumatic heart disease can result in the scarring and stiffening of heart valves, potentially causing conditions like mitral stenosis, mitral regurgitation, aortic stenosis, and aortic regurgitation. The presence of these conditions can hinder the heart's capacity to efficiently pump blood, leading to potential complications such as pulmonary hypertension, atrial fibrillation, stroke, infective endocarditis, and significant bleeding disorders (He et al. 2016; Wang et al. 2013). Untreated or severe valve problems can eventually lead to the development of heart failure increasing the risk of edema reduce exercise tolerance and hospitalization (McLeod and Pemberton 2020). Patients with RHD should undergo regular screenings for potential complications and receive ongoing monitoring and suitable interventions to effectively manage their condition and mitigate the risks of severe outcomes. This study aimed to investigate the complications associated with RHD.

People with RHD experience a range of difficulties that affect their physical, mental, and social health. Moreover, individuals with the disease often struggle with the demands of intricate medication schedules and symptom management. Many of them also lack the necessary understanding and self-care practices to effectively deal with their condition and maintain their wellbeing (Haynes et al. 2022; Mincham et al. 2008; Petricca et al. 2009; Read et al. 2023).

Numerous interventional studies have shown the importance of CDSME in improving patients' clinical indicators, such as blood pressure, pulse pressure, hemoglobin levels, mean corpuscular volume, and other hematological parameters (Jafari et al. 2020; Moon et al. 2018; Podvorica et al. 2021; Stocks 2016; Wang et al. 2014). In the same token different studies have shown CDSME improve patients depression and anxiety level ( Bhandare et al. 2024; Demircelik et al. 2016; Fredericks et al. 2012; Rodrigues et al. 2018). Research from other sources indicates that CDSME intervention is a crucial strategy and resource for enhancing medication and prophylaxis adherence, leading to a positive impact on reducing complications related to RHD (Oliveira et al. 2020; Read et al. 2018; Shimanda et al. 2024; Sletvold et al. 2022).

So far in Ethiopia, the burden of RHD is increasing, and patients lack knowledge about the disease and self-care behaviors. We assumed that implementing a CDSME intervention is the most effective approach to reducing complications related to RHD and improving clinical outcomes. To ensure successful intervention, it is essential for it to be tailored to the local context, easy to understand, and feasibly implemented within the existing healthcare infrastructure. Hence, the final objective of this study is to assess the effectiveness of CDSME intervention in enhancing clinical results and alleviating depression and anxiety in individuals with RHD.

## 1.7 Conceptual framework

Based on the existing reviewed literature, factors associated with RHD were identified to encompass several broader variable domains, such as socio-economic status, smoke exposure, nutrition, dental caries, hygiene-related factors, and the availability of health institutions, among many others. However, studies narrowed the domains of the factors based on the demonstrated interwoven relationship to attribute to the prediction of RHD. Subsequently, the factors were concerted under associated factors after a literature review, as described in Figure 1.2.

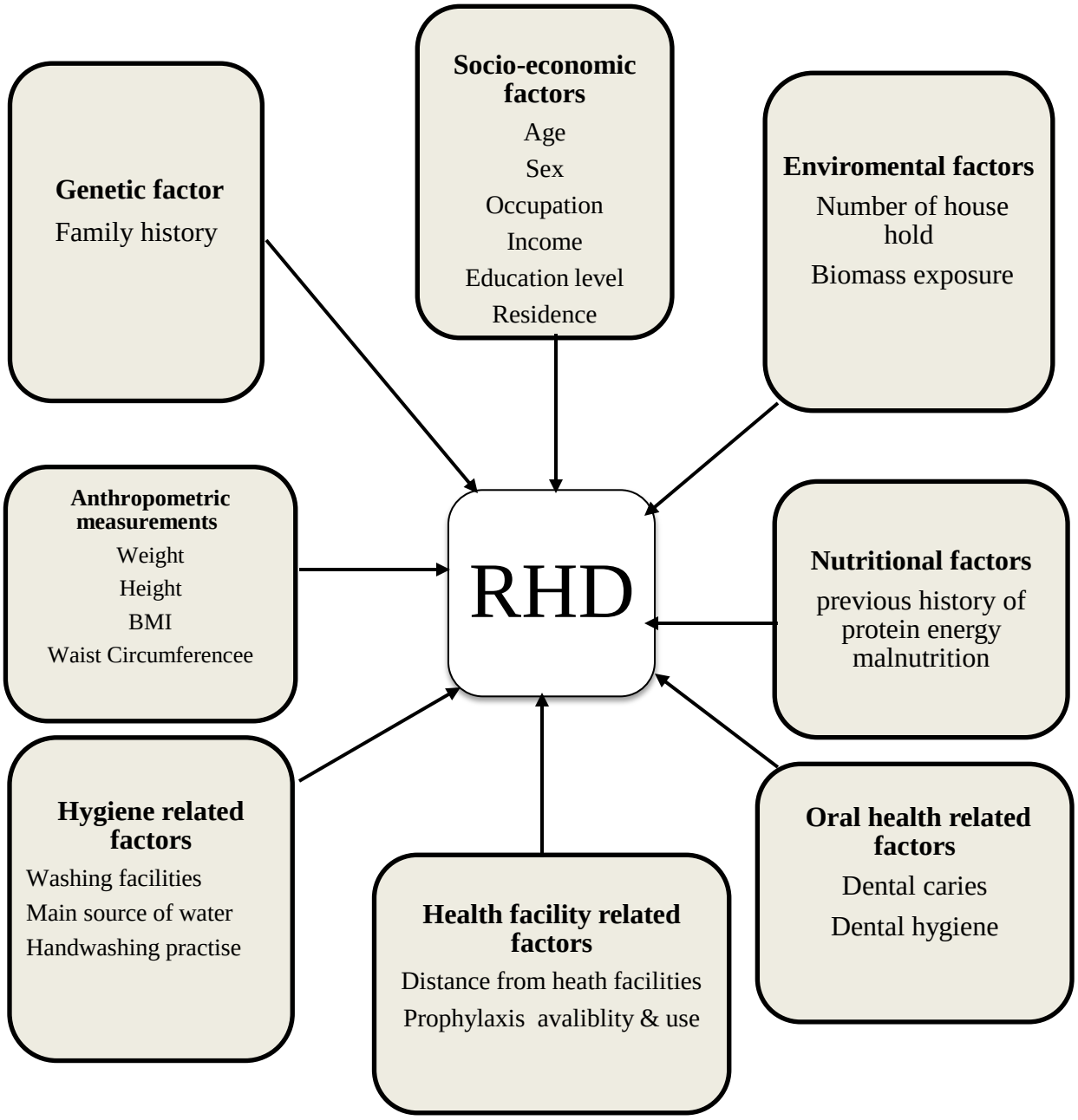



**Figure 1.2:** Schematic presentation of the conceptual framework of interrelated etiologic factors of Rheumatic Heart Disease (adapted from different literature reviews)

## 1.8 Outline of the dissertation

**Chapter 1** gives the definitions, indicators, and an overview of RHD from a global, regional, and Ethiopian perspective. **Chapter 2** provides a clear direction for the study by outlining the research questions, hypotheses, and objectives. **Chapter 3** outlines the study setting, the methodology, and the measurements. **Chapter 4** presents the pooled prevalence of RHD in Ethiopia (by sex, study setting, and regions); **Chapter 5** determines the burden and the risk factors of RHD among cardiac patients at Jimma Medical Center (JMC). **Chapter 6** analyzes the pathophysiological patterns of echocardiography among patients with rheumatic heart disease at JMC (a hospital-based echocardiographic study). **Chapter 7** examines the effect of chronic disease self-management education on improving clinical outcomes, depression, and anxiety among adult patients with RHD who are receiving medical follow-up at JMC using a quasi-experimental study design. **Chapter 8** general discussion and conclusions synthesize the findings from the various studies, which elaborate on the possible implications of the findings for programs and policies targeting RHD and also indicate future research directions. The dissertation outline is schematically depicted in Figure 1.3.

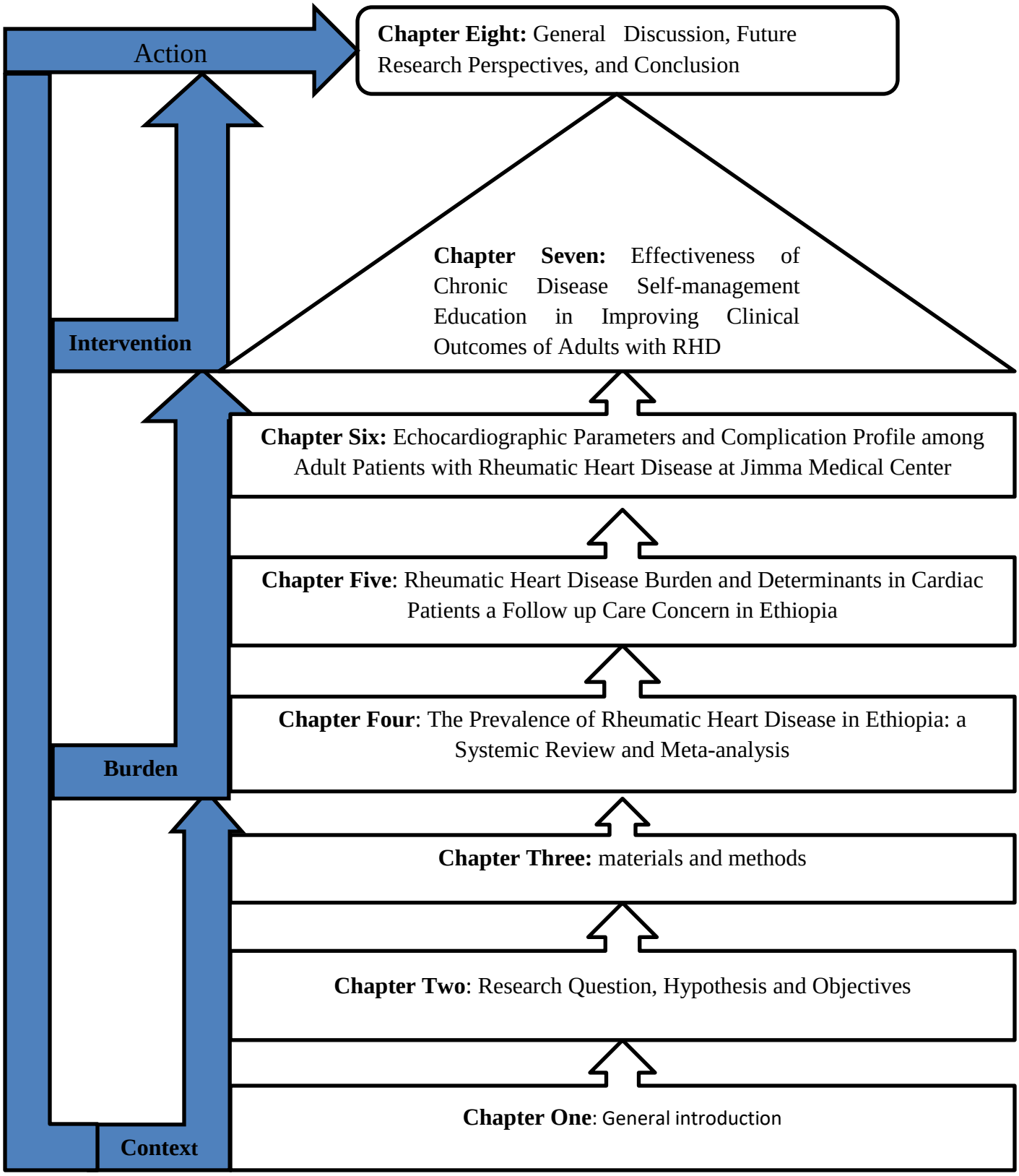



**Figure 1.3: Schematic representation of the PhD dissertation**

# Chapter Two: Research Questions, Hypotheses and Objectives

## 2.1 Research questions

1. What is the pooled prevalence of rheumatic heart disease among the general population in Ethiopia based on a comprehensive review and synthesis of existing studies?
2. What is the prevalence of rheumatic heart disease and its determinants in Southwest Ethiopia?
3. What are the echocardiographic characteristics and associated complications among patients with rheumatic heart disease look like at a cardiac clinic in Southwest Ethiopia?
4. Does chronic disease self-management education improve behavioral and clinical outcomes of patients with rheumatic heart disease in Southwestern Ethiopia?

## 2.2 Research hypotheses

1. The pooled prevalence of rheumatic heart disease among the general population in Ethiopia is not significantly different from the national or regional estimates reported in previous studies.

2. There are no significant socio-demographic, clinical, or environmental factors associated with the occurrence of rheumatic heart disease among the population in Southwest Ethiopia.

3. There are no significant differences in the echocardiographic characteristics and associated complications among patients with rheumatic heart disease at the cardiac clinic in Southwest Ethiopia.

4. Chronic disease self-management education does not have a significant influence on the behavioral and clinical outcomes of patients with rheumatic heart disease in Southwestern Ethiopia.

## 2.3 Research objectives

### 2.3.1 General objective

This study aimed to offer a contemporary evaluation of rheumatic heart disease pathophysiology, prevalence, identify determinants, analyze echocardiographic patterns, and assess the impact of chronic disease self-management education on clinical outcomes for adult patients with rheumatic heart disease at Jimma Medical Center in Southwest Ethiopia during the period from January 5, 2023, to April 1, 2024.

### 2.3.2 Specific objectives

1. Conduct a systematic review and meta-analysis to estimate the pooled prevalence of rheumatic heart disease among the all-sex and age-inclusive Ethiopian population.
2. Determine the prevalence and factors associated with rheumatic heart disease among cardiac patients attending Jimma Medical Center in Southwest Ethiopia.
3. Analyze the echocardiographic patterns among patients with rheumatic heart disease at Jimma Medical Center in Southwest Ethiopia.
4. Evaluate the effectiveness of chronic disease self-management education in improving clinical and behavioral outcomes among adult patients with rheumatic heart disease at Jimma Medical Center in Southwest Ethiopia.

# Chapter Three: Materials and Methods

## 3.1 Study setting, and period

The study was carried out at JMC, an academic institution with a variety of departments, from January 5, 2023, to April 1, 2024. JMC is a major public hospital and teaching facility located in Jimma, Ethiopia. It serves as one of the largest and most important medical institutions in Southwestern Ethiopia. The medical center has over 600 beds and provides a wide range of medical services, including internal medicine, pediatrics, surgery, and gynecology. The center serves 15 million outpatients and 16,000 inpatients each year. It provides various medical services, including echocardiography, electrocardiograms, CT scans, MRIs, and basic laboratory tests. The cardiac clinic is one of the many chronic follow-up clinics at the hospital, occurring twice weekly.

## 3.2 Study participants and criteria

We conducted a systematic review and meta-analysis to estimate the pooled prevalence of RHD in the Ethiopian population, considering data for all age groups and both sexes. For the subsequent study objectives, the study included all adult patients under medical follow-up at a cardiac clinic during the designated study period who were diagnosed with rheumatic heart disease. These patients were aged 15 years and older and had their diagnosis verified through echocardiography imaging.

### 3.2.1 Criteria

#### Inclusion criteria

**For objective 1:** Studies reporting the prevalence of RHD that were conducted in Ethiopia and published in English language between the periods of 1992 and 2022. Studies that estimated the prevalence of RHD in screening programs at schools, hospitals, and communities were included. Studies that used both echocardiographic and auscultation as methods of screening modalities. Cross-sectional studies with clear objectives and methods that have full text. Studies that report the prevalence of RHD among cardiac patient only.

**For objective 2**: Participants aged 15 years and above and included if they had a clinical diagnosis of any cardiovascular disease and were undergoing follow-up during the study period.

**For objective 3:** Participants aged 15 and above, diagnosed with rheumatic heart disease through echocardiography, were under medical follow-up at the cardiac clinic.

**For objective 4:** Participants aged 15 and older with rheumatic heart disease, confirmed by echocardiography, under cardiologist care for at least six months, and classified as NYHA functional Class II/III.

**Exclusion criteria**

**For objective 1:**Rheumatologic conditions other than RHD or solely focused on acute rheumatic fever, editorials, commentaries, and case reports were excluded from the study. Studies that had no report the prevalence of RHD at abstract.

**For objective 2 and 3:** Participants whose final diagnosis was not clearly established and not undergo through echocardiography screening

**For objective 4:** Participants who have been on follow-up for less than 6 months, as well as those classified as NYHA class I and IV.

For objective 2, 3 and 4 Participants were excluded if they had serious medical conditions such as chronic illnesses like chronic obstructive pulmonary disease, asthma, diabetes, chronic kidney disease, advanced-stage cancer. Moreover, participants needed to demonstrate the ability to effectively communicate their understanding of the study objectives and provide informed consent.

## 3.3 Sample size determination and sampling procedures

For the systematic review, eligible studies published in English language between 1992 and September 2022 was included, resulting in the final inclusion of twelve articles without imposing age restrictions. The sample size for objective two was determined using EPI Info STAT CALC Version 7.2.4.0 based on a prevalence of RHD of 40.5% from a previous study conducted at Tikure Anbesa Hospital (Yadeta et al. 2017), with a 95% confidence level, a 5% margin of error, and a population size of 2345 cardiac patients, the sample size was calculated to be 352 participants. This involved employing a simple random sampling technique, utilizing a computer-generated method from the hospital registration log book. For objective three, a sample size of 115 was calculated using EPI Info STAT CALC Version 7.2.4.0. This determination was based on a 7.5% prevalence rate of valvular dysfunction among RHD patients as reported in a

study conducted in Nigeria (Sani et al. 2007) with a confidence level of 95% and a 5% margin of error. Additionally, a non-response rate of 5% was considered in the sample size calculation. For the fourth objective, a 95% confidence level, a 5% margin of error, and a monthly population size of 315 study subjects were used. Participants included patients of either sex with RHD receiving chronic disease follow-up at JMC cardiac clinic. The sample size for objective four was calculated using Raosoftware, with parameters set at a 5% margin of error, a 95% confidence level, a monthly population size of 315, and an unknown response distribution estimated at 50%. This analysis yielded a determined sample size of 174 participants for the study.

### 3.4 Data collection and measurements

The screening initiatives for RHD in the systemic review and meta-analysis study were implemented across various settings, such as schools, hospitals, and communities, employing both echocardiographic and auscultation techniques. A systematic research strategy was employed to identify relevant studies, encompassing electronic databases and screening reference lists. The data extraction phase involved capturing details such as author information, publication date, study method, diagnostic approach, and prevalence rates categorized by community school, hospital, gender, and geographical regions.

For the second objective, data collection was conducted by four well-trained Bachelor of Science (BSC) nurses' stationed at the cardiac clinic. A structured questionnaire was utilized by interviewers to assess socio-demographic factors, anthropometric measurements, and behavioral aspects. Additionally, the participant's medical records were reviewed for any past complications. The questionnaire was initially prepared in English, translated into local languages (Amharic and Afaan Oromo), and then back translated to English to ensure consistency. For the third objective, two experienced cardiologists used a Toshiba Aplio TM ultrasound system to evaluate the degree of valvular dysfunction. The diagnoses were made in accordance with the standards set by the American Society of Echocardiography. Echocardiographic measurements such as left ventricular dimensions at end diastole and systole, left ventricular ejection fraction, aortic root diameter, and other relevant parameters are assessed in accordance with the WHF protocol.

The fourth objective was to evaluate the impact of education by collecting blood samples from patients before and after the education was provided. Venous blood samples were collected from

patients by a laboratory technician using the syringe technique. A peripheral blood morphology examination was carried out to verify analyzer flag, evaluate performance, and analyze red blood cell morphology. Detailed results were recorded on a specific form designated for laboratory result documentation.

To complement the hematological assessment, a structured questionnaire was employed to evaluate socio-demographic variables and behavioral factors among the patients.

Translations of the HADS questionnaire in local languages were utilized to assess anxiety and depressive symptoms in individuals with RHD. The HADS questionnaire comprised fourteen items divided into two subscales focusing on depression and anxiety symptoms.

Weight and height were measured using a combined height and weight scale (made in India, manufactured date: 03/20/19). Weight was measured to the nearest 0.1 kg with the participants not wearing shoes and heavy clothes, while weight was measured to the nearest 0.1 cm with the participants standing upright with the heel buttock and upper back along the same vertical plane arms at the side and looking straight forward. Body mass index (BMI) was computed by dividing the weight by the square of height, and the participants were classified as underweight, normal weight, overweight, and obese based on the WHO anthropometric guidelines.

Waist circumference (WC) was measured in cm using a stretch-resistant tape meter in the horizontal plane midway between the inferior margin of the ribs and the superior border of the iliac crest at the end of expiration. While measuring the WC, the participants were standing upright with their feet together, arms at the side, and wearing light clothes.

Blood pressure was measured on the left arm in mmHg using a calibrated sphygmomanometer (Yton sphygmomanometer, Italy, model 10220060) while the participant was in a sitting position with his/her back supported, legs uncrossed, arm supported, and cubital fossa at heart level after 5 minutes of rest. Three readings were taken with three-minute intervals, and the average of the last two readings was recorded as the final blood pressure of the respondent.

### 3.5 Data quality control

To ensure data quality, we implemented various measures. For the systematic review and meta-analysis, we conducted a thorough literature search, applied clear inclusion/exclusion criteria, double-checked the selection and extraction of studies, assessed the quality of the data, verified the accuracy of the information, and addressed any missing data. For the other objectives, we first translated the data tool into local languages and then independently retranslated it back into

English to maintain objectivity. Additionally, a trial run was conducted on a small percentage (5%) of a similar population to assess the effectiveness of the translated tool. After confirming the quality of the questionnaires, the principal investigator provided two days of training for the data collectors and two supervisors. The training focused on the objectives of the study, as well as interview and measurement techniques. The supervisor checked the completeness, accuracy, clarity, and consistency of each filled-in questionnaire on a daily basis. For objective four, the health educators received training on how to provide chronic disease self-management education and counseling based on the study's objectives. There was also a demonstration of picture-based leaflets and anthropometric measurements. During and after data collection, supervisors monitored the data collection team to ensure their adherence to the questionnaire and study protocol. The detailed data quality assurance measures are presented in the upcoming respective chapter.

### 3.6 Intervention and protocol

The detail form of intervention and protocol discussed on chapter 7

### 3.7 Data analysis

The meta-analysis was carried out using STATA Version 16.0, implementing a random effect model weighted by the inverse of variance. Subgroup analyses were stratified based on study settings, gender, and regions. Trends in the prevalence of RHD over time were investigated, and sensitivity analysis was conducted to pinpoint sources of heterogeneity and publication bias.

In addressing the second objective, data were entered into EPI Data Version 4.6 statistical software and subsequently exported to SPSS Version 25. Prior to the actual data analysis, data cleaning procedures were executed.

Descriptive statistics, including frequencies, means, and standard deviations, were computed to summarize the dependent and independent variables. Bivariable and multivariable logistic regressions were performed to ascertain the relationships between the dependent and independent variables. Initially, each independent variable was individually included in the bivariable analysis. Subsequently, variables with a p-value of $\leq 0.25$ in the bivariable analysis were collectively entered into the multiple logistic regression to control the confounding factors. Variables with a p-value of $<0.05$ in the multivariable regression were considered as determinate of RHD. The model fit was assessed using the Hosmer-Lemshow test. Odds ratio with a 95%

confidence interval were utilized to demonstrate the association between the dependent and independent variables.

Regarding the third objective, the data underwent processing and analysis using EpiData 3.1, followed by transfer to SPSS Version 25.0 for further analysis. The normality of variables was assessed using the Kolmogorov-Smirnov test, indicating that the data exhibited a normal distribution. The results of the analysis were organized by summarizing categorical and continuous data and subsequently presented using counts, percentages, and standard deviations. The Chi-square test was employed to compare the proportions of categorical variables, assessing the statistical significance of the association and determining the level of significance.

In addressing the fourth objective, data analysis was carried out utilizing SPSS software version 25.0. Descriptive statistics were utilized to present means with a standard deviation (SD) for continuous variables and a percentage for categorical variables. A two-tailed student t-test was applied to compare the continuous data sets of pretests and post-tests at a 95% confidence interval with 5% margin of error. A statistical analysis, which was all two-tailed tests, the findings was subsequently reported in percentages through narrative descriptions, tables, and figures.

### 3.8 Ethical approval

The study was conducted according to the Helsinki Declaration. Ethical approval of the research protocol was obtained from Jimma University Institute of Health with reference number JUIH/IRB277/22. Medical directors and the administrative office dean of the studies were briefed on the study objectives through a letter from Jimma University IRB office to improve collaboration. Written informed consent was obtained from each participant before enrollment and assent was obtained from adolescent patients. The study participants were assured that they were free to withdraw consent and to discontinue participation in the study without prejudice to it. Data protection and the confidentiality of the data collected were guaranteed through the study. Subsequent to the data collection phase, the information was de-identified and safely preserved in a secure storage facility, ensuring confidentiality by restricting access solely to authorized personnel. Furthermore, this study has been registered on Clinicaltrial.gov and assigned the identifier number ID: NCT06400628.

## 3.9 Dissemination of the study findings

The findings were submitted and presented at Jimma University, shared at scientific conferences, and published in international journals. Additionally, the final approved version of the findings will be shared with the Ministry of Health, Oromia Regional Health Bureaus, Jimma Zone Health Department, and other stakeholders.

Table 3.1: Summary of the study methods of the dissertation, 2023-2024

| Objectives | Designs | Approaches | Data collection methods | Study population | Sample size | Data analysis |
|---|---|---|---|---|---|---|
| **Estimate the pooled prevalence of rheumatic heart disease among Ethiopian population** | Systemic review and meta-analysis | Quantitative systematic review & meta-analysis | Searching in major databases like PubMed/Medline, SCOPUS, HINARI, and Google Scholar | All-sex and age-inclusive Ethiopian population | 12 articles included in the review and meta-analysis | Findings were Synthesized using random effect model STATA Version 16.0 software |
| **Determine the prevalence and factors associated with rheumatic heart disease among cardiac patients** | Cross-sectional | Quantitative | Survey (Interviewer administered questionnaire) | All cardiac patients attending follow-up | 340 ( male 156 and females184 ) | Bivariate & multivariate logistic regressions (SPSS Version 25) |
| **Analyze the echocardiographic patterns among patients with rheumatic heart disease** | Cross-sectional | Quantitative | Survey (Interviewer-administered questionnaire) and reviewing patients medical records | RHD patients age ≥ 15 years | 115 (29 males and 86 females) | Descriptive analysis Chi-square test was utilized to compare the proportions of categorical variables (SPSS Version 25) |
| **Evaluate the effectiveness of CDSME in improving clinical and behavioral outcomes among adult patients with RHD** | Quasi-Experimental Study | Quantitative | Survey (Interviewer-administered questionnaire) | RHD patients NYHA functional Class II/III. | 166 (Males77 and females 89) | Descriptive analysis A two-tailed Student t-test ( SPSS version 25.0) |

## Chapter Four: The Prevalence of Rheumatic Heart Disease in Ethiopia: a Systematic Review and Meta-analysis

Published on

Tropical Diseases, Travel Medicine and Vaccines

Berhanu H, Mekonnen Y, Workicho A, et al. The prevalence of rheumatic heart disease in Ethiopia: a systematic review and meta-analysis. Trop Dis Travel Med Vaccines. 2023; 9(1):16. Published 2023 Oct 13. doi: 10.1186/s40794-023-00192-y

**Abstract**

*Globally, more than 33 million people are living with RHD. A high prevalence of the disease is observed in people with poor socio-economic status, overcrowding, and low access to medical facilities. Even though different studies have been conducted in different settings, there is no reliable data regarding RHD prevalence in Ethiopia. Therefore, the aim of this systematic review and meta-analysis was to estimate the pooled prevalence of RHD in Ethiopia. PubMed/Medline, SCOPUS, HINARI, and Google Scholar databases were used to search for peer reviewed articles. Articles published in English language between the years 1992 and 2022 September were considered. The pooled prevalence of RHD was calculated using a random-effect model at a 95% confidence interval, including the weight of each study. Finally, for meta-analysis STATA Version 16.0 software was used to calculate the pooled prevalence of RHD. A total of twelve cross-sectional studies were included in the meta-analysis. Individual study prevalence ranges from 0.32% to 32.78%. The pooled prevalence of RHD was 3.19% (95% CI: 1.46–5.56%). The prevalence was higher among the population who visited hospitals at 5.42% (95% CI: 1.09–12.7%) compared to schoolchildren at 0.73% (95% CI: 0.30–1.34%) and community-based studies at 3.83% (95% CI: 3.16–4.55%). Addis Ababa had the lowest prevalence of RHD (0.75% (95% CI: 0.38–1.25%), whereas the highest prevalence was observed in the Amhara region (8.95% (95% CI: 7.21–11.06%). A significant variation in the overall estimated prevalence of RHD was not observed between males and females.*

***Trial registration Protocol registration (PROSPERO): CRD42021251553, Date of registration May 28 2021***

## 4.1 Background

Rheumatic heart disease is group A streptococcal-related cardiovascular morbidity, though it is virtually eliminated in developed nations (Carapetis et al. 2005). Globally, around 33 million people are living with the disease, of which sub-Saharan Africa, South Asia, and Oceania accounting for the highest burden of the disease (Watkins et al. 2017; Yuyun et al. 2020).

In Africa, it is one of the most common causes of heart failure and carries a harsh prognosis due to the absence of specialized centers and the availability of cardiac surgery (Essop and Peters 2014; Remenyi et al. 2016; Seckeler and Hoke 2011; Zühlke 2018).

Studies in Africa have reported that RHD accounts for up to 34% of hospital admissions related to cardiovascular disease and it is the most frequent cause of morbidity among children and young people (Sliwa and Mayosi 2013). The etiologic agent for RHD is Group A streptococcal bacterial infection, which causes acute rheumatic fever and later on advances to cause the heart muscle to swell and inflame through narrowing of the valves (Dougherty et al. 2017; Mocumbi 2015).

Factors contributing to an increased prevalence of RHD in developing nations include household overcrowding, poor hygiene, and limited access to medical services (Coffey et al. 2018; Dobson et al. 2012; Gemechu et al. 2017). Strong RHD research and development initiatives have now led to notable modifications in the elimination of the disease in industrialized nations (Seckeler and Hoke 2011).

Even though global, regional, and national burdens of RHD are reported at different times, it remains difficult to estimate the prevalence of RHD in Ethiopia. The problem could be due the absence of a routine RHD screening plan in Ethiopian health policy, as well as the small number of studies done (Mebrahtom et al. 2023).

In Ethiopia, various studies have been conducted to estimate the prevalence of RHD in different contexts. A community-based study done in rural Ethiopia using trans-thoracic echocardiography indicated that 37.5% of the participants were found to have RHD (Gemechu et al. 2017).

Another multisite echocardiography-based study done among schoolchildren shows that 19 cases per 1000 children have evidence of the disease (Yadeta et al. 2016). Like any other low-income country, Ethiopia is severely affected by RHD (Günther 2005). To the extent of our knowledge, except for a few fragmented studies, there has been no large population based study or systematic review and meta-analysis done in this country in order to assess the pooled prevalence

of RHD among all populations. Thus, the main aim of this systematic review and meta-analysis was to estimate the pooled prevalence of RHD in Ethiopia, and the findings might help policymakers revise policy.

## 4.2 Materials and methods

### 4.2.1 Outcome variables

A data extraction tool was utilized to create data from each article chosen for review, which was then presented in a table in accordance with the PRISMA protocol. The primary outcome of this review was to estimate the quantitative pooled prevalence of RHD and the secondary outcome was to identify, if any, differences among community-based studies and institutional studies (school and hospital) and investigate any regional and gender variation regarding the prevalence of RHD in Ethiopia.

### 4.2.2 Eligibility criteria

Studies reporting the prevalence of RHD that were conducted in Ethiopia and published in English language between the periods of 1992 and 2022 September were considered. Age restrictions were not used during the article retrieval process. Studies that estimated the prevalence of RHD in screening programs at schools, hospitals, and communities were included. Studies that used both echocardiographic and auscultation as methods of screening modalities were considered for analysis. Cross-sectional studies with clear objectives and methods that have full text are included in the study. Rheumatologic conditions other than RHD or solely focused on acute rheumatic fever, editorials, commentaries, and case reports were excluded from the study.

### 4.2.3 Search strategy

The reviewed studies were accessed through electronic web-based search strategies from PubMed/Medline, SCOPUS, HINARI, and Google Scholar. A three-step search strategy was utilized in this review. An initial limited search of PubMed, SCOPUS, and HINARI was undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search was undertaken across all included databases using all identified keywords and index terms. Finally, the reference list of all identified reports and articles was searched for additional studies, and only English-language studies were included.

The following search terms were used by using subject headings (MeSH in Pub Med/MEDLINE) for each database and free-text words for the concepts of "Prevalence," "Epidemiology", "Cross-Sectional Studies", "Rheumatic Heart Disease," "Child," "Adolescent," "Adult", "Community-Based Participatory Research," "Hospital-Based," "Ethiopia," "Africa South of the Sahara" Boolean operators such as (AND, OR) were used to narrow the search. The reference lists of included studies and related reviews as indicated in Table 1.

The initial search was done by experienced team members with searching and screening of titles; abstracts and full texts were conducted independently by two reviewers (KH, SM). In the case of disagreements, the third author (AW) was invited and involved to reach a consensus.

Table 4.1: Searching strategy and information sources

| **Databases** | **MeSH heading** | **Searching combination** | **Searching Date** | **Results** |
|---|---|---|---|---|
| PubMed/Medline | Rheumatic Heart Disease, Prevalence, Cross-Sectional Studies, Epidemiology, Ethiopia | ("rheumatic heart disease"[All Fields] OR (("rheumatic"[All Fields] OR "rheumatic"[All Fields]) AND ("heart"[MeSH Terms] OR "heart"[All Fields] OR "hearts"[All Fields] OR "heart s"[All Fields]) AND ("fever"[MeSH Terms] OR "fever"[All Fields] OR "fevers"[All Fields])) AND ("prevalence"[All Fields] OR "epidemiology"[All Fields]) AND "Ethiopia"[MeSH Terms] | September 30, 2022 | 28 |
| Scopus | Prevalence, Rheumatic Heart Disease, Community-based, Institution based, Ethiopia | ( TITLE-ABS-KEY ( prevalence ) AND TITLE-ABS-KEY ( "Rheumatic Heart Disease" ) AND TITLE-ABS-KEY ( community-based ) OR TITLE-ABS-KEY ( institution-based ) OR TITLE-ABS-KEY ( Ethiopia ) ) | September 30, 2022 | 36 |
| Hinari | Prevalence, Cross sectional Studies, Epidemiology, rheumatic heart disease, Ethiopia | ((Title Combined:(Prevalence)) OR (Cross Sectional Studies) OR (Epidemiology)) AND (rheumatic heart disease) AND ("Ethiopia") | September 30, 2022 | 260 |
| **Others** | | | | |
| Google Scholar | | allintitle: prevalence rheumatic heart disease Ethiopia | | 10 |

#### 4.2.4 Risk of bias assessment

The risk of bias assessment tool adopted from Hoy et al. was used as a quality assessment checklist for critical appraisal of the selected articles (Hoy et al. 2012). The risk of bias assessment was done by two authors (SM and KH). The tool includes nine items, with a maximum score of nine and a minimum score of zero. The overall risk of bias has been ranked into three categories: low, moderate, and high risk. A summary of the risk of bias for all the twelve included articles with a justification of the rating for each item is provided in Annex part (risk of bias assessment 10.6)

#### 4.2.5 Data extraction and outcome of interest

Duplicates were removed; full-text studies were retrieved for the selected abstracts; and eligible studies that lacked full text (only abstracts) from the primary authors were contacted through their email address. Individual studies yielded the following information:

1. Author name and years of publication; study design; age of the participants.
2. Diagnostic modalities.
3. Prevalence estimate reported by community, school, hospital, sex, and region.

### 4.3 Reliability of data

#### 4.3.1 Analysis of the Data

The primary outcome of this review was the pooled prevalence of RHD in Ethiopia. The meta-analysis was done by using STATA Version 16.0 and a random effects model, weighted by the inverse of variance. Heterogeneity between estimates was assessed using the I2 statistics (percentage of residual variation attributed to heterogeneity); an I2 value above 75% was taken as considerable heterogeneity within the studies (Higgins et al. 2020). The pooled prevalence of RHD and its 95% confidence intervals (CIs) were reported in the pooled analysis. Sub-group analysis was done based on study settings (community, school, and hospital), gender, and regions of the country.

The trend of RHD prevalence with publication years was and sensitivity analysis for possible sources of heterogeneity and publication bias was done by visual assessment of the funnel plot, and small-study effect was assessed by Egger's test.

## 4.4 Results

### Study selection

Overall, 334 studies were initially retrieved from different databases. After removing the duplicates, 302 studies were screened and a total of 60 eligible abstracts were screened by inclusion criteria, followed by screening of full-text studies. Finally, 12 studies satisfying the eligibility criteria were included in the meta-analysis of rheumatic heart disease (Figure 4.1).

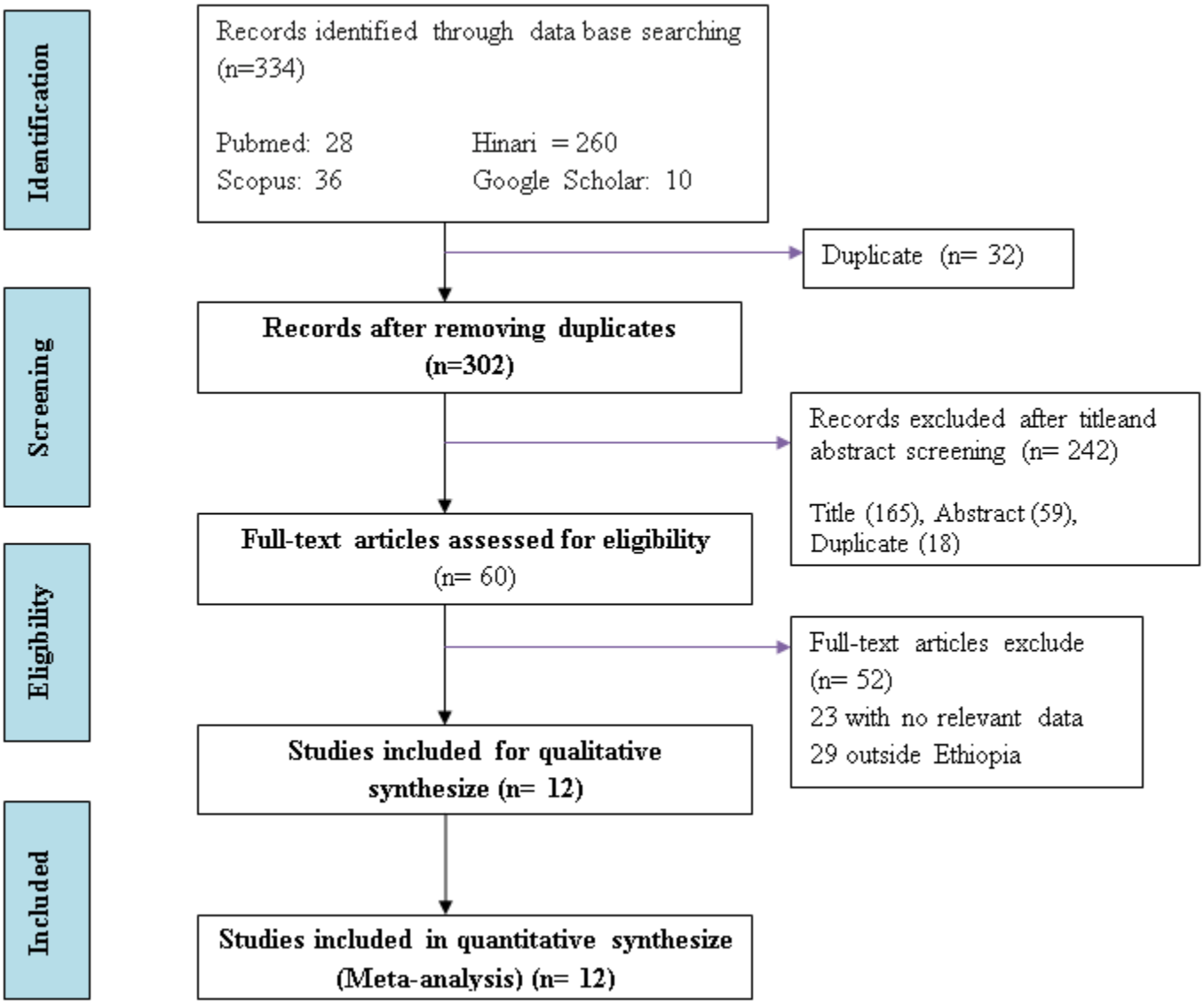



**Figure 4.1:** PRISMA flow chart for identifications of studies included in systematic review and meta-analysis on prevalence of Rheumatic Heart Diseases in Ethiopia

**Characteristics of studies included in the Meta-Analysis**

Twelve studies, with a total sample size of 33,009 participants, have been included in the meta-analysis. The prevalence of RHD is nearly similar among sexes, with 1.89 (95% CI: 0.63–3.16) and 1.95 (95% CI: 0.54–3.35) for males and females, respectively. The majority of the studies (41.6%) were conducted in Oromia region, followed by Addis Ababa (25%), while the remaining studies were conducted in South Nation Nationality and People (SNNP) (16.6%), Amhara region (8.24%), and national-level (8.4%). Two studies by Bezaye & Henok (Bezaye and Henok 2019) and Gemechu et al (Gemechu et al. 2017) included pediatric ages between 2 months and 14 years, while the studies conducted by Bacha & Abera and Moges et al. included pregnant populations (Bacha and Abera 2019; Moges et al. 2021).

Regarding study setting, six studies were hospital-based (Bacha and Abera 2019; Bezaye and Henok 2019; Engida et al. 2022; Gebremariam and Moges 2016; Habte et al. 2010; Moges et al. 2021) the other four studies were school-based (Engida et al. 2022; Oli et al. 1992; Oli K 1999; Yadeta et al. 2016) and two studies (Engel et al. 2015; Gemechu et al. 2017) were community-based studies. (Table 4.2)

To diagnose RHD, WHO echocardiography criteria for case definition, the American Society of Echocardiography with the European Association of Echocardiography standard and the World Heart Federation (WHF) criteria were used. All of the studies used a cross-sectional study design, and eleven studies used echocardiography, while one study used auscultation as a method of diagnostic approach (Oli K 1999) .

Table 4.2: Characteristics of the individual studies included in the systematic review and meta-analysis on prevalence of rheumatic heart diseases in Ethiopia

| Authors | Publication Year | Study design | Regions Ethiopia | Study Setting | Age of the participants in year | Sample size | No. of RHD | Prevalence (%) | Diagnostic Method |
|---|---|---|---|---|---|---|---|---|---|
| Anteneh et al. | 2022 | Cross Sectional | Amhara | Hospital Based | 6-103 | 849 | 76 | 18.2 | Echocardiography |
| Bacha et al. | 2019 | Cross Sectional | Addis Ababa | Hospital Based | 18-40 | 398 | 9 | 2.3 | Echocardiography |
| Moges et al. | 2021 | Cross Sectional | Oromia | Hospital Based | Mean age was 29 years | 4584 | 29 | 0.6 | Echocardiography |
| Engel et al. | 2015 | Cross Sectional | Oromia | Community based | 4-24 | 2000 | 61 | 3.05 | Echocardiography |
| Gemechu et al. | 2017 | Cross Sectional | Oromia | Community based | 6-25 | 987 | 56 | 5.7 | Echocardiography |
| Mulatu et al. | 2015 | Cross Sectional | Oromia | School based | 5-15 | 1874 | 6 | 0.32 | Echocardiography |
| Kebede Oli et al. | 1992 | Cross Sectional | SNNP | School based | 5-19 | 3235 | 15 | 0.46 | Auscultation |
| Yadeta et al. | 2016 | Cross Sectional | National | School based | 6-18 | 3238 | 59 | 1.9 | Echocardiography |
| Habte et al. | 2010 | Cross Sectional | Oromia | Hospital based | Adult (mean age was 31.4 years ) | 781 | 256 | 32.8 | Echocardiography |
| Bezaye & Henok | 2019 | Cross Sectional | SNNP | Hospital based | 2months-14 years | 2000 | 75 | 3.75 | Echocardiography |
| Gebremariam & Moges | 2016 | Cross Sectional | Addis Ababa | Hospital based | 2 months-14 years | 3672 | 19 | 0.52 | Echocardiography |
| Kebede Oli & Porteous | 1999 | Cross Sectional | Addis Ababa | School based | School children | 9388 | 60 | 0.64 | Echocardiography |

**Risk of bias assessment**

**Assessment of publication Bias**

Publication bias was evaluated using Egger's test. The publication bias funnel plot shows that there is an apparently symmetrical distribution (Fig. 4.2), and Egger's regression test was found to be significant with a p-value of p=0.001. Thus, the test provides evidence for no or undetected publication bias in the included studies. The estimated bias coefficient was 9.939 (Egger bias B=9.939 (95% CI: 5.548–14.330; p=0.001)) with a standard error of 1.971, as indicated in Table 4.3

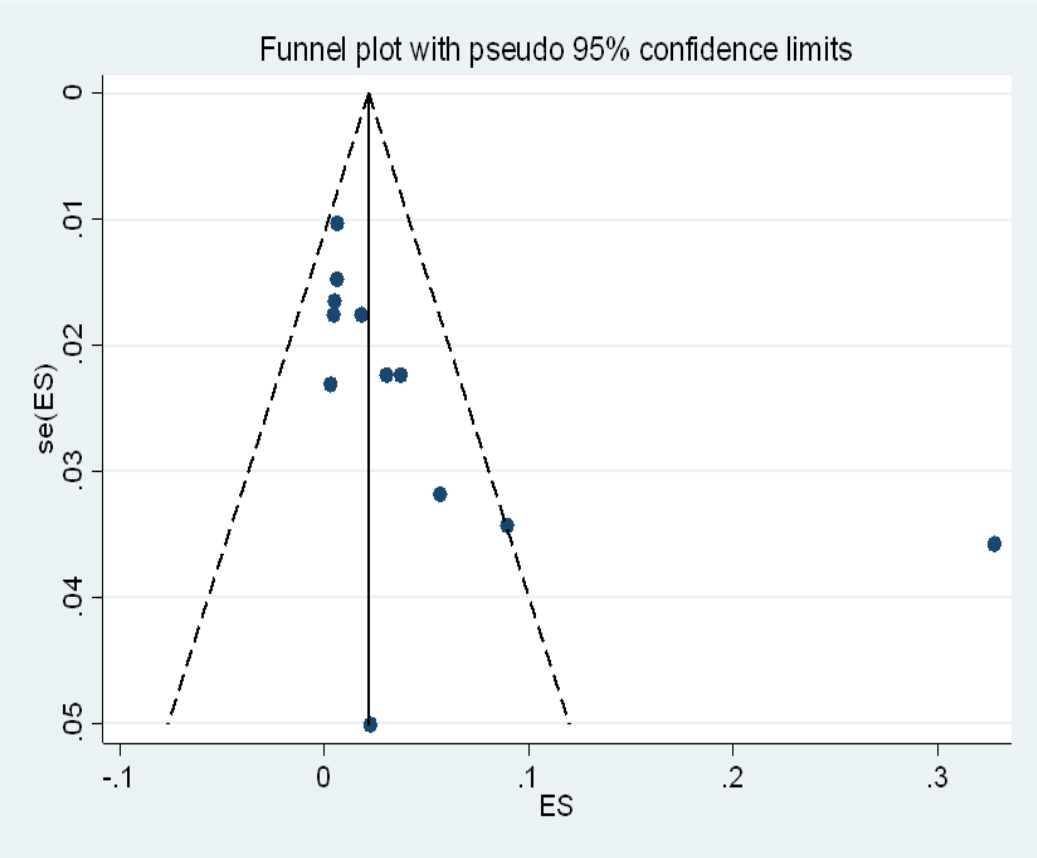



**Figure 4.2:** Funnel plot for assessment of publication bias across studies

Table 4.3: Assessment of publication bias using egger's test among studies

Note: data input format theta se_theta assumed

Egger's test for small-study effects:

Regress standard normal deviate of intervention

effect estimate against its standard error

Number of studies = 12 Root MSE = 4.157

| Std. Eff | Coef. | Std. Err. | t | P>t | [95% Conf. Interval] |
|---|---|---|---|---|---|
| Slope | -0.005 | 0.003 | -1.680 | 0.124 | -0.012-0.002 |
| Bias | 9.939 | 1.971 | 5.040 | 0.001 | 5.548-14.330 |

Test of H0: no small-study effects p = 0.001

**Prevalence of rheumatic heart disease**

The estimated pooled prevalence of RHD, reported by twelve primary studies using a fixed effect model, showed significant heterogeneity between the studies. Accordingly, a random-effect model was used to estimate pooled prevalence. In primary studies (n= 12), the prevalence of RHD ranged from 0.32% in a study conducted by Mulatu et al. (Mulatu et al. 2015) to 32.78% in a study conducted by Habte et al. (Habte et al. 2010) . In the random-effect model, the prevalence of RHD was 3.19% (95% CI: 1.46–5.56%) with significant heterogeneity between the individual studies (I2=99.07%), $p \leq 0.001$) (Figure 4.3).

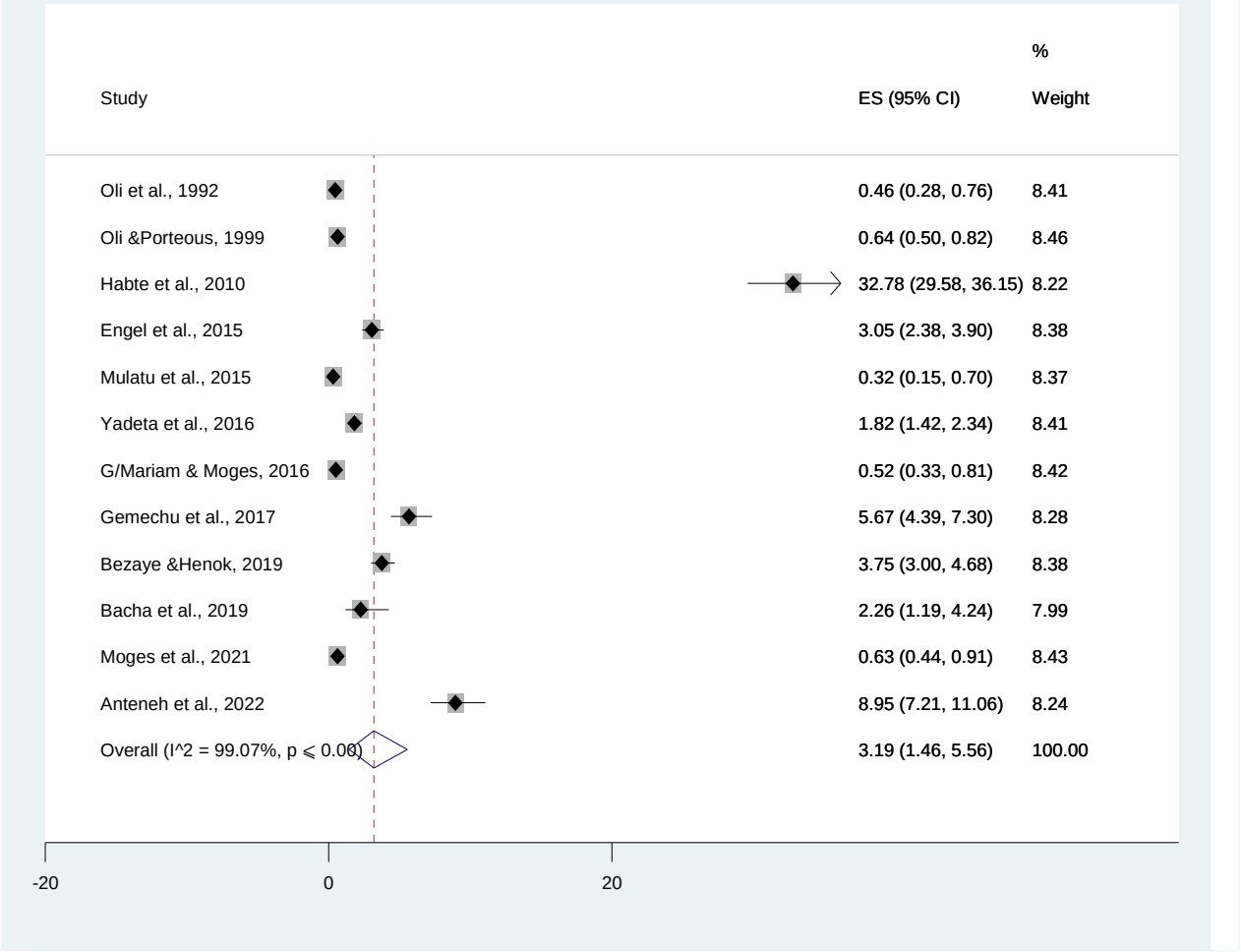



**Figure 4.3:** Forest plot on studies that quantitatively assessed pooled prevalence of rheumatic heart disease in Ethiopia

**Subgroup analysis and investigation of heterogeneity**

**Prevalence of RHD based on study setting**

Based on study location, places of study were categorized into three settings: school, hospital, and community-based. The highest prevalence was observed in the population who visited hospitals, 5.42% (95% CI: 1.09%–12.70%) compared with schoolchildren 0.73% (95% CI: 0.30% –1.34%) and community-based studies at 3.83% (95% CI: 3.16% –4.55%) (Figure 4.4)

Subgroup analysis was performed per study setting, and potential heterogeneity was detected in the prevalence estimates of RHD across studies ($I^2$ range: 99.47–99.97%; all p≤0.001).

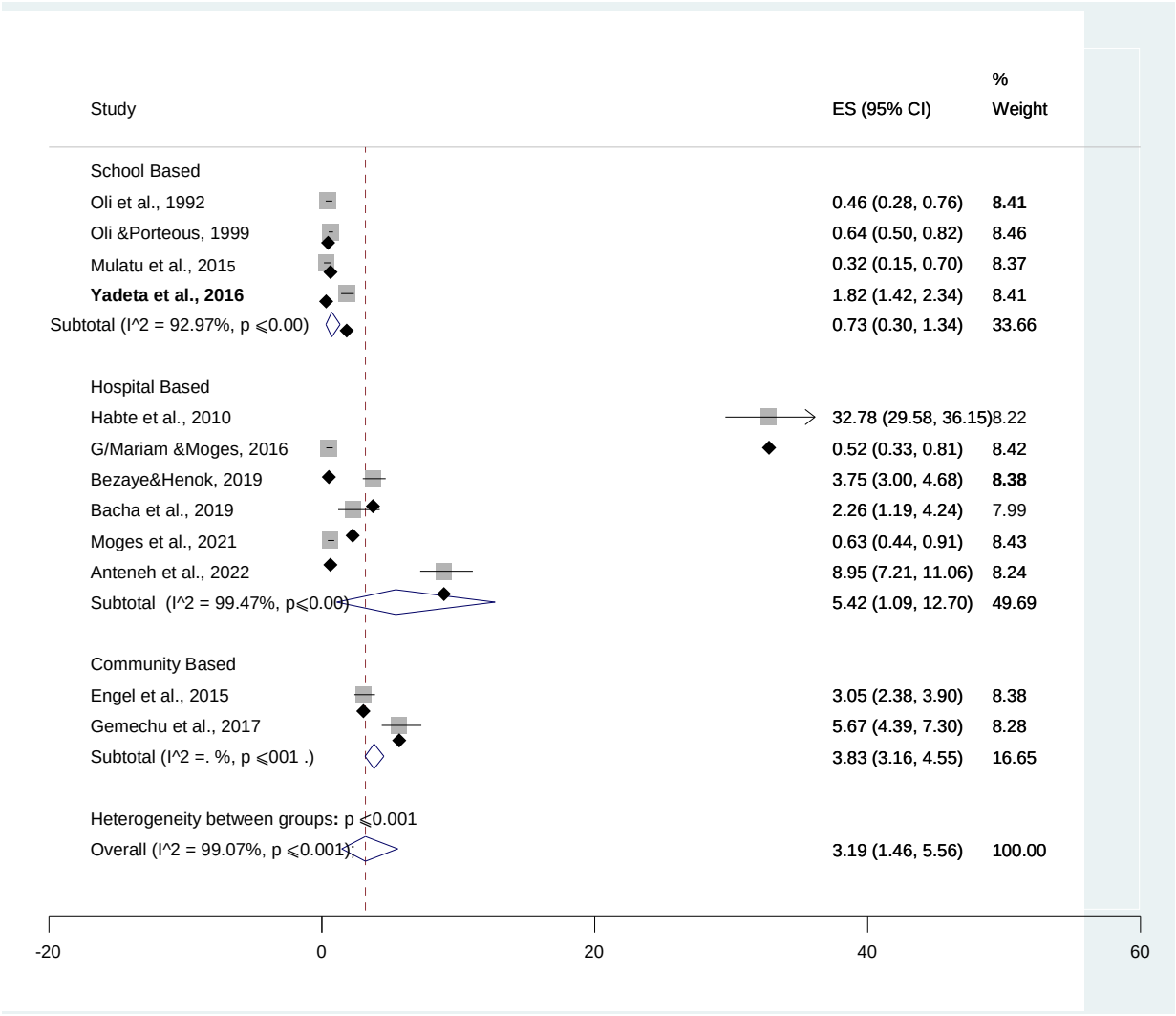



**Figure 4.4:** Forest plot on studies that quantitatively assessed pooled prevalence of Rheumatic Heart Disease in Ethiopia

**Prevalence of RHD based on region**

Based on the administrative division of Ethiopia, the study regions were grouped into five regions: SNNP, Amhara, Addis Ababa, Oromia, and National (studies done in two or more regions). RHD was less prevalent in Addis Ababa (0.75% (95% CI: 0.38%–1.25%) compared with Amhara (8.95% (95% CI: 7.21% –11.06%) (Figure 4. 5) in the region-based subgroup analysis, potential heterogeneity was detected in the prevalence estimates of RHD across studies ($I^2$ range: 99.07–99.53%; all p≤0.001).

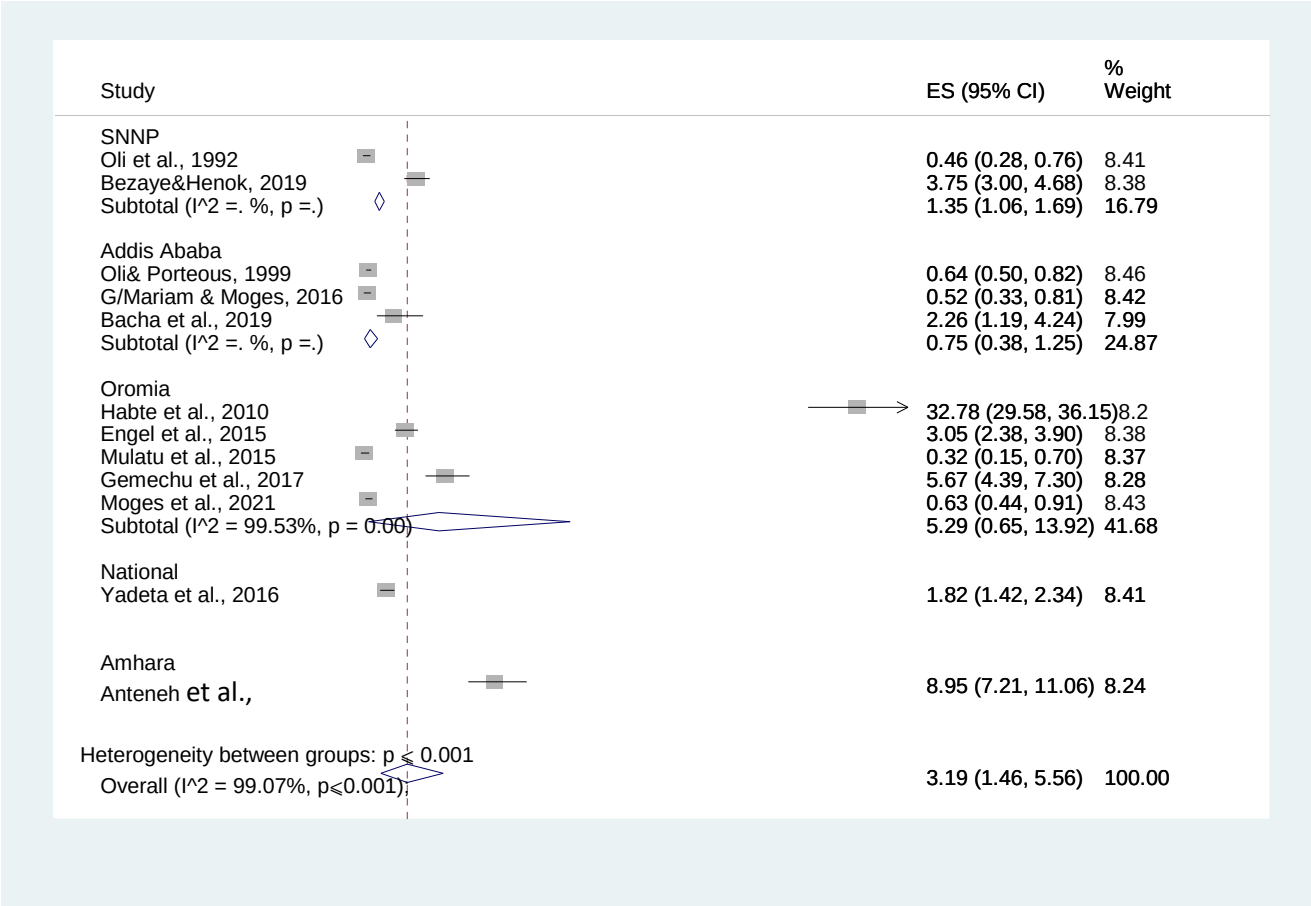
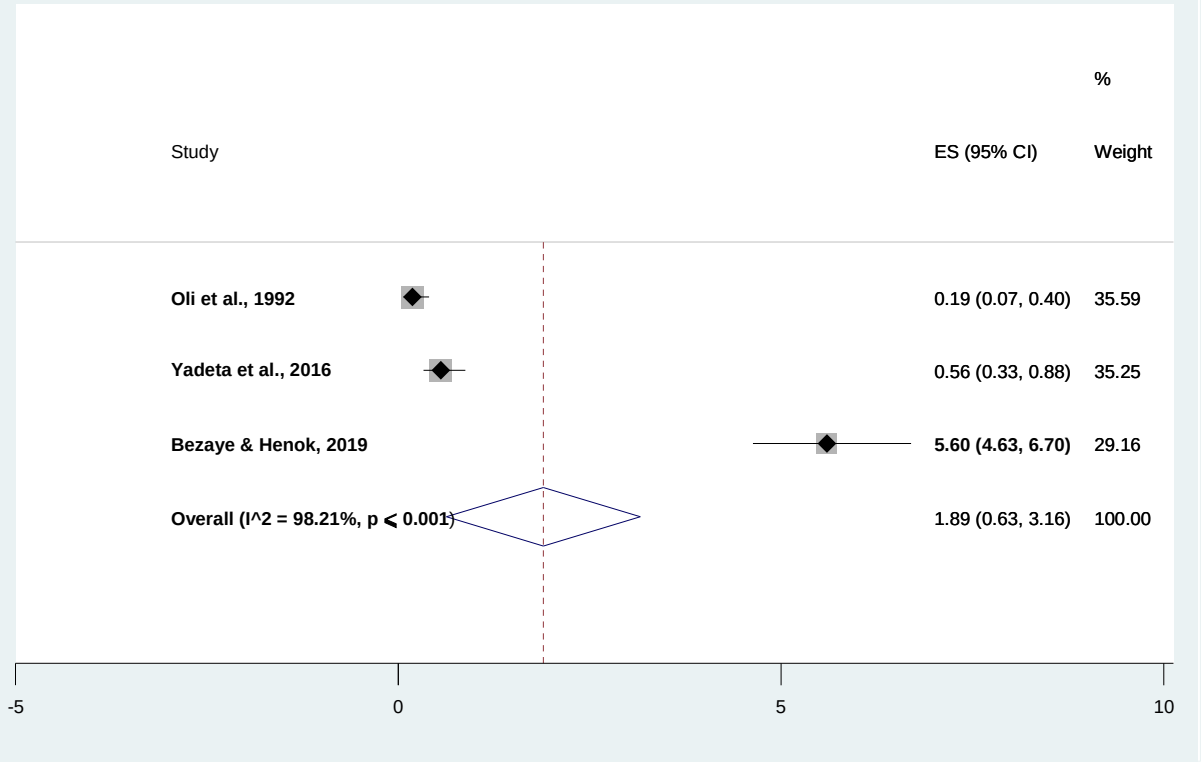



**Figure 4.5:** Subgroup analyses on the prevalence of Rheumatic Heart Disease among different regions of Ethiopia.

**Prevalence of RHD based on sex**

Subgroup studies based on gender were done for three studies, with a total population of 8476; the pooled prevalence of RHD among males was 1.89 (95% CI: 0.63–3.16%) and females was 1.95 (95% CI: 0.54–3.35 %), which was almost similar as indicated in Figure 4. 6.

(a)


Study
ES (95% CI)
%
Weight
Oli et al., 1992
0.19 (0.07, 0.40)
35.59
Yadeta et al., 2016
0.56 (0.33, 0.88)
35.25
Bezaye & Henok, 2019
5.60 (4.63, 6.70)
29.16
Overall (I^2 = 98.21%, p < 0.001)
1.89 (0.63, 3.16)
100.00
-5
0
5
10

(b)

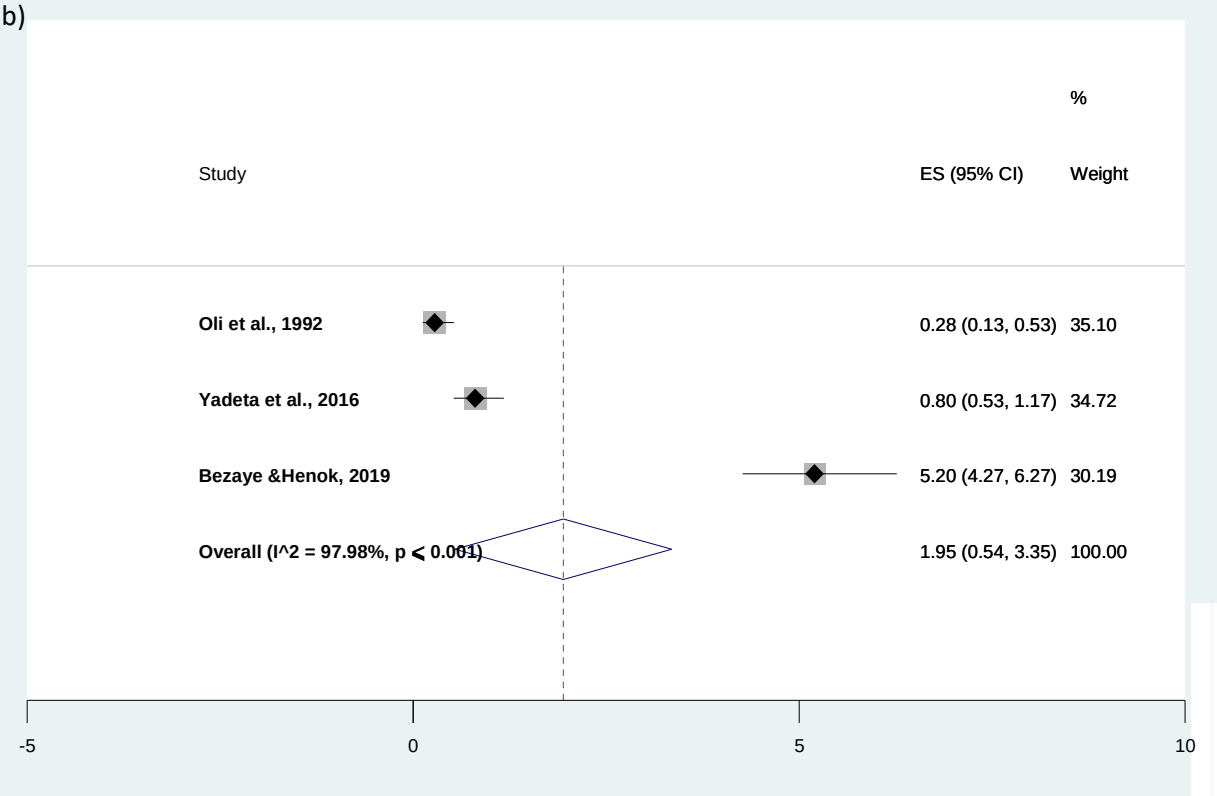

Study
ES (95% CI)
%
Weight
Oli et al., 1992
0.28 (0.13, 0.53)
35.10
Yadeta et al., 2016
0.80 (0.53, 1.17)
34.72
Bezaye &Henok, 2019
5.20 (4.27, 6.27)
30.19
Overall (I^2 = 97.98%, p < 0.001)
1.95 (0.54, 3.35)
100.00
-5
0
5
10

**Figure 4.6:** Prevalence of Rheumatic Heart Disease among males (a) and females (b) in Ethiopia

**Trends of RHD prevalence through year of publication**

The prevalence of RHD did not change between 1990 and 2000 but increased significantly from 0.64% to 32.78% between 2000 and 2010, and this pattern continued after 2020 (Figure 4.7)

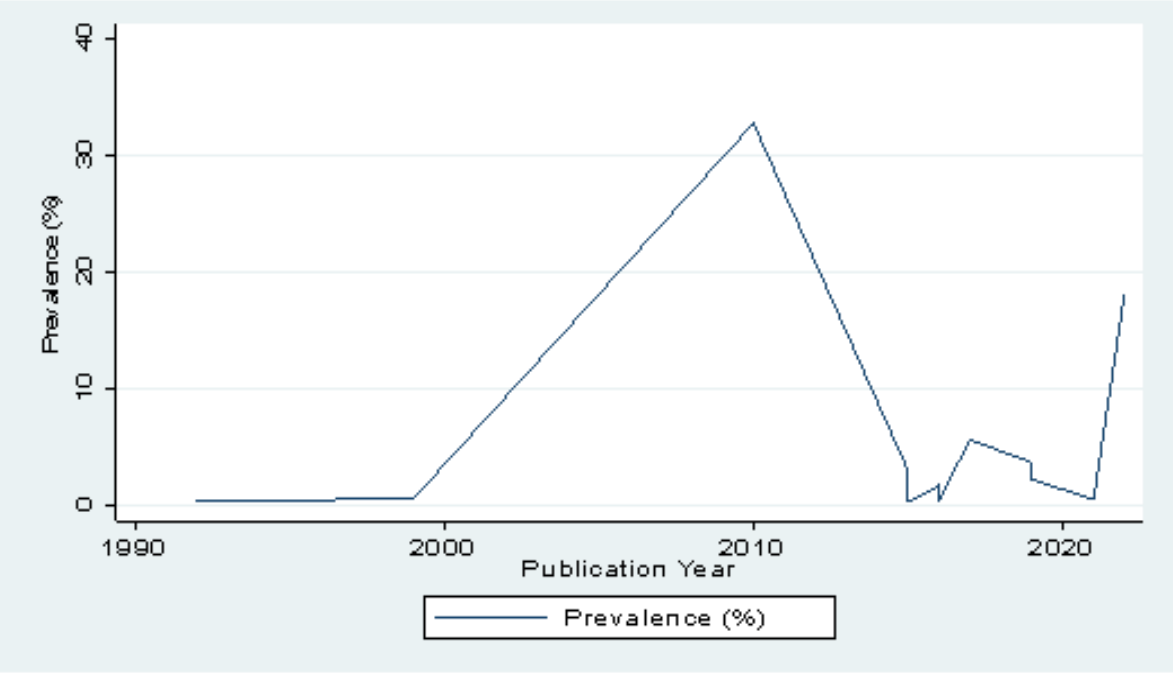



Figure 4.7: Trends of Rheumatic Heart Disease prevalence by year of publication in Ethiopia

## 4.5 Discussion

In the current systematic review and meta-analysis, the reviewers have explored published papers from different sources and finally included 12 primary studies that involved a total of 33,009 study participants. During this process, reviewers have identified a pooled prevalence of RHD as being 3.19% among the all-sex and age-inclusive Ethiopian population. For screening purposes, both the auscultation and echocardiography methods of diagnosis were employed in the study. Even though echocardiography is the gold standard for screening RHD with the best imaging contrast, careful clinical auscultation using a stethoscope remains a valuable tool for cardiac diagnosis in low-income countries (Carapetis et al. 2008; Quarato et al. 2017).

In terms of the prevalence patterns of RHD by year of publication, the prevalence remained stable in papers published in 1992 and 1999. However, there was a significant increase in prevalence between 2000 and 2010, rising from 0.64% to 32.78%. This upward trend has continued through to 2020.This could be due to the fact that the Ethiopian government is currently working to improve Ethiopians' health and well-being by providing a comprehensive package of high-quality preventive, curative, and rehabilitative non-communicable disease services in an equitable manner. This effort includes increasing the number of screenings for RHD which could enhance the number of research to increase (Memirie et al. 2022). Another possible explanation could be the efforts made by the World Heart Federation (WHF) to address RHD as a global health priority. The WHF aims to reduce the prevalence of RHD by 25% by the year 2025, which has encouraged researchers to focus on conducting studies in their respective areas.

The identified pooled prevalence of the current systematic review and meta-analysis was compared with different studies conducted at different times by different researchers. Accordingly, the current 3.19% pooled prevalence in the Ethiopian context is found to be lower as compared to the pooled prevalence reported by the study conducted in endemic areas by Rothenbuhler et al and the global systemic review done by Jean Jacques et al., where the prevalence was 12.9% and 26.1%, respectively (Jacques et al. 2019; Rothenbühler et al. 2014). In contrast, the current finding was slightly greater by a percentage than the South Asian study by Lamichhane P et al. in Nepal (Lamichhane et al. 2022) which was 2.79 percent of a comparable population. This could be due to the Nepalese government's dedication and the community's involvement through the development of an RHD registry, comprehensive program

evaluation, and improving the quality and safety of Benzathine Penicillin supplies (Regmi and Wyber 2013).

In the sub-group meta-analysis, the prevalence of RHD among individuals who visited hospitals was found to be 5.42%, which is more than 7 times higher compared to the school-based study. The possible reason for the heterogeneity among hospital-based studies and school-or community-based studies could be the straight-forward difference among study participants. The participants in hospital settings could be diseased individuals who sought healthcare services, whereas the school-level participants are notably healthy individuals. Moreover, the researchers have deployed a document review for data collection at hospitals and, on the other hand, have used face-to-face interviews for both school and community based studies. Therefore, differences in the method of data collection could also contribute to the variation in recorded prevalence.

In a separate view, the school-based pooled prevalence of RHD according to this study was 0.73%, indicating a reasonable difference from the hospital or community based pooled prevalence. In any case, the school-based pooled prevalence was found to be comparably similar to the pooled prevalence of RHD that was reported in Nepal among schoolchildren (Shrestha et al. 2012). On the contrary, the current school-based pooled RHD prevalence was higher when compared with the pooled prevalence of 0.04% in the same case among Iranian schoolchildren (Hayet et al. 2021). Even though the reasons for the disparity in the prevalence among the studies have not been clearly established, literatures ambiguously forwards the possible reasons to be differences in shortage of basic needs, overcrowding, malnutrition, low level of awareness about the disease, and accessibility of healthcare services for screening, early identification, and treatment of the disease in the Ethiopian context (Oli K and Asmera 2004).

In terms of geographical distribution, Amhara region had the highest prevalence of RHD, with Oromia region and SNNP ranking in second and third places, respectively. The possible explanations for the variation include differences in population density between regions, as well as levels of health service utilization and related water supply that is particularly low in the Amhara region compared to Oromia and SNNP regions ( Muluken et al. 2020). However, as the heterogeneity in the areas has been identified to be higher, the prevalence might not represent a real higher prevalence. Yet, the variability in the characteristics of the study setting, such as dense population, existence of many disadvantaged populations, and relatively lower healthcare

service coverage in Oromia and Ahmara regions, could support the result of the current review. Additionally, the study done by Bezaye and Henok (Bezaye and Henok 2019) included pediatric ages between 2 months and 14 years, while the studies conducted by Bacha and Abera and Moges et al. (Bacha and Abera 2019; Moges et al. 2021) included pregnant populations, which would grossly contribute to the variation among the studies.

Finally, the current review has revealed the overall sex distribution of RHD among males and females to be the same. On the contrary to this, previous studies have suggested the likelihood of a higher prevalence of RHD in females than in males of the same age for several reasons. To that end, previous research has identified the poor health-seeking behaviors of females and women who are burdened with home activities that expose them to indoor smokes produced during cooking. The higher exposure further increases the risk of upper respiratory infections among women (Alim et al. 2014). Nowadays, however, the aforementioned risk factors are relatively equally distributed among populations independent of sex due to equitable healthcare and indoor or community-based health services in the current study setting, unlike the report from Nepal, where the prevalence of RHD is higher among females (Nepal et al. 2020).

**Strength and limitations**

Data extraction and critical appraisal were done by two experienced reviewers. Besides this, sub-group analysis and sensitivity analysis were implemented to assess the degree of heterogeneity. However, the current studies lack detailed descriptions of the classification of cases as definite RHD or borderline RHD based on echocardiographic finding. The other limitation of this systematic review and meta-analysis is that not all regions of the countries are represented due to a lack of available studies.

## 4.6 Conclusion and recommendation

This review revealed that the prevalence of RHD is high in Ethiopia. The highest prevalence was observed among clients who visited hospitals compared to individuals screened at the school and community level. In terms of geographical distribution, Amhara region had the highest prevalence of RHD, followed by Oromia and SNNP, respectively. There is no significant sex difference in acquiring the disease. The review has also implicated that the study related to RHD prevalence has not been covered in all regions of Ethiopia. Therefore, the authors suggest that future research should encompass the entire geography of the country, along with additional

observational studies aimed at explicitly characterizing RHD and its risk factors, in order to provide valuable support to policymakers.

# Chapter Five: Rheumatic Heart Disease Burden and Determinants in Cardiac Patients: A Follow up Care Concern in Ethiopia

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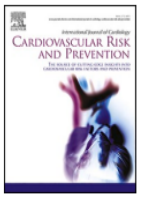

## Rheumatic heart disease burden and determinants in cardiac patients: A follow up care concern in Ethiopia

Hiwot Berhanu [a,*], Elsah Tegene [b], Morankar Sudhakar [c], Tadesse Dukessa Gemechu [b], Andualem Mossie [a]

***Abstract***

***Background:*** *Rheumatic heart disease (RHD) is a neglected tropical disease and remains one of the leading causes of cardiovascular-related deaths in Ethiopia. This study aims to assess the burden of RHD and identify its determinants in the country.*

***Methods:*** *A hospital-based cross-sectional study was employed from January 5 to April 15, 2023, among cardiac patients attending Jimma Medical Center. Socio-demographic data were collected using a structured interviewer-administered questionnaire, and echocardiographic patterns were taken by senior cardiologists. Data entered in to Epidata Version 4.6 and exported to SPSS Version 25.0 for analysis. Bivariable and multivariable logistic regressions were performed. A p value <0.05 was considered statistically significant.*

***Results:*** *A total of 340 adult patients were included in the analysis and investigated for the most frequent morbidities. Accordingly, the most frequent morbidities were RHD (n = 95, 27.9%), hypertensive heart disease (n = 92, 27.1%), ischemic heart disease (n = 54, 15.9%), and dilated cardiomyopathies (n = 54, 15.9%). Further, female sex [AOR=3.06: 95% CI 1.73–5.47], using wood (biomass fuel) for cooking [AOR=1.94: 95% CI 1.10-3.42], history of malnutrition with follow-up at health facilities [AOR=3.90: 95% CI 2.22-6.86], dental caries [AOR=2.09: 95% CI 1.12-3.87], and living in crowded households [AOR=2.02: 95% CI 1.15-3.52] were identified as determinants of RHD.*

***Conclusion:*** *This finding suggests that focusing on female healthcare, reducing biomass fuel exposure, improving nutritional status, providing regular dental care, and improving living conditions could help reduce the impacts of the disease. Moreover, conducting further research regularly will also benefit the community at large.*

## 5.1 Background

Cardiovascular disease (CVD) refers to all illness that affects the heart and circulatory system of the body including the blood vessels and the heart valves (Márquez 2020). According to estimates from the world health organization 17.9 million deaths worldwide in 2016 were attributed to CVD. The majority of CVD mortality occurs in low- and middle-income nations (Shashu 2021). Ethiopia is a nation undergoing an epidemiologic transition, with non-communicable diseases, including CVD, becoming the leading causes of disease and mortality. However, novel approaches for reducing the risks have been rarely developed and put into practice (Ali et al. 2020; Tolla et al. 2016) .

Rheumatic heart disease develops as a result of an immunological reaction initiated in the pharyngeal epithelium's innate immune components, which gradually results in valvular damage. This can lead to a number of structural and hemodynamic long-term consequences, including heart failure, atrial fibrillation, and stroke (Ellis et al. 2010; Okello et al. 2013).

Various studies in Africa have found that RHD is the most common cause of morbidity in adolescents and young adults, accounting for up to 34% of hospital admissions related to cardiovascular morbidity (Sliwa and Mayosi 2013). Patients with severe RHD in Africa frequently pass away without receiving heart surgery, and the majority of them have restricted access to surgical intervention because the continent only has 1% of the world's cardiothoracic surgeons (Vervoort et al. 2021) .

According to the Global Burden of Disease Study, the rate of disability-adjusted life years related to RHD was 10.67 million in 2019, with low and middle-income nations accounting for the majority of the burden (Ou et al. 2022). Similar to this, RHD results in significant financial losses for nations due to the early deaths of young adults and working-age individuals, with an estimated cost of 2.2 trillion dollars yearly (Belay and Aliyu 2021). Even though group A Streptococcus bacteria (GAS) is the top ten cause of death worldwide, the scientific community does not pay attention to the disease, and sub-Saharan Africa has continued to be the hotspot for RHD (Yuyun et al. 2020). A visible indicator for this is the Drakensberg Declaration, which provided momentum to a number of studies that have demonstrated that the burden of RHD is significantly higher than thought in 2005, referencing the Mozambican schoolchildren at 30 per 1000, which was an obvious proof of the reality (Mayosi et al. 2014).

Based on echocardiographic research from six major referral hospitals in Ethiopia, RHD accounts for up to 40.5% of cases (Yadeta et al. 2017). A study from Dabat Health Center in Amhara Region disclosed that the overall mortality rate in patients with RHD was 125.3 per 1000 person years and the mean age at death was 22 years (Günther 2005).

Even though RHD is a well-known complication of RF, not all RF patients develop it. A number of risk factors can render individuals more susceptible to acquiring RHD (Riaz et al. 2013). Literature highlights various factors associated with the risk of developing RHD. Genetic, socio-economic, nutritional, environmental, health facility-related factors, and hygiene-related factors all play a crucial role in influencing the likelihood of developing this condition (Zaman et al. 1998; Dobson et al. 2012; Sharma and Toor 2019; Thornley et al. 2017). A study conducted in Bangladesh reported that being a woman, urban resident, living in a brick-built house, having more than two siblings, and not brushing teeth after meals were identified as risk factors for RHD (Riaz et al. 2013). In contrast, a cross-sectional study in Tanzania indicated that overcrowding, age, and malnutrition are not risk factors for developing RHD (Kazahura et al. 2021). Similarly, a study in Assam, India, found that a low monthly income is associated with an increased risk of RHD (Baro et al. 2018). However, a study from Uganda did not demonstrate that low income is an associated factor for having RHD (Okello et al. 2012).

Except for a few studies on the prevalence of RHD in Ethiopia, there have been no comprehensive studies conducted on the risk factors for RHD in the country so far.

Therefore, this study was conducted to describe the burden of RHD and its determinants among patients who initiated follow-up at JMC cardiac follow-up clinic. The study aimed to address the World Heart Federation (WHF) non-communicable disease action plan, which was developed for the World Health Assembly in 2013. This plan calls for a 25% reduction in premature mortality from RHD by the year 2025, also known as the "25 by 25" target.

## 5.2 Materials and Methods

### 5.2.1 Study design, period, and setting

A cross-sectional study was carried out at JMC between January 5 and April 15, 2023. The facility accommodates 15 million outpatients and 16,000 inpatients annually, with multiple departments operating 24 hours a day. On average, this unit admits 102 patients each month for a variety of health issues (Kebede 2018). The facility provides a range of medical services such as echocardiography, electrocardiograms, CT scans, MRIs, and basic laboratory tests. This clinic is

just one of the several chronic follow-up clinics held at the hospital twice a week. Two adult cardiologists used a Toshiba AplioTM ultrasound system (TUS-A500, Shimoishigami, Japan) to diagnose various CVDs in accordance with the standards of the American Society of Echocardiography (Mitchell et al. 2019). In contrast, other cardiac diseases were diagnosed through echocardiography following their specific diagnostic protocols.

Echocardiographic parameters assessed include left ventricular ejection fraction, left ventricular dimensions, aortic root diameter, left atrial diameter, and tricuspid annular plane systolic excursion. Additionally, fractional shortening was measured to estimate left ventricular function, and left atrial size was assessed to determine pressure overload. Blood flow patterns across the affected valves were also analyzed to evaluate the severity of valve dysfunction.

**Study population and eligibility**

All cardiac patients attending follow-up at JMC cardiac clinic were the source population, and the study population were all selected adult cardiac patients attending follow-up at JMC cardiac clinic who fulfilled the inclusion criteria. Patients with clinical diagnosis of any cardiovascular disease who were taking follow-up during the study period were included in the study. Patients aged 15 years and above were treated as adults. However, individuals with comorbidities such as severe liver or kidney disease, uncontrolled diabetes, or active cancer were excluded from the study. Additionally, participants with serious medical conditions and those unable to provide informed consent were also excluded.

**Operational definitions**

**Rheumatic heart disease** was identified using the echocardiographic imaging criteria established by the World Heart Federation (WHF). These criteria encompass pathological features observed in two views, including jet length, velocity, and the presence of pan-systolic or pan-diastolic jets in at least one envelope. Additionally, morphological characteristics such as thickening, restricted motion of the leaflets, prolapse, coaptation defects, and excessive leaflet tip motion are considered for valve regurgitation. For mitral stenosis, a gradient increase of 4 mmHg or more is required. The evaluation also included an assessment of heart valve physiology and the severity of the dysfunction (Reméanyi et al. 2012).

**History of malnutrition and follow-up at a health facility** refers to patients who have been admitted to the hospital at least once in the past due to a diagnosis of malnutrition, with approval provided orally.

**The presence of dental caries** is the number of teeth that have fallen out or been lost by the patient due to dental caries (tooth decay), as reported by the patient and verified through clinical examination or patient history.

### 5.2.2 Sample size determination and sampling procedure

The sample size was calculated using Info STAT CALC Version 7.2.4.0, based on the assumption that the prevalence of rheumatic heart disease is 40.5%, as reported in a previous study conducted at Tikure Anbesa Hospital (Yadeta et al. 2017), With a confidence level of 95% and a margin of error of 5%, the population size of cardiac patients is 2345. Finally, a sample size of 352 was obtained by considering a 10% nonresponse rate. Lists of all cardiac patients are taken from the hospital registration log book. The study participants were selected from the hospital registration log book, which contains lists of all cardiac patients, using a simple random sampling technique facilitated by computer-generated methods until the desired sample size was reached, as illustrated in Figure 5.1.

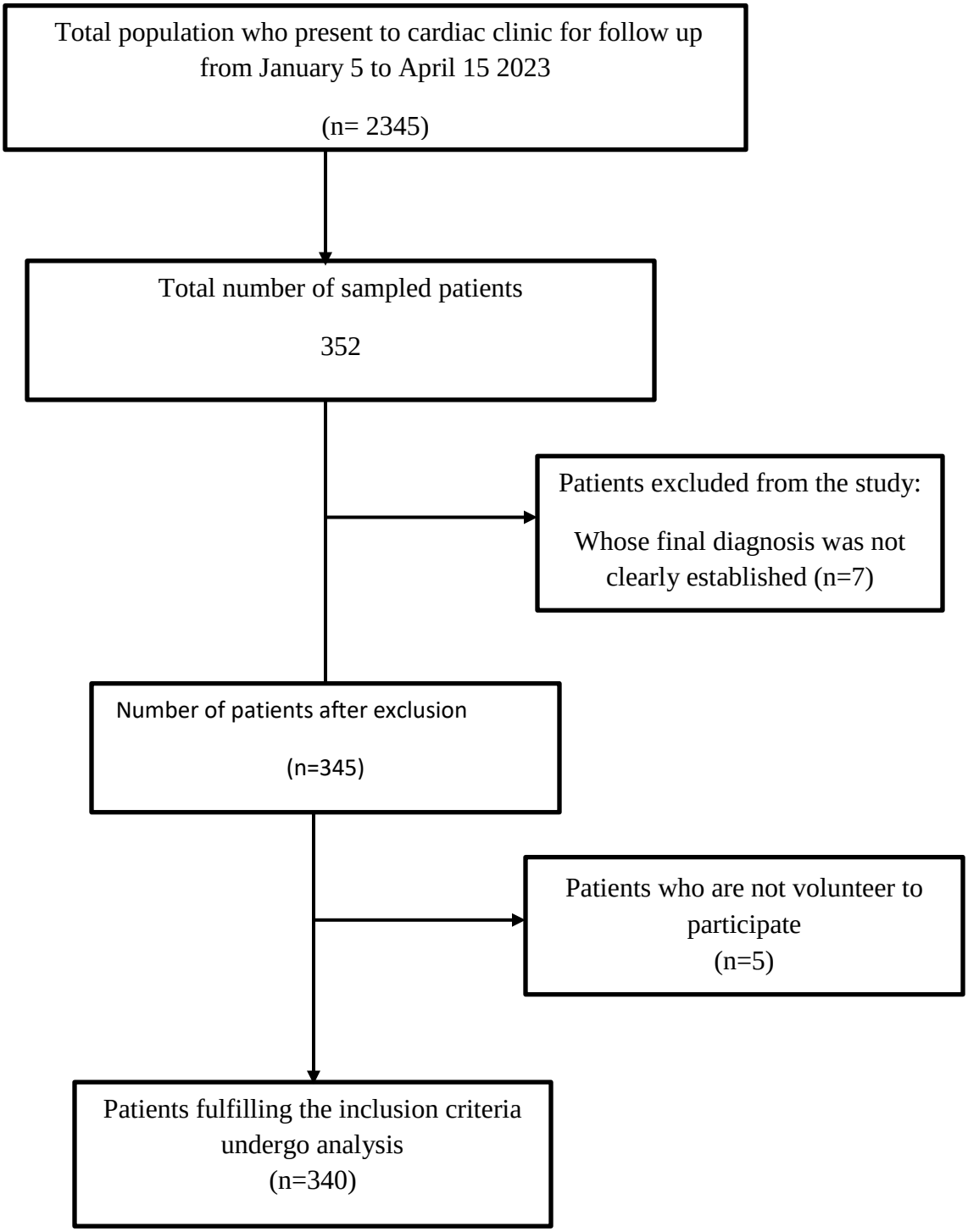


**Figure 5.1:** A flow chart showing the recruitment of study participants

### 5.2.3 Data collection tools and procedures

The detail is discussed on chapter 2

### 5.2.4 Data processing and analysis

Data were entered into EpiData Version 4.6 statistical software and exported to Statistical Package for the Social Sciences (SPSS) version 25. Data cleaning was performed before the actual data analysis. Descriptive statistics for frequencies, mean, and standard deviation were performed to summarize the dependent and independent variables. Bivariable and multivariable logistic regressions were performed to determine the association between dependent and independent variables. Binary logistic regression analysis was used to determine the crude relationship between rheumatic heart disease and independent variables that was expressed in the confidence interval, odds ratio, and p-value. Variables with a p-value of $\leq 0.25$ were selected as candidates for multiple logistic regression analysis using a backward stepwise approach. This method aimed to assess the impact of each independent variable on the dependent variable, reporting the results in terms of adjusted odds ratios, confidence intervals, odds ratios, and p-values.

Model fitness was tested with the Hosmer-Lemeshow test and multicollinearity of the variables was checked via tolerance test and variance inflation factor. Statistical significance was set at p-value of $< 0.05$.

## 5.3 Results

Socio-demographic characteristics of the participants

The study was conducted with a total of 340 participants, resulting in an impressive response rate of 97%. Among the participants, 156 individuals, accounting for 54.1%, were females. The mean ages of participants were 42.07±15.79 years, with a minimum of 15 and a maximum of 78 years. Regarding educational status, 160 (47.1%) of the respondents cannot read and write; more than one-fourth (27.4%) were farmers. The average monthly income of the recruited participants was 56 US$, as shown in Table 5.1.

Table 5.1: Socio-demographic characteristics of cardiac patients attending follow-up at JMC cardiac clinic from January 5 to April 15, 2023 (n = 340)

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Place of residence | Urban | 167 | 49.1 |
| | Rural | 173 | 50.9 |
| Sex | Male | 156 | 45.9 |
| | Female | 184 | 54.1 |
| Age (years ) | 15-24 | 44 | 12.9 |
| | 25-34 | 24 | 7.1 |
| | 35-44 | 61 | 17.9 |
| | 45-54 | 57 | 16.8 |
| | 55-64 | 91 | 26.8 |
| | ≥ 65 | 63 | 18.5 |
| Educational status | Cannot read and write | 160 | 47.1 |
| | Can read and write with no formal school attendance | 15 | 4.4 |
| | Primary school | 76 | 22.4 |
| | Secondary school | 60 | 17.6 |
| | Above secondary | 29 | 8.5 |
| Occupation | Government employ | 26 | 7.6 |
| | Merchant | 93 | 27.4 |
| | Farmer | 70 | 20.6 |
| | Self-employ | 51 | 15.0 |
| | House wife | 60 | 17.6 |
| | Others* | 40 | 11.8 |
| House hold monthly income ($ USD) | ≤35 | 106 | 31.2 |
| | 35-75 | 176 | 51.8 |
| | >75 | 58 | 17.0 |
| Distance from facilities (KM) | 1-5 | 229 | 67.4 |
| | 6-10 | 39 | 11.5 |
| | 11-20 | 25 | 7.4 |
| | 21-30 | 47 | 13.8 |
| Family size | ≤5 | 204 | 60.0 |
| | >5 | 136 | 40.0 |

* Retired, student and unemployed

**Cardiac disease distribution among patients who underwent echocardiography examinations in JMC**

Out of 340 individuals sampled with cardiovascular disorders who underwent echocardiography diagnosis, 95 (27.9%) had RHD, 92 (27.1%) had hypertensive heart disease (HHD), 54 (15.9%)

people had dilated cardiomyopathy, 12 (3.5%) individuals had congenital heart disease, and 20 (5.8%) individuals had other sorts of heart diseases. (Table 5.2)

Table 5.2: Echocardiographic diagnostic classifications by age in cardiac patients attending follow-up at JMC cardiac clinic from January 5 to April 15, 2023 (n = 340)

| **Type of cardiac disease** | **Age of cardiac patients** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **15-24** | **25-34** | **35-44** | **45-54** | **55-64** | **65 above** | **Total, (No %)** |
| Rheumatic heart disease | 29 | 19 | 24 | 17 | 4 | 2 | 95(27.9) |
| Ischemic heart disease | 0 | 0 | 8 | 11 | 19 | 16 | 54(15.9) |
| Hypertensive heart disease | 0 | 0 | 27 | 9 | 47 | 9 | 92(27.1) |
| Dilated cardiomyopathy | 15 | 0 | 0 | 10 | 10 | 19 | 54(15.9) |
| Congenital heart disease | 0 | 4 | 4 | 4 | 0 | 0 | 12(3.5) |
| Hypertrophic cardiomyopathy | 0 | 0 | 0 | 0 | 0 | 6 | 6(1.8) |
| Restrictive cardiomyopathy | 0 | 5 | 2 | 0 | 0 | 0 | 7(2.1) |
| Other types of cardiac diseases ** | 0 | 0 | 0 | 6 | 7 | 7 | 20(5.8) |
| Total | 44 | 24 | 61 | 57 | 91 | 63 | 340(100) |

**Pericardial disease, degenerative valvular disease, Cor pulmonale

**Factors associated with rheumatic heart disease**

Fourteen variables were included in the studies: place of residence, age, sex, occupation, literacy status, monthly income, BMI, distance from facilities, number of households, source of energy for cooking, source of water, history of chronic illness in the family, follow-up with malnutrition at health facilities, and presence of dental caries.

In the bivariate analysis, variables such as sex, place of residence, history of chronic illness in the family, source of water, source of energy for cooking, history of malnutrition with follow-up at a health facility, number of households living together, and presence of dental caries before the diagnosis of disease were candidate variables for multiple logistic regression (p value $\leq$ 0.25). Multivariate analysis was then performed to control confounders, and five variables like sex, main family food cooking materials, history of malnutrition with follow-up at a health

facility, presence of dental caries, and number of households living together showed a statistically significant association with RHD ($p < 0.05$) (Table 5.3).

Accordingly, by keeping all other variables constant, the odds of having RHD were 3 times higher in female patients compared to male patients (AOR = 3.06; 95% CI 1.73-5.47; p value < 0.001). Cardiac patients treated with malnutrition at health facilities were nearly four times more likely to have RHD than those without malnutrition (AOR = 3.90; 95% CI 2.22–6.86; p value < 0.001). Cardiac patients who use wood as a source of fuel for cooking had almost a two-fold risk of having RHD as compared to patients who use electricity as a source of energy (AOR = 1.94; 95% CI 1.10–3.42; p value = 0.021). Similarly, patients who had more than five households had a twofold risk of having RHD as compared to those who had fewer than five households (AOR = 2.02; 95% CI 1.15-3.52; p value = 0.013). Patients who have dental caries were two times more likely to have RHD than patients without dental caries (AOR = 2.09; 95% CI 1.12–3.87; p value = 0.019).

Table 5.3**:** Bivariables and multivariable logistic regression model of factors independently associated with RHD among cardiac patients attending follow-up at JMC cardiac Clinic, 2023 (n = 340)

| **Variables** | **Categories** | **RHD** | | **Bivariable result** | | **Multivariable result** | |
|---|---|---|---|---|---|---|---|
| | | **Yes (n)** | **No (n)** | **P value** | **COR(95%CI)** | **P value** | **AOR(95%CI)** |
| Place of resident | Rural | 42 | 125 | 0.24 | 1.3(0.82-2.1) | ____ | _____ |
| | Urban | 53 | 120 | | 1 | | |
| Sex | Female | 70 | 114 | 0.001 | 3.22(1.91-5.41) | 0.001 | 3.06(1.73-5.47) |
| | Male | 25 | 131 | | 1 | | 1 |
| Number of house hold living together (family size) | >5 | 50 | 88 | 0.001 | 0.031(0.19-0.51) | 0.013 | 2.02(1.15-3.52) |
| | ≤5 | 45 | 157 | | 1 | | 1 |
| Sources of water | Spring | 21 | 71 | 0.14 | 1.5(0.9-2.7) | _____ | _____ |
| | River | 13 | 25 | 0.58 | 0.8(0.4-1.8) | _____ | _____ |
| | Tap | 61 | 144 | | 1 | | |
| Source of energy for cooking | Animal waste | 5 | 8 | 0.09 | 0.37(0.11-1.20) | 0.391 | 0.56(0.15-2.10) |
| | Wood | 54 | 82 | 0.01 | 0.35(0.21-0.58) | 0.021 | 1.94(1.10-3.42) |
| | Electric power | 36 | 155 | | 1 | | 1 |
| History of chronic disease in the family | Yes | 52 | 149 | 0.21 | 1.2(0.81-2.10) | _____ | _____ |
| | No | 43 | 96 | | 1 | | 1 |
| History of malnutrition and follow-up at health facility | Yes | 67 | 81 | 0.001 | 0.20( 0.12- 0.34) | 0.001 | 3.90(2.22-6.86) |
| | No | 28 | 164 | | 1 | | 1 |
| Presence of dental caries | Yes | 37 | 45 | 0.001 | 0.35(0.20-0.59) | 0.019 | 2.09(1.12-3.87) |
| | No | 58 | 200 | | 1 | | 1 |

## 5.4 Discussion

Evidence indicates that CVDs are the primary contributors to illness and death globally. The number of CVD cases in Ethiopia doubled in 2017 as compared with 1990 which is explained by rapid population growth, with an increased ageing population (Ali et al. 2021). Nevertheless, there are a limited number of studies available to show the burden, distribution, and determinants of CVDs, including RHD, in nations with limited resources. Therefore, the objective of this study was to assess the prevalence of RHD and identify its determinants among cardiac patients receiving care at the follow-up clinic.

In the present study, the overall prevalence of RHD was found to be 27.9%, making it the most common cause of cardiovascular disorders among the participants. This result aligns closely with a similar study conducted in South Ethiopia (29.7%) (Tesfaye et al. 2020). However, the studies in south India (Manjunath et al. 2014),Uganda (Beaton et al. 2012), reported a high portion of RHD, which was 64.3% and 55.4%, respectively. Furthermore, the magnitude of RHD in the current study is much higher than in other studies in North Ethiopia (Engida et al. 2022), the south-west region of Cameron (Nkoke et al. 2017), and the Nigerian Savannah (Sani et al. 2007), where the range is between 6.7% and 18.2%. Genetic variations, economic status, cultural practices, access to healthcare, and public health initiatives could also be credible explanations for the differences observed in the studies.

According to the present finding, female sex was significantly associated with having rheumatic heart disease. This finding is supported by several studies (Engida et al. 2022; Negi et al. 2020; Nkoke et al. 2017; Sani et al. 2007). In contrast, research by Mutagaywa et al. reveals that there are no variations in the occurrence of RHD with regard to sex (Mutagaywa et al. 2020). None of the literature we appraised was able to identify an explanation for the difference in sex-specific prevalence. There is no established explanation for the increased prevalence of RHD among women in our population. Gender disparities in healthcare access exist in many regions of Ethiopia; females face barriers to accessing healthcare services compared to males due to limited financial resources, cultural norms, and geographic challenges, which can all contribute to delayed or inadequate medical care (Demsash and Walle 2023). The other possible genetic or biological reason could be due to the effect of estrogen on B cells, resulting in increased antibodies and autoimmune disease responses to infections, vaccines, and auto antigens that make females more susceptible to RHD contrast with the effects of androgens, which inhibit B-

cell maturation, decrease antibody production, and suppress the development of autoimmune diseases (Mutagaywa et al. 2020; Shrestha et al. 2012). Studies also suggest that menopause effect with increased blood pressure increased sympathetic tone, abnormal lipid metabolism, increased fat distribution, and increased deposition of collagen and elastin in the heart. These factors may accelerate aortic and mitral valve degeneration and calcification (Huxley 2007). In addition to this, pregnancy causes hyper dynamic circulation, and cardiovascular changes like increased blood volume, heart rate and cardiac output which might disclose an undiagnosed valvular lesion in an asymptomatic patient (Youssef 2021).

In the current study, using wood (biomass fuel) as a major source of energy for cooking has shown a significant association with having RHD. This finding is supported by previous studies conducted in the United Kingdom (Phillips et al. 2017) and Sri Lanka (Whiteman et al. 2020) . This could be due to the fact that biomass fuel produces toxic smoke, when inhaled, serves as an endogenous source of localized inflammation by increasing the level of anti-endothelial cell antibodies and further increasing the number of circulatory neutrophils and monocytes (Azad et al. 2012). In addition, it has been noted that low levels of autoantibodies can be triggered by smoke exposure. Initial exposure to biomass smoke may induce a sensitization phase characterized by low levels of cross-reactive antibodies. Upon subsequent streptococcal infection, these antibodies may increase significantly, contributing to the development of RHD (Rastogi et al. 2018).

The other factor that shows an association with RHD is history of malnutrition and follow-up at a health facility. This study is consistent with studies conducted in Bangladesh (Zaman et al. 1998), India (Saxena et al. 2011). In contrast, a cross-sectional study in Tanzania found that malnutrition is not a risk factor for developing RHD (Kazahura et al. 2021). The possible justification might be that malnutrition can weaken the immune system, make individuals more susceptible to infections, impair the tissue repair process, and increase the severity of valve damage. Malnutrition can also lead to chronic inflammation and increased oxidative stress in the body. This inflammatory response can contribute to the progression of RHD by exacerbating damage to the heart valves and promoting a pro-inflammatory environment that further fuels the disease process (Passos et al. 2021).

In the current study, the presence of dental caries was identified as independent risk factor for RHD. Patients who had dental caries were two times more at risk of developing RHD compared

to patients without dental caries. This is supported by studies conducted in New Zealand (Thornley et al. 2017), Australia (MacDonald et al. 2021),and Turkey (Onsuren et al. 2022). The possible mechanism could be that dental caries can provide a breeding ground for bacteria, including streptococcal pyogenes, within the oral cavity. When dental caries progresses and cavities deepen, it can lead to the exposure of the dental pulp, which contains blood vessels and nerves. Bacteria can reach the pulp, allowing them to enter the bloodstream (Michalik et al. 2020). Furthermore, the presence of dental caries can also contribute to a generally weakened immune response. The constant exposure to oral bacteria and the resulting chronic inflammation can disrupt the immune system's balance, potentially making the body more susceptible to infections (Galler et al. 2021).

Finally, this study justified having an association with RHD is the number of households living together. Patients who have more than five households have a doubled risk of developing RHD compared to their counterparts. This study is supported by studies in Uganda (Okello et al. 2012) and Bangladesh (Riaz et al. 2013). Conversely, a separate study conducted in India did not find any association between household crowding and the presence of RHD (Nandi et al. 2001).This might be due to the fact that in overcrowded households, where individuals live in close proximity, the transmission of GAS bacteria is more likely, and there is also an increased risk of reinfection and recurrences. At the same time, in overcrowded households, access to healthcare services may be limited, leading to delayed or inadequate treatment for streptococcal infections that might lead to repeated episodes of inflammation in the heart valves, which can eventually result in damage and the development of RHD (Avire et al. 2021).

**Limitation of the study**

The primary limitation of the study is that it only includes patients from a hospital setting, which hinders the ability to generalize the findings to the general population. Another limitation is the small number of patients with RHD, which reduce a precise statistical analysis of the disease's risk factors. Additionally, relying on patients' self-reported history to confirm past malnutrition and dental caries may introduce bias. Furthermore, the cross-sectional design of the study prevents the establishment of a cause-and-effect relationship.

## 5.5 Conclusion and recommendation

In the present study, the majority of cardiac illnesses are related to RHD. Specifically, sex, using wood (biomass fuel) for cooking, malnutrition, the presence of dental caries, and living with more than five households were identified as contributing factors to the problem. In the study population, females had a threefold greater chance of having RHD than males. To address these challenges, targeted healthcare programs specifically for women should be developed, utilizing the grassroots government structures of women's development armies in Ethiopia to raise awareness about RHD and its risk factors. Moreover, engaging with community health workers or local organizations to raise awareness about RHD and its risk factors, based on the study findings, is crucial. Such initiatives can greatly enhance public health education and preventive strategies. To mitigate health risks associated with overcrowding, malnutrition, indoor pollution, and dental caries, additional interventions are necessary. These should include introducing modern cooking technologies, ensuring access to routine dental care, promoting good oral hygiene practices, and encouraging healthy nutrition. Likewise, conducting awareness campaigns that educate the public about RHD, its risk factors, and preventive measures, while engaging community leaders for effective outreach, will be vital in combating this pressing health issue. Finally, we strongly recommend that future studies focus on assessing the degree and severity of valve dysfunction in patients with RHD. Comprehensive evaluations will offer valuable insights into the progression of RHD and its effects on cardiac function. This enhanced understanding can improve clinical knowledge and inform healthcare policies, ultimately leading to better management of the condition.

# Chapter Six: Echocardiographic Parameters and Complication Profiles among Adult Patients with Rheumatic Heart Disease at Jimma Medical Center

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***Abstract***

***Background:*** *Despite the fact that patients with rheumatic heart disease need early medical attention and follow-up, most patients in developing countries tend to present with debilitating complications. The objective of this study was to evaluate the echocardiographic features of adult individuals diagnosed with RHD and examine the associated complications among patients who started follow-up at Jimma Medical Center's cardiac follow-up clinic.*

***Methods:*** *A prospective cross-sectional study was conducted at JMC between January 5 and April 15, 2023. Echocardiographic patterns were taken by senior cardiologists; socio-demographic variables, anthropometric measurements, and behavioral factors were collected through a structured questioner.*

***Result:*** *The study recruited a total of 115 participants, of whom 86 (74.8%) were female and 29 (25.2%) were male. The mean age of the patients was 32.31 (SD± 12.16) years. The mitral valve was affected in 98.26% of cases, while the aortic and tricuspid valve abnormalities were diagnosed in 49.5% and 21.7%, respectively. The most frequent combinations of valve lesions were mitral regurgitation (MR) + mitral stenosis (MS) + aortic regurgitation (AR) (15.7%), followed by MR + AR + TR (8.7%). The occurrence of MR+MS+AR was higher in females (17.4%) compared to males (10.3%), whereas the occurrence of MS+MR was higher in males (24.1%) compared to females (20.9%). Females have a severely reduced ejection fraction compared to males (84.8% vs. 15.2%, p = 0.044). Nearly two-thirds (63.5%) of individuals experienced RHD-related complications; the most commonly encountered complications were pulmonary hypertension (26.1%) and atrial fibrillation (19.1%).*

***Conclusion****: RHD predominantly affects individuals in their active and productive years, particularly females. Most patients have multiple valve lesions.*

***Key words****: rheumatic heart disease, echocardiography, complication, Ethiopia*

## 6.1 Background

Rheumatic heart disease, a post-streptococcal complication of RF, is a disorder characterized by the impairment of one or multiple heart valves, resulting in significant structural and hemodynamic abnormalities (Franczyk et al. 2022) .

According to the Global Burden of Disease Study, the prevalence of RHD was 142.6 per 100,000 people in 2015, largely impacting low- and middle-income countries (Watkins et al. 2017). Despite the fact that patients with RF/RHD require early medical attention and follow-up, a significant number of patients in developing nations tend to present with debilitating complications such as heart failure, pulmonary hypertension, and arrhythmias (Desta et al. 2023). In the diagnosis and management of RHD, echocardiography has the ability to detect up to 10 times more cases compared to relying solely on clinical examination (Marijon et al. 2009; Saxena 2015). Likewise, echocardiography is an indispensable tool by providing valuable information about the severity of valve lesions, left ventricular (LV) chamber size, LV function, and pulmonary artery pressure, which are important indicators of cardiac health (Seitler et al. 2023). Moreover, strain echocardiographic imaging has gained popularity as a prognostic and diagnostic tool for patients with valvular heart disease by offering valuable functional insights about left atrial reservoir strain and improving understanding of cardiac function as compared to the conventional echocardiography techniques (Cvijic and Voigt 2020; Sonaglioni et al. 2021).

A study conducted in Nigeria Savannah showed that mitral regurgitation was the commonest echocardiographic diagnosis present in 65.9% of the patients, followed by aortic valve disease in 19.5% of cases (Sani et al. 2007). Similarly, according to the report of the Global Rheumatic Heart Disease Registry, the majority (63.9%) of patients with RHD had moderate-to-severe multi-valvular disease, complicated by heart failure (33.4%), pulmonary hypertension (28.8%), atrial fibrillation (AF) (21.8%), stroke (7.1%), infective endocarditis (4%), and major bleeding disorder (2.7%) (Zühlke et al. 2015).

In the same token, a study conducted in Nepal discovered that the majority of patients were women, accounting for 71.3% of the total sample, and the average age was 44.24±14.24 years. The majority of the patients were presented to have severe mitral stenosis (41.2%) followed by severe mitral regurgitation (19.8%) (Nepal et al. 2020).

Ethiopia, a nation heavily affected by RHD, experiences a significant burden from the disease (Berhanu et al. 2023) . Echocardiographic analysis across six major referral hospitals in Ethiopia has revealed that RHD constitutes as much as 40.5% of the reported cases (Yadeta et al. 2017). Similarly, a study conducted at Dabat Health Centre in the Amhara region reported the highest prevalence of RHD-related mortality worldwide, with a rate of 125.3 per 1000 people. The study also highlighted that the average age at the time of death was 22 years (Günther 2005).Therefore, the objective of this study was to evaluate the echocardiographic parameters, and related complications in patients diagnosed with rheumatic heart disease.

## 6.2 Materials and Methods

### 6.2.1 Study design and setting

From January 5 to April 15, 2023, a cross-sectional study was carried out at JMC, which is an academic institution with various departments. The center serves 15 million outpatients and 16,000 inpatients each year, with various departments operating 24 hours a day. One of its departments, internal medicine, includes a cardiac unit. This unit admits an average of 102 patients per month who present with various complaints related to cardiac problems. Additionally, the hospital runs a cardiac clinic twice a week as part of its chronic follow-up services, providing ongoing care and support to individuals with chronic cardiac conditions.

**Study participants**

The study included all patients who were consecutively under medical follow-up at the cardiac clinic during the designated study period and diagnosed with rheumatic heart disease. The patients included were aged 15 years and above and had their diagnosis verified through echocardiography imaging.

**Echocardiographic parameter**

Following the recommendations established by the American Society of Echocardiography, two adult cardiologists evaluated rheumatic heart disease using a Toshiba AplioTM ultrasound system (TUS-A500, Shimoishigami, Japan) (Mitchell et al. 2019). The diagnosis of RHD was made using the WHF echocardiographic imaging criteria. The criteria for valve regurgitation include morphological features (thickening, restricted leaflet motion, prolapse, coaptation defect, excessive leaflet tip motion) and pathological characteristics (seen in two views, jet length, velocity, pan-systolic/pan-diastolic jet in at least one envelope). The criteria for the diagnosis of mitral stenosis were signs of increased flow speed through the mitral valve, indicated by a mean

pressure gradient greater than 4mmHg. Mitral stenosis severity was evaluated using planimetry and pressure half-time, and classified as mild if the mitral valve area (MVA) exceeded 1.5 cm2, moderate if MVA ranged from 1.1 to 1.5 cm2, and severe if MVA was less than 1.0 cm2 (Omran et al. 2011; Reméanyi et al. 2012). The severity of valvular dysfunction was categorized as mild, moderate, and severe, following the guidelines provided by the American College of Cardiology/American Heart Association (ACC/AHA) (Baumgartner et al. 2009).

### 6.2.2 Data Collection Tool and Procedures

Data were collected by four trained BSc nurses assigned to the cardiac clinic. They used an interviewer-administered structured questionnaire to assess socio-demographic variables, anthropometric measurements, and behavioral factors. Additionally, participants' medical charts were reviewed to document any previous complications.

The questionnaire was initially developed in English and then translated into two local languages, Amharic and Afaan Oromo. It was retranslated back into English to ensure consistency. Data collection involved face-to-face interviews, allowing nurses to guide participants through the questionnaire and address any questions they had.

### 6.2.3 Sample Size Determination and sampling Procedure

The sample size was determined using Epi Info STAT CALC version 7.2.4.0, considering the following assumptions: a prevalence of RHD patient 7.5%, based on a previous study conducted in Nigeria,(Sani et al. 2007) a confidence level of 95%, and a margin of error of 5%. Taking into account a non-response rate of 5%, a sample size of 115 was obtained.

### 6.2.4 Data Analysis

The data was processed and analyzed using Epidata 3.1, and then transferred to SPSS version 25 for further analysis. The Kolmogorov–Smirnov test was used to evaluate the normality of variables and revealed that the data was normally distributed. The outputs of the analysis were then sorted by summarizing categorical and continuous data and finally resented using counts, percentages, and standard deviations. Chi-square test was utilized to compare the proportions of categorical variables, evaluating the statistical significance of the association and determining the level of significance.

## 6.3 Results

In the study, a total of 115 participants were recruited, of which 86 (74.8%) were female and 29 (25.2%) were male, representing a 1:2.5 sex ratio. The mean age of the patients was 32.31 ±

12.16 years, with an age range of 16 to 66 years. The age group with the highest proportion of patients with RHD was 25–34 years, accounting for 40 individuals (34.8%), following the age group of 35–44 years, with 31 patients (27.0%), as shown in (Table 6.1).

Table 6.1: Socio-demographic characteristics of patients with RHD at JMC cardiac Clinic from January 5 to April 15, 2023, (n=115)

| Characteristics | n (%) |
|---|---|
| Male | 29(25.2) |
| Female | 86(74.8) |
| Current khat chewers | 62(53.9) |
| Alcohol users | 10(8.7) |
| **Characteristics** | **Mean ±SD** |
| Mean age in years | 32.31±12.16 |
| Mean BMI | 19.67±3.12 |
| Mean systolic blood pressure | 114.46±18.41 |
| Mean diastolic blood pressure | 74.13±14.59 |
| Waist circumference | 78.51±12.75 |

**Echocardiographic parameters**

**Pathological Valve Lesions**

In the majority of cases, the mitral valve was found to be the most involved, accounting for 98.26% of the cases. The aortic valves were the second most commonly involved valve, seen in 49.5% of the cases and tricuspid valve is involved in 21.7% of the cases. Among isolated valve involvement cases, mitral regurgitation was the most common, observed in 15 individuals (13%), followed by mitral stenosis, which accounted for 3 cases (2.6%), and aortic regurgitation, which was present in 1 case (0.9%). The majority of the patients were found to have multiple valve lesions. The most common combination of multiple valve diseases observed was MR+MS+AR and MR+AR+TR, accounting for 15.7% and 8.7% of the cases, respectively. The occurrence of MR+MS+AR was more common among females (17.4%) than in males (10.3%), while the occurrence of MS+MR was higher in males (24.1%) compared to females (20.9%). Combined MR+AR was present in 7.8% of patients with a p value of 0.008, as presented in (Table 6.2)

Table 6.2: Classification of valvular lesions in adults with RHD at JMC Cardiac Clinic from January 5 to April 15, 2023 (n = 115)

| Valvular lesion | Male, n (%) N = 29 | Female, n (%) N = 86 | Overall, n (%) N = 115 | p value |
|---|---|---|---|---|
| MR only | 4(13.8) | 11(12.8) | 15(13) | 0.619 |
| MS only | 0(0) | 3(3.5) | 3(2.6) | 0.30 |
| AR only | 0(0) | 1(1.2) | 1(0.9) | 0.99 |
| MS+MR | 7(24.1) | 18(20.9) | 25(21.7) | 0.717 |
| AR +AS | 0(0) | 1(1.2) | 1(0.9) | 0.99 |
| MR+AS | 2(6.9) | 6(7) | 8(7) | 0.98 |
| MR+TR | 2(6.9) | 6(7) | 8(7) | 0.98 |
| MR+AR | 4(13.8) | 5(5.8) | 9(7.8) | 0.008* |
| MS+AR | 0(0) | 8(9.3) | 8(7) | 0.97 |
| MR+MS+AR | 3(10.3) | 15(17.4) | 18(15.7) | 0.36 |
| MR+AR+ TR | 5(17.2) | 5(5.8) | 10(8.7) | 0.692 |
| MS+MR+TR | 2(6.9) | 5(5.8) | 7(6.1) | 0.50 |
| MR+AR+AS | 0(0) | 2(1.3) | 2(1.6) | 0.99 |

*Association between valvular lesion and sex

MR: mitral regurgitation; MS: mitral stenosis; AR: aortic regurgitation; AS: aortic stenosis; TR, tricuspid regurgitation

**Severity of valvular dysfunction**

Among the patients with RHD, mitral valve disease (MR or MS) was the most common valve disease present in 98.26% of the cases. Mitral regurgitation was identified as the most prevalent severe valvular lesion, representing 35.65% of all cases followed by aortic regurgitation (AR) at 18.26% as shown in (Table 6.3)

Table 6.3: Severity of valve lesion among adults with RHD attending at JMC cardiac Clinic from January 5 to April 15, 2023, (n=115)

| Type of valve dysfunction | Severity of valve dysfunction | | | |
|---|---|---|---|---|
| | Total n (%) | Mild | Moderate | Severe |
| MR | 93(80.86) | 8(6.95) | 44(38.26 ) | 41(35.65 ) |
| MS | 61(53.04) | 12(10.43) | 33(28.69) | 16(13.91) |
| AR | 49(42,60) | 8(6.95) | 20(17.39) | 21(18.26) |
| AS | 11(9.56) | 4(3.47) | 3(2.60) | 4(3.47) |
| TR | 17(14.78) | 4(3.47) | 8(6.95) | 5(4.34) |

**Echocardiographic parameters**

Nearly one-fifth of the study participants (18.3%) have severely reduced left ventricular systolic function; the mean left ventricular systolic dimension (LVSd) was 54.4±8.3mm. Severely reduced left ventricular posterior wall end diastole and end systole (LVPWd) function is observed among 16.5% of the patients, and the mean LVPWd was 10.01±1.18 mm.

Twenty-six percent of the participants have severely reduced ejection fractions. Whereas the mean left ventricular ejection fraction (EF) in percentage was 55.2±9.13. High number of females have low level of ejection fraction compared to males (84.8% vs 15.2%, p= 0.044).

One third of the participants (28.7%) have a decreased Tricuspid annular plane systolic exertion (TAPSE), and the mean TAPSE was 17.53±2.8mm.

Regarding fractional shortening, 26% of the patients have severely reduced systolic function, with a mean value of 30.47±6.03. Half of the patients have severely enlarged left atrium, and the mean left atrial diameter was 41.87±10.55mm as presented in (Table 6.4)

Table 6.4: Echocardiographic parameters severity classification among adults with RHD at JMC cardiac clinic from January 5 to April 15, 2023 (n = 115)

| Echocardiographic parameters | Severity of classification | n=115(%) |
|---|---|---|
| Left ventricular internal diameter end diastole (LVIDd) | Normal | 64(55.7) |
| | Mildly increased | 4(3.5) |
| | Moderately increased | 8(6.9) |
| | Severely increased | 39(33.9) |
| Left ventricular systolic dimension (LVSd) | Normal | 83(72.2) |
| | Mildly reduced systolic function | 5(4.3) |
| | Moderately reduced systolic function | 6(5.2) |
| | Severely reduced systolic function | 21(18.3) |
| Left ventricular posterior wall end diastole and end systole. (LVPWd) | Normal | 87(75.7) |
| | Mildly increased | 1(0.9) |
| | Moderately increased | 8(6.9) |
| | Severely increased | 19(16.5) |
| Left ventricular Ejection Fraction (EF) | Normal | 69(60) |
| | Mild dysfunction | 5(4.4) |
| | Moderate dysfunction | 11(9.6) |
| | Severe dysfunction | 30(26.0) |
| Tricuspid annular plane systolic excursion (TAPSE) | Normal | 82(71.3) |
| | Decreased | 33(28.7) |
| Fractional shortening (FS) | Normal | 59(51.4) |
| | Mildly reduced | 9(7.8) |
| | Moderately reduced | 17(14.8) |
| | Severely reduced | 30(26) |
| Aortic root diameter | Normal | 71(61.7) |
| | Mild dilated | 6(5.2) |
| | Moderately dilated | 14(12.2) |
| | Severely dilated | 24(20.9) |
| Left atrial diameter | Normal | 27(23.5) |
| | mild enlarged | 4(3.5) |
| | moderate enlarged | 35(30.4) |
| | severe enlarged | 49(42.6) |
| Main pulmonary diameter | Normal | 107(93.1) |
| | Mildly enlarged | 8(6.9) |
| | Moderately enlarged | - |
| | Severely enlarged | - |

**Complication related to Rheumatic heart disease**

Among 115 patients, 73 (63.5%) have rheumatic heart disease-related complications. Pulmonary hypertension accounts for 26.1%, followed by atrial fibrillation (19.1%), left ventricular thrombus (6.1%), stroke (4.3%), valvular cardiomyopathy (4.3%), and infective endocarditis (3.5%) as presented in (Figure 6.1)

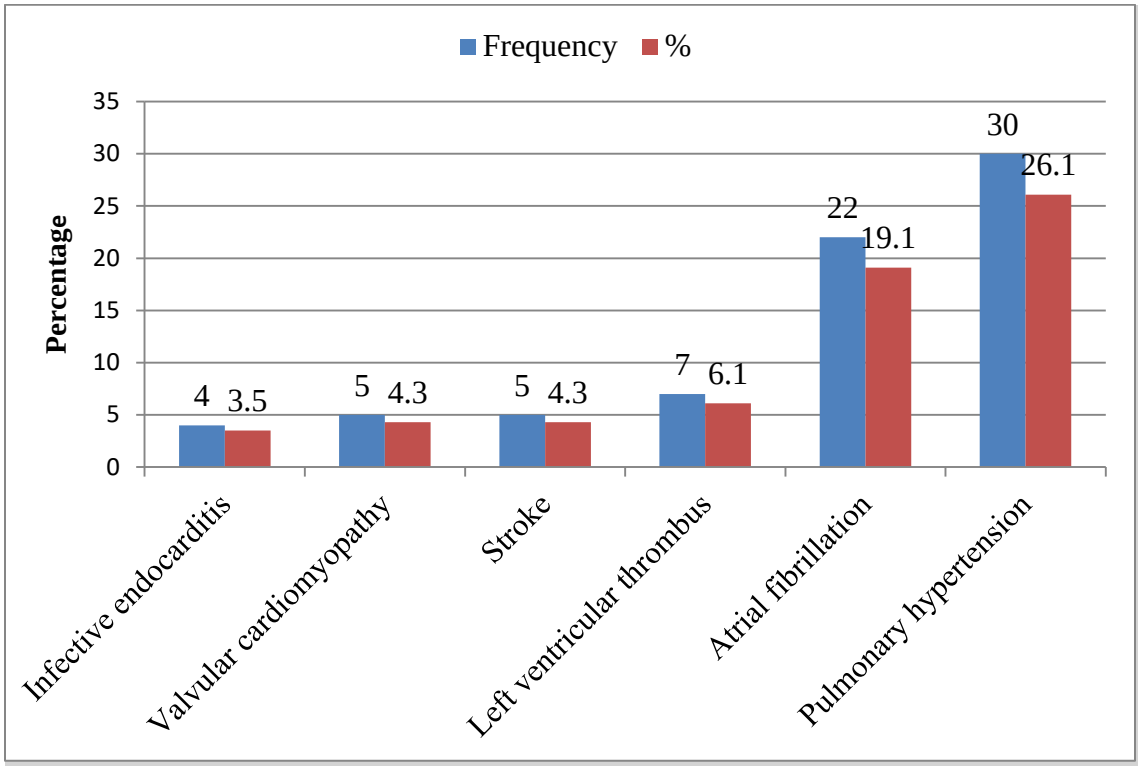


**Figure 6.1:** Complications related to rheumatic heart disease

## 6.4 Discussion

The current study, conducted within a hospital setting, presents data on the echocardiographic characteristics of rheumatic heart disease, the extent of valve dysfunction, and complications encountered in the Jimma Medical Center cardiac clinic. Our study investigated the age group with the highest proportion of patients with RHD, which was found to be between 25 and 44 years, accounting for the majority of the cases (61.8%). This study is consistent with the study conducted in the Northern Territory of Australia. Where the highest prevalence of RHD is typically observed during adulthood, specifically between the ages of 25 and 45 (Lawrence et al. 2013). A similar, published study at the National Heart Center of Nepal by Koirala PC et al.,

reported as RHD to be more prevalent among individuals aged 10 to 40 years, with a higher occurrence among females (Koirala et al. 2018).

The gender distribution in this study demonstrated a male-to-female ratio of 1:2.5, indicating a higher proportion of female participants. Similar proportion of studies are reported by Adem et al and (Adem et al. 2020) and Zühlke, Liesl et al. (Zühlke et al. 2015). Even though the exact reasons for this gender disparity are not fully understood, the higher percentage of RHD in females can be attributed to several factors, like stronger immune responses in females, potential genetic predispositions, and social and cultural factors such as limited healthcare access could be the possible explanation.

This study revealed that the mitral valve was the most affected valve, accounting for 98.2%, followed by the aortic valve, observed in 49.5% of the participants. Likewise the study conducted at St. Paul's Hospital Millennium Medical college (SPMMC) also demonstrated that the mitral valve was the valve most frequently affected valve, accounting for 95.6% of individuals followed by aortic valve (61.5%) of individuals (Adem and Mulatu 2022). In isolated valve involvement cases, the most common valvular impairment observed was mitral regurgitation, accounting for 13%, followed by mitral stenosis, which accounted for 2.6%, and aortic regurgitation, which was present in 0.9% of individuals. This study is comparable to the study conducted in Nigeria Savanna, which reported that mitral regurgitation (38.0%) is the commonest valve, followed by mitral stenosis (7.8%), and pure aortic regurgitation (3.1%) (Sani et al. 2007). The most common combination of multiple valve diseases observed was MR+MS+AR accounting for 15.7% of the cases, Whereas a study conducted in central Nepal reported that combined mitral plus aortic valve lesions were the commonest valve lesions contributing 9.78 percent (Koirala et al. 2018).

According to this study, the occurrence of MR+MS+AR was more common among females (17.4%) than in males (10.3%). This study is comparable to the study by Koirala PC et al., in which MR+MS+AR were higher in females (36.49%) compared to males (15.25%) (Koirala et al. 2018). Similarly, the current study also found that the occurrence of MS+ MR was higher in males (24.1%) compared to females (20.9%) and combined MR+AR was present in 7.8% of patients and was statistically significant in relation to sex with a p value of 0.008. This study supports the study conducted by Adem et al and Mulatu., where MS+MR was more prevalent among males (35.6%) than females (28.3%) (Adem and Mulatu 2022).

In general, most of the individuals involved in the present study exhibited more severe valvular dysfunction than mild valvular dysfunction. In particular, MR and AR were identified as having severe levels of dysfunction. This study is consistent with a study conducted by SPMMC (Adem and Mulatu 2022) and a study in the northern part of Ethiopia (Engida et al. 2022). On the contrary, the current finding revealed that high number of severe form of valvular lesion compared to the study by a multisite echocardiography-based study conducted in Ethiopia (Yadeta et al. 2016) and north India (Raina 2013) that indicate the majority of patients presented with mild valvular lesions. The variations in the studies could be due to the differences among study participants. The participants with severe forms of valvular dysfunction are from hospital settings and presented with symptoms of heart failure, while participants with mild valvular lesions are individuals at school and notably healthy individuals without symptoms.

Regarding the echocardiographic findings, nearly one-fifth of the study participants (18.3%) have severely reduced left ventricular systolic dysfunction; the mean LVSd was 54.4±8.3mm; this study resembles a study by Rudiktyo et al., where the patients have a mean of 56.63 ± 8.57mm (Rudiktyo et al. 2023).

This study discovered that the mean left ventricular posterior wall end diastole and end systole (LVPWd) was found to be 10.01±1.18mm. This finding is higher than a study conducted in Multan, Pakistan, where the mean LVPWd was reported as 7.13 ± 1.95mm (Shahid et al. 2022) and another study by Meel et al. from South Africa also reported a mean LVPWd of 8.5 ± 1.5mm (Meel et al. 2020). Differences in LVPWd among studies may be attributed to various factors. Firstly, variations in the characteristics of the study populations, such as age, sex, and ethnicity, can influence ventricular wall thickness and contribute to different mean values (Chen et al. 2016). The other possible factor could be due to discrepancies in the measurement techniques employed to assess LVPWd can impact the accuracy of the measurements and variances in image acquisition, echocardiographic equipment, and measurement protocols (Letnes et al. 2021).

In our study, a quarter of the participants (26%) exhibited a severely reduced ejection fraction, while 49 individuals (42.6%) had a severely dilated left atrium, and 33 participants (28.5%) experienced a decline in tricuspid annular plane systolic excursion (TAPSE). Similarly, a study carried out in Dares Salaam, Tanzania, among RHD patients with arrhythmia revealed that 80 individuals (20.5%) had reduced TAPSE, 20 participants (5.1%) displayed a severely reduced

ejection fraction, and 263 individuals (67%) exhibited a severely dilated left atrium (Makatu et al. 2023).

In terms of complications observed in our study, a majority of participants (63.5%) experienced complications related to RHD. Among these complications, pulmonary hypertension accounted for 26.1%, while atrial fibrillation occurred in 19.1% of cases. Other complications included left ventricular thrombus (6.1%), stroke (4.3%), valvular cardiomyopathy (4.3%), and infective endocarditis (3.5%). This study is comparable with a study conducted in Nigeria where the major RHD related complications were pulmonary hypertension in 72.1% of cases, valvular cardiomyopathy in 31.8% of cases, and functional tricuspid regurgitation in 30.2%, atrial fibrillation in 10.1% of cases, while left ventricular thrombus occurred in 2.3% of cases (Sani et al. 2007). Whereas a study conducted in a tertiary hospital in Addis Ababa shows that complications related to RHD account for 83.6% of cases. The most common complication encountered was heart failure (61.4%), followed by pulmonary hypertension (59.3%), malnutrition (50.7%), and infectious endocarditis (3.6%) ( Gezachew and Eshetu, 2023).

**Limitation of the study**

The main limitation of a study is that it exclusively includes patients from a hospital setting, which can limit the ability to generalize the findings to the general population. The other limitation of the study is that it is unable to use cardiac MRI, which is a better tool for visualizing the valve anatomy. Likewise, the study used conventional echocardiography instead of strain echocardiography due to the unavailability of strain echocardiography, which could have provided additional functional information regarding left atrial reservoir strain in the study. Further studies should be designed to evaluate the potential role of strain echocardiographic imaging in patients with rheumatic heart disease.

## 6.5 Conclusion and recommendation

The current study reveals that rheumatic heart disease predominantly affects individuals in their active and productive years, particularly females. A majority of the patients included in the study have multiple valve lesions. Mitral valve was the commonest valve affected. Approximately two-thirds of patients experienced RHD related complications, with pulmonary hypertension and atrial fibrillation being the most common. As a result, it is recommended to regularly conduct echocardiography for individuals diagnosed with RHD, with a particular emphasis on females and younger adults to facilitate early detection and treatment of the disease before complications

arise. Additionally, we recommend implementing educational interventions to encourage effective lifestyle management. By providing patients with the necessary knowledge and skills to make informed choices that improve their health and support the management of the disease

# Chapter Seven: Effects of Self-Management Education on Clinical Outcomes of Adults with Rheumatic Heart Disease: a Quasi-Experimental Study

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**Abstract**

*As the burden of rheumatic heart disease increases in Ethiopia, there is a growing need for low-cost interventions to mitigate its impact. This study aimed to assess the effectiveness of chronic disease self-management education (CDSME) on clinical outcomes, depression, and anxiety among patients with RHD. A quasi-experimental study was deployed among 166 patients with RHD at JMC between April and July 2024. A multi-component CDSME was endured for four consecutive months. Data were analyzed using SPSS version 25.0. Systolic blood pressure decreased from 131.31 mmHg (SD±15.68) at pre-education to 113.77 mmHg (SD±20.98) at post-education (t- 12.251, p<0.001). Diastolic blood pressure decreased from 94.87 mmHg (SD±19.41) pre-education to 79.28 mmHg (SD±9.33) post-education (t-12.306, p<0.001). Hemoglobin level changed from 11.97 g/dl (SD±1.99) to 13.84 g/dl (SD±1.37) after the intervention (t -11.96, p < 0.001). Similarly, hospital depression subscale decreased from 11.93 (SD±3.43) to 9.48 (SD±3.67) (t - 8.37, p < 0.001) post intervention. Regarding the hospital anxiety subscale, the mean score before education program was 8.59 (SD±2.91) and decreased to 7.30 (SD±1.97) (t -6.44, p < 0.001) after education. This intervention is simple, cost-effective, and has the potential to be scaled up and implemented in the current healthcare system in Ethiopia.*

***This study was registered under the ClinicalTrials.gov with an identifier number ClinicalTrials.gov on 2/5/2024 ID: NCT06400628***

**What is known about this topic?**

Empower patients with chronic conditions to actively manage their health and improve their quality of life.

Patients with rheumatic heart disease experience various physical and emotional symptoms. This is especially important for people with low socioeconomic status because they have difficulties performing suitable self-management.

**What does this article add?**

Improves knowledge, skills, and self-management behaviors among patients with RHD in Ethiopia.

Reduced rheumatic heart disease-related complications among patients by utilizing CDSME in Ethiopia.

## 7.1 Background

Rheumatic heart disease, a neglected tropical chronic disease, disproportionately affects low-income countries, causing preventable morbidity and mortality (Antunes 2020). Globally, over 40.5 million individuals have been impacted by RHD, leading to 1,100,000 cases of heart failure and 320,000 deaths annually (Yingying et al. 2022). Poignantly, the financial toll is equally far-reaching, with nations losing a whopping 2.2 trillion dollars yearly due to premature deaths of the working-age population (Watkins and Daskalakis 2015). Consequently, individuals living with RHD face a multitude of problems and tragedies that impact various aspects of their lives. From the burden of adhering to a complex medication regimen to managing their daily lives. Moreover, many individuals with RHD lack the knowledge and skills to effectively cope with their illness and manage their well-being (Coffey et al. 2018; Dixit et al. 2021).

According to recent reports from Uganda, individuals with RHD face numerous health challenges. These patients frequently experience physical, emotional, and social issues, living in fear of the future due to limited awareness about the disease and self-management (Nalubwama et al. 2023). Similarly, Sheikh et al. discovered that anxiety and depression are prevalent among those living with RHD, indicating a common coexistence of these mental health conditions (Sheikh et al. 2019). Likewise, studies have shown that individuals with RHD are at a higher risk of malnutrition due to inadequate knowledge about proper dietary requirements (Thorup et al. 2020). In reflecting the cruelty and widespread nature of the condition, the research conducted in Addis Ababa revealed that over half of patients with RHD (50.7%) suffered from malnutrition (Desta et al. 2023). Furthermore, findings by Klein et al. indicated that a significant portion of patients with RHD experienced nutritional deficiencies and anemia (Klein et al. 2019). Significantly, findings from a study conducted in India suggest that a substantial number of individuals diagnosed with RHD, around 46%, failed to comply with the recommended antibiotic prophylaxis. This indicates a deficiency in disease awareness within this specific population, thereby complicating their health status (Chowdhury and Chakraborty 2017).

On the other hand, several studies recommend chronic disease self-management education as a way to empower patients with the knowledge, skills, and abilities needed for self-care. This education is tailored to the specific needs, goals, and life experiences of individuals with chronic illnesses, guided by evidence-based standards (Vainauskienė and Vaitkienė 2021). Numerous studies have shown that implementing a CDSME program leads to improved self-care behaviors,

enhanced decision-making skills, increased problem-solving abilities, and better engagement and collaboration with healthcare professionals. These improvements have resulted in better clinical outcomes and an enhanced quality of life for patients with RHD (Dessie et al. 2021; Vainauskienė and Vaitkienė 2021; Zhao et al. 2020).

Similar studies conducted in Nepal demonstrated the effectiveness of education and awareness-raising interventions in improving knowledge and promoting health-seeking behaviors among patients with RHD. Specifically, the study revealed that self-management education significantly increased the proportion of participants possessing good knowledge of self-management practices for the disease, rising from 6% to 37.6% in the post-intervention group (Regmi and Sanjel 2019). In the Ethiopian context, however, the prevalence of RHD is substantial, exacerbated by a lack of self-management education that results in inadequate understanding of the disease and suboptimal self-care practices. It is hypothesized that implementing chronic disease self-management education interventions can effectively mitigate RHD-related complications and enhance clinical outcomes. Accordingly, this study aimed to evaluate the effectiveness of locally tailored Chronic Disease Self-Management Education interventions in improving clinical outcomes among adults with RHD.

## 7.2 Materials and Methods

### 7.2.1 Study design, setting and period

A quasi-experimental study was conducted from April to July 2024, involving a single group of consecutively sampled adults of both sexes receiving medical care at JMC, a teaching and referral tertiary hospital located in Oromia, Ethiopia. The study included pre-test and post-test assessments to evaluate the impact of an educational intervention. The intervention was provided once a month for four consecutive months: on April 1, May 31, June 30, and July 31, 2024. Both clinical and laboratory measurements were comprehensively assessed before the initiation of the intervention and after the completion of all educational sessions. A summary of the study time lines is presented in Figure 7.1.

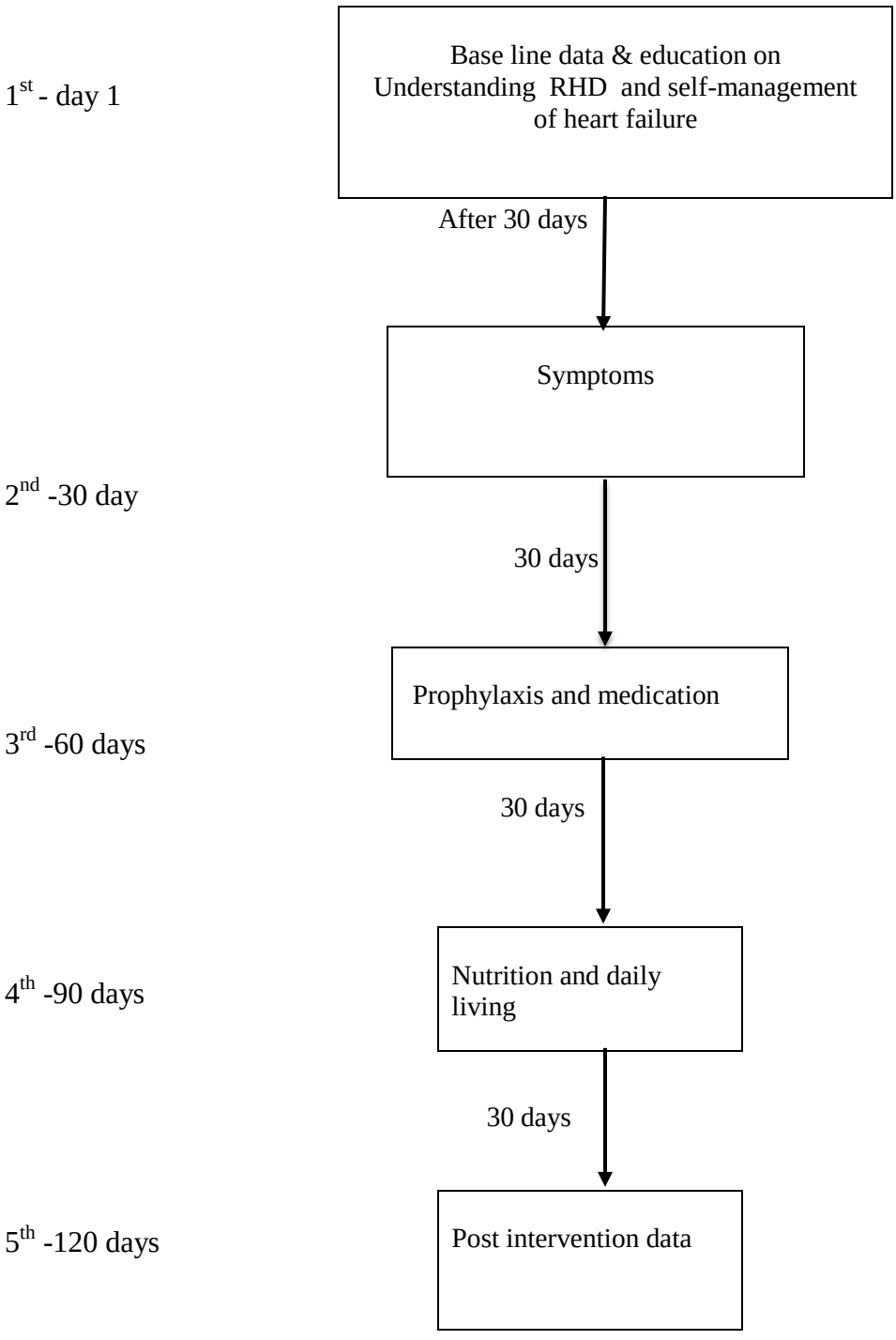


**Figure 7.1:** A summary of the study time lines

### 7.2.2 Sample size, sampling technique and criteria

The sample size for the study was determined using Raosoftware, considering a margin of error of 5%, a confidence level of 95%, a monthly population size of 315, and an unknown response distribution estimated at 50%. This resulted in a calculated sample size of 174 study subjects, as detailed in Figure 2. Participants included patients of either sex with rheumatic heart diseases receiving chronic disease follow-up at Jimma Medical Center cardiac clinic.

**Criteria**

**Inclusion:** The study included patients aged 15 years and older, with a confirmed diagnosis through echocardiography imaging of rheumatic heart disease by a cardiologist for at least 6 months and classified as New York Heart Association (NYHA) functional Class II/III.

**Exclusion:** patients under serious medical conditions, the existence of chronic illnesses like chronic obstructive pulmonary disease or asthma, diabetes, chronic kidney failure, stroke, or advanced-stage cancer. Participants also needed to demonstrate the ability to effectively communicate, understand the study's objectives, and provide informed consent.

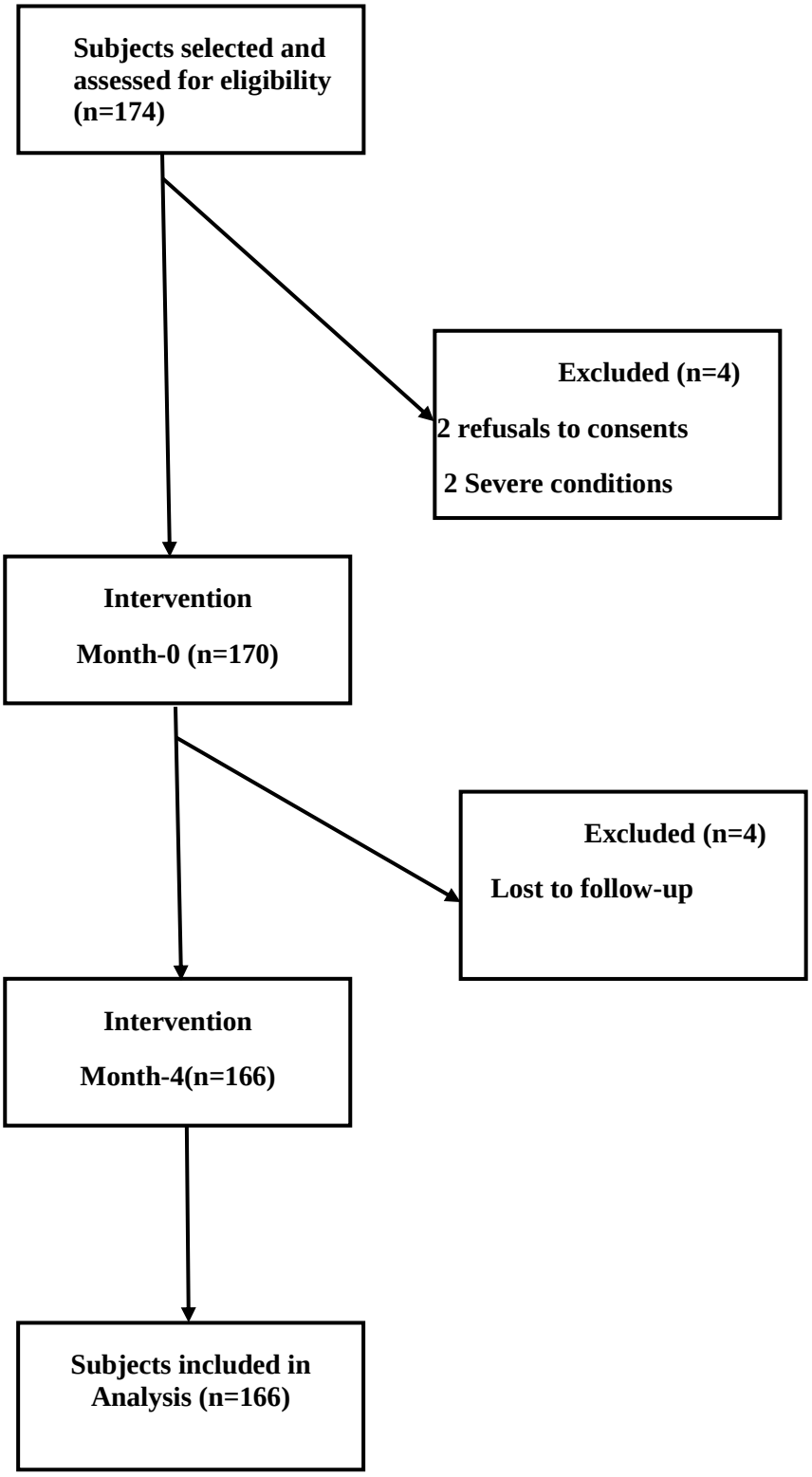


**Figure 7.2:** Study identification and selection flow diagram

**Interventions and protocols**

A multi-component, one-to-one nurse-led and chronic disease patient-centered self-management education intervention was introduced using a translated educational guideline for chronic disease self-management. The validated guideline helped to ensure the intervention covered all important topics for patients to better manage their condition. The study involved collecting baseline data before the initiation of the intervention to serve as a pretest dataset. This baseline data included important information on patients' current knowledge of self-care, adherence to follow-up, substance behaviors, hematologic parameters and health status related to their chronic condition prior to the educational sessions. Following the collection of baseline data, education sessions were provided to the enrolled participants on a monthly basis for four months. The sessions were conducted in a face-to-face approach to allow for personal interaction and the ability to enhance clarity. The sessions were limited to duration of 30 to 45 minutes based on the individual participant's health condition and learning styles. The thematic areas covered in the sessions were based on validated educational guidelines to ensure that all important self-management topics were addressed. Example topics included medication management, healthy lifestyle behaviors such as diet and exercise, monitoring symptoms and knowing when to contact a healthcare provider, and stress management techniques. Nurses leading the sessions were able to tailor content and examples to the specific chronic conditions of the enrolled participants.

The education session was developed based on heart failure management guidelines produced by the American Heart Failure Society, the Joanna Briggs Institute's (JBI) evidence-based manual, and the Ethiopian Ministry of Health (Duffy 2005; FMOH 2016; Lindenfeld 2010). All enrolled patients participated in a series of educational sessions led by experienced nurse educators. The program's content was reviewed by experts in cardiology, nutrition, and public health. Face-to-face education methods were utilized, and participants were provided with an educational leaflet containing information on RHD, heart failure, self-reported symptoms, and self-care behaviors.

After the fourth and final educational session was completed, follow-up data was collected from the same subjects using the same data collection tool as the baseline. This follow-up data served as a post-test dataset to measure any changes following the intervention and allowed researchers to analyze the effectiveness of the multi-component, nurse-led chronic disease self-management education program in empowering those with chronic conditions. The contents of the self-management program are presented in Table 7.1.

Table 7.1: Components and contents of chronic disease self-management education program at JMC, southwest Ethiopia

| Theme | Contents | Strategy of intervention | Responsibility | Adherence assessment tool |
|---|---|---|---|---|
| Understanding rheumatic heart disease and self-management of heart failure | 1.Introduction<br>2.Knowledge about RHD and heart failure<br>Definition, etiology, symptoms, complications, diagnosis, and treatment<br>3.Updating the patient's current disease status<br>4. Self-management of heart failure in patients with RHD | Leaflets with take home message (in local languages ) counseling and face to face discussion on disease risk factors, symptoms management, prophylaxis, nutrition and daily living | Trained nurse educators, supervisor and principal investigators | Number of participants who received the leaflets |
| Symptoms | 1. Monitor the symptoms of patients on a monthly basis and during their unscheduled follow-up visits.<br>Assess factors that worsen and alleviate the symptoms.<br>Verify the use of self-symptom checklists<br>Evaluate and implement strategies for managing and retraining<br>2.Education<br>Symptoms of heart failure, measure<br>Signs of heart failure requiring immediate attention, assessment<br>- Question and answer | | | Frequency of symptoms |
| Prophylaxis and medication | 1.Importance of Prophylaxis in preventing recurrence of Acute rheumatic fever and disease severity<br>2.Schedule regular follow-up visits, Injection site care, common side effect of benzathine penicillin<br>3. Providing information about the medication's details and purpose.<br>4. Assessing the challenges and potential adverse reactions associated with the medication/prophylaxis.<br>5. Establish a routine follow up for consistent medication and prophylaxis usage through the utilization of a self-care calendar<br>6.Question and answer | | | Medication adherence questionnaire |
| Nutrition and dietary management | 1. Dietary considerations for individuals with heart failure.<br>2.Restrictions on dietary intake of salt, fluid<br>3.Importance of balanced diet and meal plan<br>4. Important dietary factors to consider for individuals taking warfarin medication.<br>5. Develop a routine of regularly monitoring weight as frequently as possible.<br>-Question and answer | | | Food frequency questionnaire |
| Routine, daily living` | 1.Relaxation, stress management,<br>2.Avoid alcohol intake , khat chewing ,smoking<br>3. Incorporate regular physical activity routine by utilizing a self-care calendar.<br>-Question and answer | | | Self-report questionnaire |

**Tools, Parametric Measurements and Tests**

In the evaluation of post-education changes, complete blood counts (CBC) of individual participants were analyzed using a five-differential Unicel DxH 800 Coulter cellular analysis system (Beckman Coulter, Ireland). A trained laboratory technician collected a 4 mL venous blood sample from patients using the syringe technique. Additionally, a peripheral blood morphology examination was conducted to validate the flags generated by the automated hematology analyzer, assess its performance, and examine RBC morphology. The air-dried smear was stained with Wright stain and carefully observed with a 100X oil immersion objective by laboratory technologists. The results of each participant were meticulously documented on a form specifically designed for laboratory result registration.

To complement the hematologic parameters, a structured questionnaire was used by interviewers to assess socio-demographic variables and behavioral factors of the patients. Translated versions of the Hospital Anxiety and Depression Scale (HADS) questionnaire in local languages (Amharic and Affan Oromo) were used to measure anxiety and depressive symptoms in RHD patients. The HADS questionnaire consisted of fourteen items divided into two subscales for depression and anxiety. Scores on the HADS scale ranged from 0 to 3, with 0 indicating the lowest value and 3 representing the highest severity of anxiety and depression. The final score was calculated by adding the subscale values, resulting in total scores ranging from 0 to 21. This score range allowed for classification into three levels: normal (0-7), borderline (8-10), and abnormal. (11-21) (Conduta and Hipertensiva 2011).

Measurements of weight and height were taken using a combined height and weight scale (manufactured in India, production date: March 17, 2017). Weight measurements were recorded to the nearest 0.1 kg with participants not wearing shoes or heavy clothing. Height measurements were taken to the nearest 0.1 cm with participants standing upright, aligning the heel, buttocks, and upper back along the same vertical plane, arms at the sides, and gaze directed straight ahead.

Blood pressure was assessed on the left arm in mmHg using a sphygmomanometer (Yton sphygmomanometer, Italy, model 10220060). Participants were seated with back support, legs uncrossed, arm supported, and cubital fossa at heart level after a 5-minute resting period with arms at the sides and gaze forward.

**7.2.4 Ethical approval and consent for participation**

The study was conducted according to the Helsinki Declaration. Ethical approval of the research protocol was obtained from Jimma University Institute of Health with reference number JUIH/IRB/277/23. Written informed consent was obtained from each participant before enrollment.

Furthermore, this particular study has been registered on ClinicalTrials.gov and is assigned the identifier number ClinicalTrials.gov ID: NCT06400628.

**Operational Definitions**

**Adherence to medication:** During the four-month intervention period, the participants were expected to take their medications as prescribed by their physicians. Those who consistently took 80% or more of the prescribed medications were classified as good adherents, whereas individuals who took less than 80% of the medications were deemed to have poor adherence. Participants who failed to attend all educational sessions were categorized as non-adherent to the guidelines. Meanwhile, individuals who discontinued their involvement in the study were identified as lost to follow-up.

**Heart failure requiring immediate attention** refers to a critical medical condition where the heart is unable to pump blood effectively, leading to severe symptoms such as shortness of breath, extreme fatigue, and fluid buildup in the lungs or other parts of the body.

**Self-care calendar** a personalized schedule or plan that includes specific daily activities, such as medication reminders, dietary guidelines, exercise routines tailored to the individual needs of cardiac patients.

**Self-symptom checklists** refer to picture based check lists indicators that individuals with cardiac conditions can use to monitor their health status on a regular basis.

**Data analysis**

The data analysis was conducted using SPSS software version 25.0. Descriptive statistics were employed to present means with standard deviation (SD) for continuous variables and percentages for categorical variables. A two-tailed Student t-test was utilized to compare the continuous datasets of pretests and post-tests at a 95% confidence interval and a 5% margin of error. A statistically significant result was defined as a p-value less than 0.05 for all statistical analyses, which were all two-tailed tests. The findings were then reported in percentages through narrative texts, tables, and figures.

## 7.3 Results

**Socio-demographic characteristics of the participants**

The study included a total of 166 participants with mean ages of 32.64±13.53 years, of which 89 (53.6%) were female and 77 (46.4%) were male. Residentially, 101 (60.8%) of the participants were from rural settings, while 65 (39.2%) were urban dwellers, and 63 (38%) of the participants could not read or write. Regarding the extent of heart failure, 111 (66.9%) was classified under New York Heart Association (NYHA) classification II. (Table 7.2)

Table 7.2: Socio-demographic characteristics of patients with RHD at JMC Southwest Ethiopia 2023

| Variables | Category | Frequency | Percentage |
|---|---|---|---|
| Place of residence | Urban | 65 | 39.2 |
| | Rural | 101 | 60.8 |
| Sex | Male | 77 | 46.4 |
| | Female | 89 | 53.6 |
| Age (years ) | 15-24 | 58 | 34.9 |
| | 25-34 | 37 | 22.3 |
| | 35-44 | 35 | 21.1 |
| | 45-54 | 24 | 14.5 |
| | 55-64 | 8 | 4.8 |
| | ≥ 65 | 4 | 2.4 |
| Marital status | Single | 76 | 45.8 |
| | Married | 62 | 37.3 |
| | Divorced | 26 | 15.7 |
| | Separated | 2 | 1.2 |
| Educational status | Cannot read and write | 63 | 38.0 |
| | Primary school | 59 | 35.5 |
| | Secondary school | 34 | 20.5 |
| | Above secondary | 10 | 6 |
| Occupation | Government employ | 10 | 6 |
| | Merchant | 35 | 21.1 |
| | Farmer | 25 | 15.1 |
| | Self-employ | 12 | 7.2 |
| | Students | 20 | 12 |
| | Unemployed | 64 | 38.6 |
| New York Heart Association (NYHA) | NYHA class II | 111 | 66.9 |
| | NYHA class III | 55 | 33.1 |
| Hospitalization | None | 87 | 52.4 |
| | Once in the last year | 36 | 21.7 |
| | >1 in the last year | 43 | 25.9 |
| Duration of illness | ≤ 5 years | 121 | 72.8 |
| | >5 years | 45 | 27.2 |

**Components and effect indicators of chronic disease self-management education**

Table 7.3 summarizes the effect of an educational intervention on patients' clinical measurements before and after the intervention. Accordingly, the mean systolic blood pressure of the participants decreased from 131.31 mmHg (SD±15.68) at pre-education to 113.77 mmHg (SD±20.98) at post-education (t -12.251, $p<0.001$).The diastolic blood pressure decreased from 94.87 mmHg (SD±19.41) pre-education to 79.28 mmHg (SD±9.33) post-education (t-12.306, $p<0.001$).The mean Hemoglobin level increased from 11.97 g/dl (SD±1.99) before the intervention to 13.84 g/dl (SD±1.37) after the intervention (t -11.96, $p < 0.001$). Whereas, white blood cell count and platelet distribution width remain unchanged.

Table 7.3: Effect indicators and measurement values of patients with RHD chronic disease self-management education

| Parameters | Mean, SD | | t- test | p -value |
|---|---|---|---|---|
| | Before education | After education | | |
| Body Weight (Kg) | 58.01±11.25 | 57.06±11.39 | 1.445 | 0.148 |
| Systolic blood pressure (mmHg) | 131.31 ±15.68 | 113.77±20.98 | 12.25 | <0.001 |
| Diastolic blood pressure (mmHg) | 94.87±19.41 | 79.28±9.33 | 12.30 | <0.001 |
| Pulse pressure (mmHg) | 45.46 ±9.23 | 43.25±10.24 | 4.74 | <0.001 |
| Pulse rate (Beat /minute) | 107.97±24.74 | 91.57±16.80 | 8.57 | <0.001 |
| Hemoglobin Conce. (g/dl) | 11.97±1.99 | 13.84±1.37 | 11.96 | <0.001 |
| Hematocrit level (%) | 37.05±5.19 | 42.50±4.20 | 11.49 | <0.001 |
| RBC counts millions/$mm^3$ | 4.23±0.57 | 4.75±0.59 | 9.22 | <0.001 |
| WBC counts /µl | 7.23±3.52 | 7.18±2.16 | 0.19 | 0.846 |
| Platelets counts/µl | 243.95± 87.88 | 262.23± 65.20 | 3.07 | 0.02 |
| RBC distribution width (RDW-SD) | 40.66±8.45 | 42.51±7.76 | 4.43 | <0.001 |
| Mean corpuscular volume/fL | 79.97±5.10 | 85.64±6.69 | 10.109 | <0.001 |
| Mean corpuscular hemoglobin/pg | 26.54±2.77 | 28. 29±2.17 | 7.967 | <0.001 |
| Platelet distribution width/percentage | 12.46±3.55 | 12.38±2.28 | 0.317 | 0.751 |
| Mean platelet volume/fL | 9.94±1.36 | 10.36± 1.23 | 4.86 | <0.001 |

**Effect of chronic disease self-management education intervention on depression and anxiety**

Describes the mean score for the HADS depression subscale, which decreased from 11.93 (SD±3.43) at the pre-test to 9.48 (SD±3.67) ($t = 8.37$, $p < 0.001$) at the post-test. Regarding the HADS anxiety subscale, the mean score before the education program was 8.59 (SD±2.91) and decreased to the mean score of 7.30 (SD±1.97) ($t = 6.44$, $p < 0.001$) after education as presented figure 7.4.

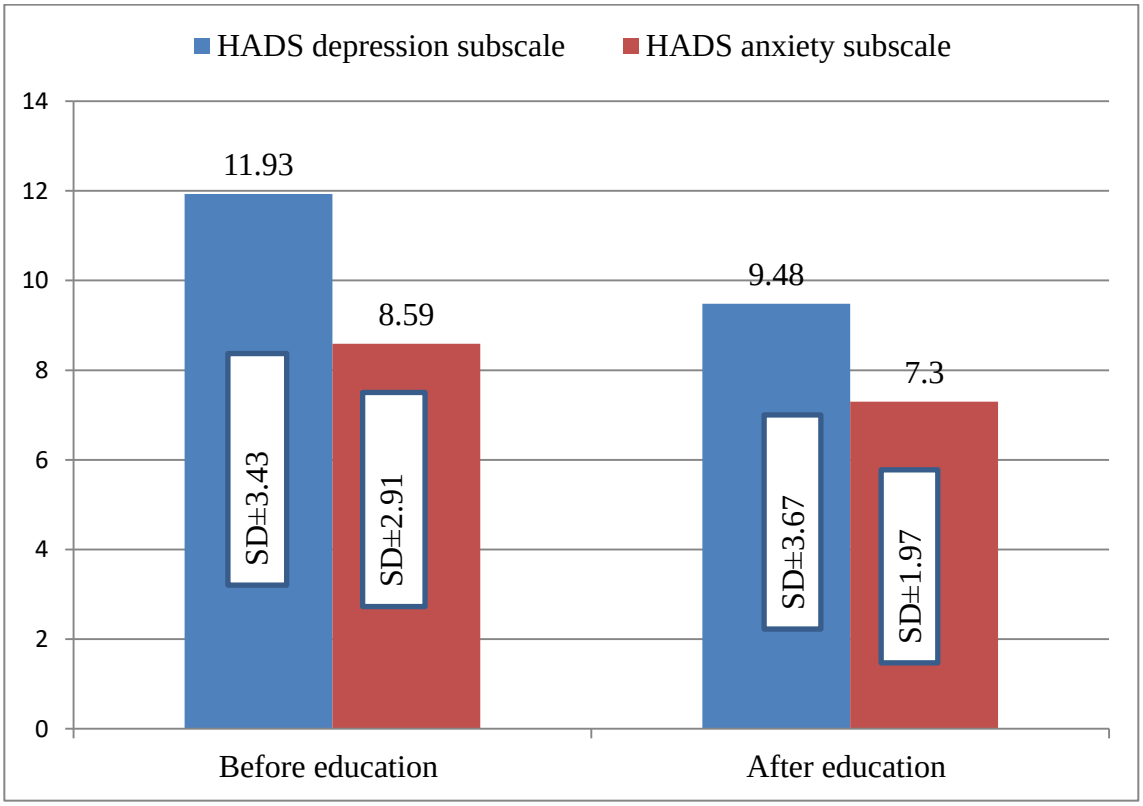


**Figure7.3:** Hospital Anxiety and Depression subscales among patients with RHD.

## 7.4 Discussion

This study assessed the impact of an educational intervention program designed to assist healthcare providers in promoting chronic disease self-management education for patients with rheumatic heart disease, with the ultimate goal of enhancing patient quality of life. During the study, a nurse-led multicomponent face-to-face chronic disease self-management education (CDSME) program was delivered over a period of four consecutive months. The effectiveness of the intervention was measured through the analysis of clinical and laboratory indicators specifically complete blood counts. The educational program was structured around five key themes: comprehension of rheumatic heart disease and heart failure self-management, prophylaxis and medication management, nutritional considerations, and guidance on daily routines and activities.

Baseline data was taken prior to the initiation of the intervention, and patient education was conducted at 30, 60, 90, and 120 days. Accordingly, a significant improvement was observed in patients' clinical outcomes as well as their levels of depression and anxiety when comparing pre-education and post-education phases.

In the current study, both systolic blood pressure and diastolic blood pressure was improved after the intervention. This study is similar with a study conducted among Pristina and Korean outpatients with

heart failure, where there was a significant change in participants blood pressure after education session (Moon et al. 2018; Podvorica et al. 2021). The reason behind the decrease in blood pressure among patients may be attributed to factors such as receiving education on reducing salt intake, improving adherence to medication. The other possible reason for the decrease in blood pressure in our study could be due to the abstinence of the participants from khat, where the majority of the participants used to take this substance, and cathinone appears to be the main ingredient of khat responsible for elevated blood pressure by increasing sympathetic tone, increasing heart rate, increasing myocardial contractility, and causing prolonged vasoconstriction (Getahun et al. 2010).

Despite the frequent recommendation for heart failure patients to monitor their weight regularly in order to identify deterioration and prevent hospitalization, many individuals still struggle to adhere to this practice due to a lack of knowledge about weight monitoring and the necessary skills to recognize sudden weight gain. This study showed a slight decrease in weight gain from (58.01±11.25) to (57.06±11.39), but this change was not found to be statistically significant. The results of this study are consistent with the findings of a study conducted by Wang et al., which showed that self-management education enhances weight monitoring and contributes to positive changes in patients' weight (Wang et al. 2014).

In this current investigation, a decrease in the average pulse rate (PR) was observed among the study participants. The PR improved from (107.97±24.74) to (91.57±16.80). This finding is consistent with a previous study conducted by Siavoshi et al. and Aizawa et al, which also demonstrated a reduction in heart rate among coronary artery patients through the implementation of a cardiac rehabilitation program and lifestyle educational interventions (Aizawa et al. 2009; Journal 2012) . The improvement in PR in our study could be due to sufficient follow-up time (four months) and the contents of education, which aimed to improve drug compliance, relaxation, and stress management. On the contrary, the results of this study contradict with a study conducted by Jafari et al. (Jafari et al. 2020) which found no significant influence of educational interventions on patients' heart rate. The discrepancy between the two studies could potentially be attributed to factors such as the limited sample size or the insufficient one-month follow-up period, which may not have allowed enough time for a reduction in PR.

In this particular study, we identified that the majority of the participants had abnormal values for different hematological parameters at baseline measurements, and different blood parameters were measured, including hemoglobin, hematocrit level, red blood cell distribution width, mean corpuscular volume, and other parameters, in order to assess the effectiveness of CDSME. The findings revealed a

significant improvement in hemoglobin count, with levels increasing from (11.97±1.99) before education to (13.84±1.37) after education. This study aligns with a similar investigation conducted at Alexandria Main University Hospital, where self-management strategies resulted in an improvement in the average hemoglobin level where there is a noticeable change before and after the program (from 10.33 ± 0.50 to 12.11 ± 0.85, respectively) (Mowla et al. 2018).Similar to this, the mean coursculpular volume (MCV) in this study improved from (79.97±5.10) to (85.64±6.69). The result of this study is consistent with a study conducted by Creary et al., which states increased MCV after education (Creary et al. 2022). The change in hemoglobin and MPV could be because of the educational component of the intervention, which focused on nutrition and provided guidance on the types of foods that can help enhance the levels of Hg and MPV.

Our study examined the effect of education on mean platelet volume (MPV) and platelet count, which changed pre-education from 9.94±1.36 to 10.36±1.23 at post-education. Similarly, platelet count improved from 243.95± 87.88 to 262.23± 65.20. These improvements could be attributed to factors such as good drug adherence and advice provided to patients regarding important dietary considerations while taking medication like warfarin (for patients on anticoagulants), which might optimize and stabilize platelet function.

Numerous studies have extensively documented the high prevalence of depression and anxiety among individuals diagnosed with rheumatic heart disease (Dixit et al. 2021; Sheikh et al. 2019; Tadele et al. 2021). According to a study conducted by Vasconcelos et al., it was found that among individuals diagnosed with RHD, approximately 34% of patients' experienced major depression, while 54% of RHD patients were found to be suffering from generalized anxiety disorder (Vasconcelos et al. 2022). The result of this study has also approved that there is improvement of HADS depression subscale from (11.93±3.43) pre intervention to (9.48±3.67) post intervention p value <0.001and HADS anxiety subscale improved from (8.59±2.91) to (7.30±1.97) p value of< 0.001. This finding is similar to the study by Demircelik et al., which proves nurses lead education interventions effective in improving the HADS anxiety subscale from( 6.1 ± 0.7 to 4.2 ± 0.58) while the HADS depression subscale improved from (5.4 ± 0.6 to 3.5 ± 0.53) (Demircelik et al. 2016). The result of this study contradicts the study by Lemay et al., which states that no significant change is observed in the HADS score after education (Lemay et al. 2019). The variations observed could be due to our study's utilization of diverse educational approaches, such as face to face education , question-and-answer, and the provision of educational leaflets, which might increase patients understanding of their perception of the disease and give them confidence about how to live with RHD. Additionally, the implementation

of a comprehensive educational program encompassing various aspects of participants' lifestyles, including family support and ongoing patient follow-up, might have contributed to the discrepancies.

**Limitation of the study**

As there is no control group in a quasi-experimental study, there is a risk of potential bias. A control group is not aligned to determine the effectiveness of the study between groups. The other limitation of this study is that, due to the four-month duration of the study, we could not measure the compliance of benzathine penicillin since it has to be measured for one year.

## 7.5 Conclusion and recommendation

The results of the educational intervention indicate significant improvements across various physiological and psychological parameters. Systolic and diastolic blood pressure, pulse pressure, and pulse rate showed statistically significant decreases, suggesting a positive impact on cardiovascular health. Moreover, the increase in hemoglobin count, hematocrit level, red blood cell count, mean corpuscular volume, and mean corpuscular hemoglobin further supports the beneficial effects of the intervention on participants' blood profiles. Notably, improvements in platelet count, red blood cell distribution width, and mean platelet volume also signify positive changes. On the psychological front, the reduction in scores on the HADS depression and anxiety subscales post-intervention implies an enhancement in mental well-being among participants. In light of this, healthcare service providers should prioritize sustained monitoring, lifestyle adjustments, and customized individual support or counseling sessions to elevate the quality of life for patients with RHD. It is imperative to conduct further research to examine how these interventions impact program enhancement parameters.

# Chapter Eight: General Discussion, Future Research Perspectives, and Conclusion

## 8.1 Introduction

According to the report of the World Health Organization, an estimated 40.5 million people worldwide are currently affected by RHD (WHO 2019). Similarly, RHD also causes a loss of 11.5 million years of life to disability, with 320,000 deaths recorded each year, mostly occurring in low-income countries (Belay and Aliyu 2021; Corsenac et al. 2016). Ethiopia is a country which is significantly affected by RHD (Mebrahtom et al. 2023). Despite a few studies that have been conducted in the country, the true burden of RHD in Ethiopia remains underestimated. The lack of accurate data on the prevalence and impact of RHD continues to be a challenging public health issue of major concern in the country.

Understanding the risk factors for RHD is a very important and crucial factor in preventing RHD-related morbidities, complications, and mortalities (Kazahura et al. 2021; Palafox et al. 2017). A number of risk factors can render individuals more susceptible to acquiring RHD. However, socioeconomic and environmental factors like poor housing, under nutrition, overcrowding, and poverty also heavily influence the incidence and severity of RHD (Karthikeyan and Mayosi 2009; Marijon et al. 2012; Seckeler and Hoke 2011). Compounding these risks, widespread lack of awareness about RHD persists in affected populations. Different studies have reported that 34–87% of patients and their families had poor knowledge about RHD (Isezuo et al. 2023; Naz et al. 2023; Sayed et al. 2021). This lack of awareness is particularly problematic, as it prevents timely treatment of streptococcal infections and access to preventative strategies. Addressing the risk factors is crucial for reducing the burden of this preventable heart disease. Although patients with RHD require prompt medical attention and ongoing follow-up, a considerable number of patients in developing countries tend to present with disabling complications, such as heart failure, pulmonary hypertension, and arrhythmias, due to the lack of echocardiographic screening (Desta et al. 2023; Ong 2020; Zühlke et al. 2015). Timely echocardiographic screening is important to protect the overall outcomes of individuals with RHD and manage their condition based on its severity.

Understanding the extent of valvular damage is essential for a variety of reasons. It enables tailored management strategies based on disease severity, allowing for more appropriate interventions and monitoring, and provides valuable prognostic information with a better long-term outlook. In resource-limited settings, the severity classification helps prioritize the allocation of care and resources to those with the most urgent clinical needs. It also guides the implementation of preventive measures, such as early treatment of streptococcal infections, to mitigate disease

progression. Furthermore, the classification facilitates more accurate monitoring of disease trends and the evaluation of the effectiveness of interventions over time, informing decision-making by healthcare providers and policymakers. Overall, the classification of RHD severity is crucial for optimizing patient management, improving outcomes, and informing public health strategies to address this important cardiovascular condition.

Chronic disease self-management education empowers patients with the knowledge, skills, and abilities to self-care. It caters to the unique needs, goals, and life experiences of individuals with chronic illnesses, guided by evidence-based standards (Vainauskienė and Vaitkienė 2021). Studies have demonstrated that the implementation of a CDSME program has resulted in enhanced self-care behaviors, improved decision-making skills, increased problem-solving abilities, and greater engagement and collaboration with healthcare professionals, which has improved clinical outcomes and an enhanced quality of life for patients with cardiac disease (Dessie et al. 2021; Vainauskienė and Vaitkienė 2021; Zhao et al. 2020). Therefore, studying the burden, severity, risk factors of a disease, and then developing targeted interventions organized around coherent themes, is crucial for managing the disease and reducing complications, mortality, and disability in future generations. This comprehensive approach is essential for achieving the Sustainable Development Goal 3, which aims for a 25% reduction in premature mortality from non-communicable diseases by 2025. Additionally, it is particularly relevant for the secondary prevention of RHD, where identifying and addressing the underlying factors can significantly improve long-term outcomes and reduce the burden on individuals and healthcare systems.

## 8.2 Summary of the main findings

The main findings of this research arise from four consecutive studies: systematic review and meta-analysis, cross-sectional and quasi experimental study designs (chapter 4-7). The trend and the burden of RHD, risk factors for RHD, severity of the disease, and chronic disease self-management education intervention were applied in the study area (Jimma Medical Center) to investigate the effectiveness of chronic disease self-management education interventions for improving clinical outcomes and reducing depression and anxiety among patients with RHD.

In chapter 4, the pooled prevalence and the trend of RHD in Ethiopia was measured using systemic review and meta-analysis (published on BMC Tropical Diseases, Travel Medicine and Vaccines 13 October 2023 Trop Dis Travel Med Vaccines 9, 16 (2023). https://doi.org/10.1186/s40794-023-00192-y)

Chapter 5, Burden and its determinants of rheumatic heart disease were identified using a cross-sectional study design (Submitted).

Chapter 6, Echocardiographic Parameters and Complication Profiles among Adult Patients with Rheumatic Heart Disease at Jimma Medical Center (published on Dove press Vascular health and risk management 2024 Apr 4. doi:10.2147/VHRM.S451957 )

Chapter 7, Effectiveness of chronic disease self-management education in improving clinical outcomes, depression, and anxiety among patients with rheumatic heart disease: a quasi-experimental study (published on Current problems in cardiology, vol. 49, 11 102796. 17 Aug. 2024, and doi:10.1016/j.cpcardiol.2024.102796). In addition, this intervention is registered on clinicaltrial.gov with the identifier number NCT06400628.

Our studies found that the prevalence of RHD in Ethiopia is high. In terms of publication trends, there were only two studies published between 1990 and 2000. However, after 2000, the number of publications increased, reflecting a growing interest in the disease.

Notably, between 2000 and 2010, the reported prevalence of RHD rose significantly from 0.64% to 32.78%. Additionally, the number of studies on RHD has continued to rise, with a noticeable increase in publications after 2020. On the other hand, RHD was investigated as one of the most frequent morbidities among patients who visit cardiac clinics. The major determinants associated with RHD were female sex, using wood (biomass fuel) for cooking, history of malnutrition with follow-up at a health facility, dental caries, and living in crowded households. Our study also shows that the majority of the patients were found to have multiple valve lesions and have rheumatic heart disease-related complications. Our study also provided an important insight into the significance of chronic disease self-management education intervention as crucial tool for patients living with RHD in the existing health service. This is particularly relevant given that the current health service system and policies in Ethiopia do not adequately recognize RHD as a major public health concern. In fact, Ethiopia currently lacks any specific policies addressing the management and treatment of RHD.

This highlights the need for the health care system and policymakers to place greater emphasis on supporting self-management education programs for RHD patients. Such interventions can play a vital role in improving clinical outcomes for individuals living with this chronic cardiovascular condition. The study underscores the importance of developing targeted policies and strengthening the health system's capacity to better address the growing burden of RHD in the country.

## 8.3 Implication of the findings

The findings from this PhD research indicate that the study on RHD did not cover all geographical areas, as evidenced by the limited number of studies and publications available on the topic. This underscores the need for strengthening RHD surveillance and research in the country. The high and varying prevalence of RHD across different population groups in Ethiopia calls for the development of targeted public health policies and interventions to address this significant cardiovascular disease burden. Improving access to early diagnosis, treatment, and prevention strategies should be prioritized.

This study has shown that the risk factors for RHD are multifactorial, requiring a multi-sectorial approach that targets broader determinants. This includes raising awareness, introducing cleaner cooking technologies, improving access to dental care, and implementing comprehensive RHD action plans across the health system and other relevant sectors. Addressing these underlying social, behavioral, and environmental factors, in addition to strengthening clinical management, will be crucial in reducing the significant cardiovascular health burden of RHD in Ethiopia.

It is important to emphasize the significance of regular echocardiographic screening, particularly for females and younger adults. This can help in early detection and treatment before complications arise, ultimately improving outcomes for those affected by this disease.

The key implication of this interventional study on RHD in Ethiopia is that it addresses the growing burden of RHD in the country by demonstrating the effectiveness of a nurse-led, multi-component CDSME program in improving clinical outcomes for RHD patients. .

This low-cost, scalable intervention highlights the feasibility of implementing effective management strategies for RHD in resource-limited settings like Ethiopia, and the positive results provide a strong foundation for further research and the potential replication and scale-up of the CDSME approach in other parts of the country and potentially in other regions facing a high burden of RHD.

## 8.4 Methodological considerations: strength and limitations with future research direction

The strengths and limitations of each study are presented in their respective chapters. This study was conducted at a large teaching and referral hospital that serves a wide geographic area. The hospital (JMC) was intentionally selected because it receives a high volume of patient referrals from various surrounding regions, allowing the study to capture a diverse and representative population. The study revealed a high prevalence of RHD in the study area and identified risk factors using a cross-sectional study. It is recommended that a case-control study design be used for future research.

We recommend that future researchers use more robust research designs to fill the gaps identified in the current study. Given the relatively short duration of our 4-month intervention, we were limited in our ability to assess a comprehensive range of clinical parameters. We suggest that future studies allocate a longer intervention period to enable a more thorough evaluation of additional relevant clinical outcomes, as this would provide a stronger evidence base to draw conclusions about the impacts of the intervention.

## 8.5 Conclusion

- ✓ The prevalence of RHD is high in Ethiopia, with a pooled prevalence of 3.19%, highest in hospital visitors (5.42%), followed by community studies (3.83%) and schoolchildren (0.73%).
- ✓ It has been identified RHD as a major cause of cardiac disease, including female sex, biomass use, malnutrition, dental caries, and overcrowding as determinant factors
- ✓ It has been identified RHD as a major cause of cardiac disease, including female sex, biomass use, malnutrition, dental caries, and overcrowding as determinant factors.
- ✓ RHD predominantly affects individuals in their active and productive years, particularly females.
- ✓ A majority of the patients included in the study have multiple valve lesions. Mitral valve was the commonest valve affected.
- ✓ Approximately two-thirds of patients experienced RHD related complications, with pulmonary hypertension and atrial fibrillation being the most common.
- ✓ CDSME had a positive impact on patients' clinical outcomes, including blood pressure, pulse rate, red blood cell indices, and platelet counts.
- ✓ CDSME intervention was effective in reducing the levels of depression and anxiety among study participants.

## 8.6 Recommendations

- ✓ The high prevalence of rheumatic heart disease across Ethiopia regions emphasizes the urgent need to strengthen RHD surveillance, research, and access to early diagnosis, treatment, and prevention strategies in the country.
- ✓ The risk factors for RHD in Ethiopia are complex, necessitating a collaborative, multi-sector response to tackle this public health issue. Key strategy should include raising community awareness, introducing cleaner cooking technologies, improving access to dental care, and implementing comprehensive RHD action plans across the health system and other relevant sectors.

- ✓ Efforts should be made to educate patients and the general public about the key risk factors for RHD. Additionally, the importance of early detection and prompt treatment of RHD should be widely communicated.
- ✓ Regular echocardiographic examinations should be conducted for individuals diagnosed with RHD, with a particular emphasis on females and younger adults. This will help to facilitate early detection and treatment of the disease before complications arise.
- ✓ Because of the burden of RHD increases in Ethiopia, there is a growing need for low-cost interventions to mitigate its impact.
- ✓ CDSME had a positive impact on patients clinical outcomes, including blood pressure, pulse rate, red blood cell indices, and platelet counts. In addition to this, CDSME was effective in reducing the level of depression and anxiety among the participants.
- ✓ Addressing current policy, guideline, and program deficiencies is imperative to empower RHD patients, prevent complications, and reduce the unacceptably high morbidity and mortality associated with this treatable condition.

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10. ANNEXES

## 10.1 Curriculum Vitae of the candidate

CURRICULUM VITAE (CV) FOR

**Hiwot Berhanu Meshesha**

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**1)** Full Name: **Hiwot** **Meshesha** **Berhanu**

First Middle Last

**2)** Date of birth: **June 21 , 1988**

**3)** Nationality: **Ethiopian**

**4)** Education/degrees received

- **Master of medical physiology (MSC)** – from Jimma University
- **Bachelor of Science (BSc)** in Public health officer – from University of Gonder

Current position: **Assistant Professor at** Jimma University (JU)

**5)** Language proficiency: **English, Amharic, & Affan-oromo**

**6) Contact information**

Email: hiwed2010@gmail.com

Cell phone: +2519 17324642

P.O. Box 378 | Jimma University

**7)** Total work experience**: 14 years**

**EMPLOYMENT RECORDS:**

| Positions held | Institution | Year |
|---|---|---|
| PhD fellow | Jimma University | 2021 to present |
| Assistant Professor & Researcher | Jimma University (JU) | 2021 to Present |
| Lecturer of Medical Physiology at Jimma University, Jimma-Ethiopia | Jimma University (JU) | 2016 – 2021 |
| Graduate Assistant of Medical Physiology at Jimma University, Jimma-Ethiopia | Jimma University (JU) | 2015 – 2016 |
| Private clinic coordinator at district level, Jimma-Ethiopia | Serbo/Jimma zone | 2014 – 2015 |
| Zonal RMNCH Project coordinator at FIDO(NGO), Jimma-Ethiopia | Jimma Zone | 2012 – 2014 |
| Staff in government health institution; North shewa Gimbichu health center with different roles( clerked patients at outpatient department ,participated in outreach | North showa | 2011 – 2012 |

| | | |
|---|---|---|
| services, managerial decisions and OTP coordinator, and other community based nutritional services like screening using anthropometric measurements & growth monitoring | | |

**8) GRANT WRITING & ADMINISTRATION**

I worked on two research grants: one international and one local grant

**Research Grant #1**

**Name of project:** A Developmental Project on Advocacy Efforts to Maximize concerted Commitment of Subnational Level Stakeholders on the Passage and Future Harmonization: a road safety advocacy developmental project following a call from the Global Road Safety Partner ship

**Specific project setting:** This project was funded by GRSP under the Award Number ETHXX-RD22-1391

**Project feature**: Advocacy aims to inform and influence change to policies, legislation, and structures by targeting decision-makers who have the power to make the requested change on drunk driving, speeding, helmets usage.

**My roles**: I participated in the research, grant writing, protocol development, and working on scoping review. Furthermore, I organized a 1 days' workshop in Jimma university (with Jimma university staffs and key informants) to develop the blue print of the intervention. The research project is ongoing and I am leading the project with other scholars from Jimma University.

**Research Grant #2**

**Name of project:** Driver Related Causes of Road Traffic Accidents, and Their Association with near-misses and actual driving accidents in Jimma Zone Drivers working in public transportation

**Specific project setting:** This project was funded by postgraduate and research coordinating office, Institute of health, Jimma University.

**Project feature:** Jimma Zone, the general objective of this study was to assess the prevalence of driver related causes of road traffic accidents in Jimma zone commercial drivers

**My roles:** I participated as principal investigator, leader of a grant project, responsible for designing the research, developing the grant proposal, and managing the project's execution. The project is completed

**1) Trainings received**

a. Comprehensive Systematic Reviews organized by Jimma University JBI Center of EBHC and University of Adelaide, May 31 – June 4, 2021 @ Jimma, Ethiopia

b. JBI Clinical fellowship (The Ethiopian center for evidence based health care provided by JBI at Jimma University, Jimma -Ethiopia), May 5-9,2018
c. Scientific writing skill organized by Jimma University Jointly with University of Oslo at Jimma University, Jimma –Ethiopia, Sept 12-16,2016 G.C
d. Integrated refreshment training on reproductive maternal, newborn and child health organized by JSI/L10K and Jimma zonal health departments, Jimma –Ethiopia, October5-20,2013
e. Mobile health survey technology organized by JSI/L10K, Jimma -Ethiopia February 6-9,2013
f. Newly developed volunteerism training approach by Jimma Zonal Health Department and Fayyaa Integrated Development Organization in collaboration with JSI/ L10K .September 11-13,2013
g. Providers initiated HIV counseling and testing organized by Gondar university in collaboration with CDC .Nov 7-11 2010

## 9) SCIENTIFIC PUBLICATIONS

| |
|---|
| **1. Berhanu H,** Tegene E, Gemechu TD, Sudhakar M, Mossie A. Rheumatic heart disease burden and determinants in cardiac patients: A follow up care concern in Ethiopia International Journal of Cardiology Cardiovascular Risk and Prevention ;2024 ; 24 (2) : :https://doi.org/10.1016/j.ijcrp.2024.200352 |
| **2.Berhanu H**, Gemechu TD, Sudhakar M, Tegene E, Mossie A. Effects of self-management education on clinical outcomes of adults with rheumatic heart disease: A quasi-experimental study. Curr Probl Cardiol. 2024; 49(11):102796 doi: 10.1016/j.cpcardiol.2024.102796. |
| **3. Berhanu H**, Mossie A, Morankar SN, Gemechu TD, Tegene E. Echocardiographic Parameters and Complication Profiles Among Adult Patients with Rheumatic Heart Disease at Jimma Medical Center. *Vasc Health Risk Manag*. 2024; 20:157-166. Published 2024 Apr 4. doi:10.2147/VHRM.S451957 |
| **4. Berhanu, H**., Mekonnen, Y., Workicho, A. *et al.* The prevalence of rheumatic heart disease in Ethiopia: a systematic review and meta-analysis. *Trop Dis Travel Med Vaccines* 9, 16 (2023). https://doi.org/10.1186/s40794-023-00192-y |
| **5.Berhanu H,** Feyissa GT, Geleta D, Sudhakar M. Diabetes mellitus self-management education at Jimma University Medical Center: evidence-based implementation project. JBI Evid Implement. 2022 Feb 18. doi: 10.1097/XEB.0000000000000312. Epub ahead of print. PMID: 35185132. |
| **6**.Wondie A, Taderegew MM, Girma B, Getawey A, Tsega D, Terefe TF, Mitiku S, **Berhanu H.** Obstructive sleep apnea risk and its associated factors among type 2 diabetes mellitus patients at Wolkite university specialized hospital, Wolkite, Southern Ethiopia, 2021. A comparative cross-sectional study. Diabetol Metab Syndr. 2022 Oct 27; 14(1):157. doi: 10.1186/s13098-022-00931-9. PMID: 36303199; PMCID: PMC9607780. |
| **7. Berhanu, H.** Darge T Pathophysiology of Rheumatoid Associated Lung Diseases. Biomed J Sci & Tech Res 30(1)-2020. BJSTR.. DOI: 10.26717/BJSTR.2020.30.004884 . |
| **8.** Abdissa, G., Geleta, D., **Berhanu, H**., & Edilu, B. (2020). Nursing Care Practices at Jimma University Medical Center: A Retrospective Cross - Sectional Study in Ethiopia. *International Journal of Biomedical Engineering, 6*, 7. DOI: 10.11648/j.ijbecs.20200601.12 |
| **9**. Jemere T, Mossie A, **Berhanu H,** Yeshaw Y. Poor sleep quality and its predictors among type 2 diabetes mellitus patients attending Jimma University Medical Center, Jimma, Ethiopia. BMC |

Res Notes. 2019;12(1):488. https://doi.org/10.1186/s13104-019-4531-6

**10.** Adem A, **Berhanu H**, Geleta D (2018). Breastfeeding practices among infants & young children less than two years of age in East-central Ethiopia: A community- based cross- sectional study. Accepted at OMICS Journal Pregnancy & Child health.doi 10.4172/2376-127X.1000374

**11. Berhanu H**, Mossie A, Tadesse S, Geleta D (2018). Prevalence and pattern of primary insomnia among adults in Jimma Town, Southwest Ethiopia: A community based cross-sectional study.http://www.academic journals. org/JPHE DOI: 10.5897/JPHExxxx

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**10) International Conference Presentations (related to PhD dissertation)**

- Oral presentation at the 5th Annual Conference of Santé Medical College held in Addis Ababa, Ethiopia, on November 12, 2022. The title of the presentation is "*Prevalence of Rheumatic Heart Disease in Ethiopia: A Systematic Review and Meta-Analysis."*
- Oral presentation at the 1st Annual Conference of the Ethiopian Neurologic Society (ENS) held in Addis Ababa, Ethiopia, from May 10-12, 2024. The title of the presentation is "Effectiveness of Chronic Disease Self-Management Education in Improving Clinical Outcomes, Depression, and Anxiety."
- Oral presentation on gLocal solution (online presentation) prepared by JBI at Adelaide in Australia in collaboration with Pushagari Center for Evidence held from June 5-7, 2024. The title of the presentation is "Effectiveness of Chronic Disease Self-Management Education in Improving Clinical Outcomes, Depression, and Anxiety."

**11) REFERENCES**


| | |
|---|---|
| Professor Andualem Mossie (current staff) | Jimma University Department of Physiology, Jimma-Ethiopia |
| | Mobile:+251(0)966764380 Email andualemm2000@gmail.com |
| Professor Zeleke Mekonen (current colleague) | Jimma University Department of Microbiology, Jimma-Ethiopia. Mobile:+251(0)917765427, Email: zelekemekonnen@gmail.com |

## 10.2 Conference participations and Certificates

Ethiopian Neuroscience Society (ENS)

የኢትዮጵያ ኒርቭ ሳይንስ ማህበር (ኢነሳማ)

CERTIFICATE OF ATTENDANCE

This certificate is awarded to:

HIWOT BERHANU MESHESHA

For participating as **Speaker** on the 1st Annual Conference of Ethiopian Neuroscience Society (ENS) with the theme **"Fostering Neuroscience for Societal Wellbeing"** on "Effectiveness of chronic disease self-management education in improving clinical outcomes, depression, and anxiety among patients with rheumatic heart disease: a quasi-experimental study" and Movement Disorders School (MDS) from 10th to 12th May, 2024 G.C at Elilly International Hotel, Addis Ababa, Ethiopia.

**Samson Sahile (PhD)**
President
Ethiopian Neuroscience Society (ENS)

**Amadi Ogonda Ihunwo (Professor)**
Society of Neuroscientists of Africa (SONA)
Representative, University of the Witwatersrand,
South Africa

JBI
Pushpagiri Centre for Evidence Based Practice (PCEBP)
A JBI Centre of Excellence
CERTIFICATE of RECOGNITION
awards this certificate to
Hiwot Berhanu Meshesha
For paper presentation at
gLocal Solution Room 2024, conducted on 07.06.2024
Topic: "Effectiveness of chronic disease self-management education in improving clinical outcomes, depression, and anxiety among patients with rheumatic heart disease: a quasi-experimental study"
Nisha Kurian
Director
JBI
Pushpagiri Centre for Evidence Based Practice (PCEBP)
A JBI Affiliated Group

# CERTIFICATE

## of Appreciation

Santé Medical College awards this certificate to

## Hiwot Berhanu

For presenting a research paper at the Sante Medical College's 5th Annual Research Conference on RTA, November 12, 2022.

Dr. Ahmedin Nurhussien
Dean

SANTE
MEDICAL COLLEGE

011-3727434
011-3727364
Sante Medical College

Dr. Daniel Fekade
Research and Publication Officer

JBI

# CERTIFICATE
## OF ATTENDANCE

This is to certify that

**Hiwot**
**Berhanu Meshesha**

attended

**Comprehensive Systematic Review Training Program**

**Module 1:** Introduction to Evidence-Based Healthcare and the Systematic Review of Evidence

**Jimma**
**Ethiopia**

**31 May 2021**

**Prof Zoe Jordan, PhD**
Executive Director
JBI, University of Adelaide
Adelaide, South Australia

## 10.3 Information sheet

**Title of Research Project**: Echocardiographic-Based Study on Rheumatic Heart Disease Burden, Pathophysiology, and the Effectiveness of Self-Management Education in Southwestern Ethiopia: A Multiple Study Design

**Institution**: Jimma University institute of health, department of biomedical sciences

**Name of sponsor**: Jimma University

Name of Principal Investigator: Mrs. Hiwot Berhanu

Phone Number of Principal Investigator: +125(0)917324642

### A. Purpose and background

I am----------from Jimma town. I'm here to collect data for the study on rheumatic heart disease receiving healthcare service in this hospital from 2023 to 2024. We would like to use your information and perform an echocardiography to examine your heart condition. Samples collected during care will be used for further study. The purpose of your participation in this

research is to help the researcher understand magnitude of rheumatic heart disease, risk factors for RHD, patterns of echocardiography, and the effect of chronic disease self- management education on clinical outcomes in patients with RHD in our area. You have been selected as a possible participant in this study because you were randomly chosen to be one of the participants.

**B. Procedures**

If you agree to participate in this research study, I would like to ask you some questions about your socioeconomic and demographic factors, behavioral factors, measurement of blood pressure, height, weight, echocardiography examination and carefully a 4ml of blood is taken from your arm under supervision of the prime investigator with your consent. You may feel a little pain as is normal with standard phlebotomy and the amount of blood drawn will not affect your health.

**C. Risks**

Participation is voluntary, and no negative consequences will be attached. Your answers will be written and later used for analysis. It may cause minimal discomfort but, will not cause you any physiological, financial and psychological harm. The research team will follow your condition if any problem happened.

**D. Confidentiality**

The records from this study will be kept as confidential as possible. No individual identities will be used in any reports or publications resulting from the study. All data that will enter analysis will be changed anonymous, coded, and stored separately from any names or other direct identification of the participants. Research information will be kept in locked files at all times. Only research personnel will have access to the files, and only those with an essential need to see names or other identifying information will have access to that particular file. After the study is completed at the end of 2025 all information will be avoided carefully.

**E. Benefits of participation**

There will be no direct benefit to you from participating in this research study. The anticipated benefit of your participation in this study is to inform the type of cardiac problem you have and informing the necessary measures you need to take to prevent complication related to cardiac disease. The study will also come-up with the precise investigating modalities related to RHD

that will indirectly benefit you and your community. However, the current medical care of you will be followed closely throughout your hospital stay.

F. **Voluntary participation**

Your decision whether or not to participate in this study is voluntary and will not affect your relationship with the JMC. If you choose to participate in this study, you can withdraw your consent and discontinue participation at any time without prejudice.

**G. Questions**

If you have any questions about the study, please ask me or contact Mrs. Hiwot Berhanu by calling 0917324642. You can also contact Jimma University IRB with any questions about the rights of research participants or research related concerns.

**H. STATEMENT OF CONSENT BY THE PATIENT**

I_____ have been told of the contents of this research form and I have adequate information about the research and understood it and I do agree to participate in this study.

Name of patients---------- sign ---------- Date----------

**INTERVIEWER'S STATEMENT**

I have explained the purpose and benefits of this study to the respondent to the best of my knowledge and conviction, s/he has understood and has given consent.

Interviewer: _____ signature: _____date: _____

## 10.4 English version questionnaire for data collection

Jimma University institute of health, department of biomedical sciences (Post Graduate Program)

Echocardiographic-Based Study on Rheumatic Heart Disease Burden, Pathophysiology, and the Effectiveness of Self-Management Education in Southwestern Ethiopia: A Multiple Study Design

1. Questionnaire Identification No_____
2. Name of Health facility _____

3. Date data collected (DD/MM/YY)_____

4. Time the data collection started (HH:MM) _____

5. Time the data collection ended (HH:MM)_____

6. Name of data collector_____

7. Signature of data collector_____

8. Name and signature of Laboratory expert_____

**Part one: Socio demographic data**

| No | Questions/Variables | Responses | Response code |
|---|---|---|---|
| 101 | Place of residence? | 1. Urban 2. Rural | |
| 102 | Age (in years) | _____years | |
| 103 | Sex | 1.Male<br>2.Female | |
| 104 | Marital status? | 1. Single<br>2. Married<br>3. Separated<br>4. Widowed<br>5. Cohabited<br>6. Divorced | |
| 105 | Religion | 1. Orthodox<br>2. Protestant<br>3. Muslim<br>4. Catholic<br>5. Others , specify | |
| 106 | Education level | 1. Cannot read and write<br>2. Can read and write with no formal school attendance<br>3. Primary school<br>4. Secondary school<br>5. Above secondary | |
| 107 | Occupation | 1. Governmental employee<br>2. Merchant<br>3. Farmer<br>4. Housewife | |

| | | | |
|---|---|---|---|
| | | 5. Other, specify | |
| 108 | Average monthly income (in Ethiopian Birr) | _____ | |
| 109 | What the main source of energy household used to cook foods for the family? | 1.Electric power<br>2. Animal waste<br>3. Wood<br>4. Other, specify | |
| 110 | Do you have Previous history of Upper respiratory tract infection | 1.yes<br>2.No | |
| 111 | If you your answer is yes for the above question have you take any medical (treatment) for it and what type of treatment you got | | |
| 112 | Is there any chronic illness in your family? | 1.yes<br>2.No | |
| 113 | If the answer is yes for question 112 what is the name of the identified disease? | | |
| 114 | Numbers of house hold living together? | | |
| 115 | What is the main source of water you are using for cooking? | 1. Spring water<br>2. River water<br>3. Tap water<br>4. Packed water<br>5. Other, specify_____ | |
| 116 | How many times do you wash your hand within a day? | | |
| 118 | Do you visit heath facilities when you got sick? | 1 .Yes<br>2. No | |
| 119 | If the answer is "yes" for question 118 how frequent you visit health facilities | 1. Rarely<br>2. Sometimes<br>3. Occasionally<br>4. Always | |

| | | | |
|---|---|---|---|
| 120 | The distance of health facilities from your house in kilometers? | | |
| 121 | Do you have history of dental caries? | 1. Yes<br>2. No | |
| 122 | If the answer is “yes” for question 121 what type of treatment you use? | _____ | |
| 123 | How many times per week do you brush your teeth? | | |
| 124 | What are the numbers of children below five year in the home? | _____ | |
| 125 | Have you diagnosed and had followed-up at health facility with malnutrition? | 1. Yes<br>2. No | |

**Part two: Medication and prophylaxis**

| | Medication and prophylaxis adherence | |
|---|---|---|
| SN | Question | Answer |
| 201 | Type of medications you are using currently? | _____ |
| 202 | Duration of the disease since diagnosis? | _____ |
| 203 | For how long have you been on medication? | _____ |
| 204 | Did you ever forget to take your medicine? | 1.Yes 2.No |
| 205 | Did you ever have problems remembering to take your medication? | 1.Yes 2.No |
| 206 | When you feel better, do you sometimes stop taking your medicine? | 1.Yes 2.No |

| | | |
|---|---|---|
| 207 | Sometimes if you feel worse when you take your medicine, do you stop taking it? | 1.Yes 2.No |
| 208 | Do you use prophylaxis for prevention of complication? | 1.Yes 2.No |
| 209 | What type of prophylaxis are you using currently? | 1. Injection<br>2. Tablets |

**Part III: Physical measurements**

| Anthropometric measurement | |
|---|---|
| Weight (in kg) | |
| Height (in cm) | |
| BMI | |
| West circumference (in cm) | |

| Blood Measurements | | | |
|---|---|---|---|
| | **Reading I** | **Reading II** | **Reading III** |
| Systolic blood pressure (mmHg) | | | |
| Diastolic blood pressure (mmHg) | | | |
| Random blood sugar measurement | _____mg/dl | | |

| parameters | Mean | |
|---|---|---|
| | **Before education** | **After education** |
| Body Weight (Kg) | | |
| Systolic blood pressure, mmHg | | |
| Diastolic blood pressure mmHg | | |
| Pulse pressure mmHg | | |
| Pulse rate Beat /minute | | |
| Hemoglobin Conce. g/dl | | |

| | | |
|---|---|---|
| Hematocrit level (%) | | |
| RBC count millions/mm3 | | |
| WBC count /µl | | |
| Platelets count/µl | | |
| RBC distribution width (RDW-SD) | | |
| Mean corpuscular volume/fL | | |
| Mean corpuscular hemoglobin/pg | | |
| Platelet distribution width/percentage | | |
| Mean platelet volume/fL | | |

**Hospital Anxiety and Depression Scale (HADS)**

Tick the box beside the reply that is closest to how you have been feeling in the past week.

Don’t take too long over you replies: your immediate is best

| D | A | | D | A | |
|---|---|---|---|---|---|
| | | **I feel tense or 'wound up':** | | | **I feel as if I am slowed down:** |
| | 3 | Most of the time | 3 | | Nearly all the time |
| | 2 | A lot of the time | 2 | | Very often |
| | 1 | From time to time, occasionally | 1 | | Sometimes |
| | 0 | Not at all | 0 | | Not at all |
| | | | | | |
| | | **I still enjoy the things I used toenjoy:** | | | **I get a sort of frightened feeling like 'butterflies' in the stomach:** |
| 0 | | Definitely as much | | 0 | Not at all |
| 1 | | Not quite so much | | 1 | Occasionally |
| 2 | | Only a little | | 2 | Quite Often |
| 3 | | Hardly at all | | 3 | Very Often |
| | | | | | |
| | | **I get a sort of frightened feeling as ifsomething awful is about to happen:** | | | **I have lost interest in my appearance:** |
| | 3 | Very definitely and quite badly | 3 | | Definitely |
| | 2 | Yes, but not too badly | 2 | | I don't take as much care as I should |
| | 1 | A little, but it doesn't worry me | 1 | | I may not take quite as much care |
| | 0 | Not at all | 0 | | I take just as much care as ever |
| | | | | | |
| | | **I can laugh and see the funny side of things:** | | | **I feel restless as I have to be on the move:** |
| 0 | | As much as I always could | | 3 | Very much indeed |
| 1 | | Not quite so much now | | 2 | Quite a lot |
| 2 | | Definitely not so much now | | 1 | Not very much |
| 3 | | Not at all | | 0 | Not at all |

| | | | | | |
|---|---|---|---|---|---|
| | | **Worrying thoughts go through my mind:** | | | **I look forward with enjoyment to things:** |
| | 3 | A great deal of the time | 0 | | As much as I ever did |
| | 2 | A lot of the time | 1 | | Rather less than I used to |
| | 1 | From time to time, but not too often | 2 | | Definitely less than I used to |
| | 0 | Only occasionally | 3 | | Hardly at all |
| | | | | | |
| | | **I feel cheerful:** | | | **I get sudden feelings of panic:** |
| 3 | | Not at all | | 3 | Very often indeed |
| 2 | | Not often | | 2 | Quite often |
| 1 | | Sometimes | | 1 | Not very often |
| 0 | | Most of the time | | 0 | Not at all |
| | | | | | |
| | | **I can sit at ease and feel relaxed:** | | | **I can enjoy a good book or radio or TV program:** |
| | 0 | Definitely | 0 | | Often |
| | 1 | Usually | 1 | | Sometimes |
| | 2 | Not Often | 2 | | Not often |
| | 3 | Not at all | 3 | | Very seldom |

Please check you have answered all the questions

Scoring

Total score: Depression (D) --------- Anxiety (A) ---------

0-7 =Normal

8-10 = Border line abnormal (borderline cases)

11-21= Abnormal cases (cases)

**10.5 Concise summaries of the 2012 World Heart Federation criteria for the echocardiography diagnosis of rheumatic heart disease**

**Echocardiographic criteria for individuals aged ≤20 years**

**Definite RHD (either A, B, C, or D):**

A) Pathological MR and at least two morphological features of RHD of the MV

B) MS mean gradient ≥4 mmHg*

C) Pathological AR and at least two morphological features of RHD of the AV‡

D) Borderline disease of both the AV and MV

**Borderline RHD (either A, B, or C):**

A) At least two morphological features of RHD of the MV without pathological MR or MS

B) Pathological MR

C) Pathological AR

**Normal echocardiographic findings (all of A, B, C, and D);**

A) MR that does not meet all four Doppler echocardiography criteria (physiological MR)

B) AR that does not meet all four Doppler echocardiography criteria (physiological AR)

C) An isolated morphological feature of RHD of the MV (e.g. valvular thickening) without any associated pathological stenosis or regurgitation

D) Morphological feature of RHD of the AV (e.g. valvular thickening) without any associated pathological stenosis or regurgitation

**Echocardiographic criteria for individuals aged >20 years**

**Definite RHD (either A, B, C, or D):**

A) Pathological MR and at least two morphological features of RHD of the MV

B) MS mean gradient ≥4 mmHg*

C) Pathological AR and at least two morphological features of RHD of the AV, only in individuals aged<35 years‡

D) Pathological AR and at least two morphological features of RHD of the MV

**Echocardiographic criteria for pathological regurgitation**

**Pathological MR**

(All 4 Doppler echocardiographic criteria must be met)

1. Seen in two views
2. In at least one view, jet length ≥2 cm‖
3. Velocity ≥3 m/s for one complete envelope
4. Pan-systolic jet in at least one envelope

**Pathological AR**

(All 4 Doppler echocardiographic criteria must be met)

1. Seen in two views
2. In at least one view, jet length ≥1 cm‖
3. Velocity ≥3 m/s in early diastole
4. Pan-diastolic jet in at least one envelope

**Morphological features of RHD**

**Features in the MV**

- AMVL thickening¶ ‖ ≥3 mm (age-specific)#
- Chordal thickening
- Restricted leaflet motion**
- Excessive leaflet tip motion during systole‡‡

**Features in the AV**

- Irregular or focal thickening§§
- Coaptation defect
- Restricted leaflet motion
- Prolapse

Congenital, acquired and degenerative heart disease should always be excluded as the etiology of MV and

AV abnormalities. Echocardiographic features should be interpreted in conjunction with other indicators of risk for RHD (e.g. demographics and regional differences) and clinical findings.

**Important considerations**

| |
|---|
| *Congenital MV anomalies must be excluded. Furthermore, inflow obstruction due to non-rheumatic mitral annular calcification must be excluded in adults. |
| ‡Bicuspid AV, dilated aortic root, and hypertension must be excluded. |
| §Combined AR and MR in high prevalence regions and in the absence of congenital heart disease is regarded as rheumatic. |
| ‖A regurgitant jet length should be measured from the vena contract to the last pixel of regurgitant color (blue or red) |
| ¶AMVL thickness should be measured during diastole at full excursion. Measurement should be taken at the thickest portion of the leaflet, including focal thickening, beading, and nodularity. Measurement should be performed on a frame with maximal separation of chordae from the leaflet tissue. Valve thickness can only be assessed if the images were acquired at optimal gain settings without harmonics and with a frequency ≥2.0 MHz. |
| #Abnormal thickening of the AMVL is age-specific and defined as follows: ≥3 mm for individuals aged ≤20 years; ≥4 mm for individuals aged 21–40 years; ≥5 mm for individuals aged >40 years. Valve thickness measurements obtained using harmonic imaging should be cautiously interpreted and a thickness up to 4 mm should be considered normal in those aged ≤20 years. |
| **Restricted leaflet motion of either the anterior or the posterior MV leaflet is usually the result of chordal shortening or fusion, commissural fusion, or leaflet thickening. |
| ‡‡Excessive leaflet tip motion is the result of elongation of the primary chords, and is defined as displacement of the tip or edge of an involved leaflet towards the left atrium resulting in abnormal coaptation and regurgitation. Excessive leaflet tip motion does not need to meet the standard echocardiographic definition of MV prolapse disease, as that refers to a different disease process. This feature applies to only those aged <35 years. In the presence of a flail MV leaflet in the young (≤20 years), this single morphological feature is sufficient to meet the morphological criteria for RHD (that is, where the criteria state “at least two morphological features of RHD of the MV” a flail leaflet in a person aged ≤20 years is sufficient). |
| §§In the parasternal short axis view, the right and non-coronary aortic cusp closure line often appears echogenic (thickened) in healthy individuals and this should be considered as normal. |

### 10.6 Risk of bias assessment

Risk of bias is done using the Hoy et al prevalence study quality assessment tool which ,the tool has major three components and graded as low ,moderate and high risk.

(1) Low risk (0-3), (2) moderate risk (4-6) finally high risk (7-9) Adapted from Hoy et al (2012

**Table 2: Critical Appraisal Tool**

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Anteneh et al. 2022 | *External Validity* | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | The study particpant age was greter than 24 |
| 2 | Was the sampling frame a true or close representation of the target population? | 0 | The study samples were drawn from the target population |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | All patients are included after echocardiography diagnostic tests |
| 4 | Was the likelihood of non-response biasminimal? | 0 | All 849 patients include cardiac clinic are included |
| | *Internal Validity* | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 1 | Data was collected directly from the patients |
| 6 | Was an acceptable case definition used in the study? | 0 | There is clear case defination |
| 7 | Was the study instrument that measured the parameter of interest shown to have reliability and validity (if necessary)? | 1 | Not well mentioned |
| 8 | Was the same mode of data collection used for all subjects? | 0 | Similar modeof datacollection were used |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Yes,approperate parameters used |
| Overall risk of Bias | | 3- low risk | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Engel et al. 2015 | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | Only Individuals from 4 - 24 years of age were included in the study. |
| 2 | Was the sampling frame a true or close representation of the target population? | 1 | The sampling frame was a list of one particular area within the overall target population |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | Appropriate randomized selection was taken |
| 4 | Was the likelihood of non-response bias minimal? | 0 | The response rate for the study was 99% |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | Data was collected directly from pupils from school |
| 6 | Was an acceptable case definition used in the study? | 0 | Clear case definition was used |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 0 | The researcher used evidence-based echocardiographic diagnostic criteria of the World Heart Federation (WHF). |
| 8 | Was the same mode of data collection used for all subjects? | 0 | Similar mode of data collection techniques used |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Both numerator and denominator were used appropriatly |
| | Overall risk of Bias | 2 (low risk) | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Mulatu et al 2016 | *External Validity* | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | The study take place in Shashemene among Primary School Students , unable to represent the whole Ethiopia population |
| 2 | Was the sampling frame a true or close representation of the target population? | 1 | The sampling frame was a list of one particular area within the overall target population |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | The study uses appropriate sampling methods |
| 4 | Was the likelihood of non-response bias minimal? | 1 | Response rate was not reported |
| | *Internal Validity* | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | Data collected directly from the subjects |
| 6 | Was an acceptable case definition used in the study? | 0 | Yes, acceptable case definition were used in the document |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 0 | The 2006 WHO echocardiography criteria for case definition of RHD were used. |
| 8 | Was the same mode of data collection used for all subjects? | 0 | Across all individuals the same mode of data collection were used |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Yes, appropriate parameters were used |
| | Overall risk of Bias | 3- low risk | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Habte et al. 2010 | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 0 | The study include age groups ,sex and place of recidence |
| 2 | Was the sampling frame a true or close representation of the target population? | 0 | Yes |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | The study use the whole study popollation (censes take place) |
| 4 | Was the likelihood of non-response bias minimal? | 1 | Records of 56 patients were incomplete |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 2 | Data were extracted from the patient charts. |
| 6 | Was an acceptable case definition used in the study? | 1 | Cases were not well defined |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 0 | Pretest was done |
| 8 | Was the same mode of data collection used for all subjects? | 1 | Data were collected only from patient chart |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Yes, appropriate parameters were used |
| | Overall risk of Bias | 5 moderate risk | More than 3 domians were at high risk |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Moges et al. (2021) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | The study do not represent the whole popolation it represent only pregnant mothers on ANC follow up |
| 2 | Was the sampling frame a true or close representation of the target population? | 1 | The sampling frame was a list of only pregnant women with<br>VHD managed at JUMC during the study period |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 1 | The study particpants taken purposively |
| 4 | Was the likelihood of non-response bias minimal? | 1 | response rate was not reported |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | data collected directly from the subjects |
| 6 | Was an acceptable case definition used in the study? | 1 | Cases were not well defined |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 0 | Two-dimensional trans-thoracic<br>Echocardiography was used to diagnose cardiac<br>disease and was performed according to American<br>Society of Echocardiography Guideline |
| 8 | Was the same mode of data collection used for all subjects? | 0 | Across all individuals the same mode of data collection were used |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Yes, appropriate parameters were used |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Bacha et al. (2019) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | The study include only pregnant popolation |
| 2 | Was the sampling frame a true or close representation of the target population? | 0 | Yes |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | Systematic<br>random sampling was used to select the samples |
| 4 | Was the likelihood of non-response bias minimal? | 0 | 5% of non-response rate was considered in the study |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | Yes ,data collected directly |
| 6 | Was an acceptable case definition used in the study? | 1 | Cases were not well defined |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 1 | Not mentioned |
| 8 | Was the same mode of data collection used for all subjects? | 0 | yes |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Yes, appropriate parameters were used |
| | Overall risk of Bias | 3 low risk | More than 3 domians were at high risk |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Gemechu (2016) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | Only 6-25 years of age included |
| 2 | Was the sampling frame a true or close representation of the target population? | 1 | Jimma zone only cannot represent rural Ethiopia |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 1 | Initially purposive then systematic and no census |
| 4 | Was the likelihood of non-response biasminimal? | 0 | The response rate is 82% |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | Yes ,data collected directly |
| 6 | Was an acceptable case definition used in the study? | 0 | RHD on the basis of the WHF criteria |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 1 | pretested was not done |
| 8 | Was the same mode of data collection used for all subjects? | 0 | Yes, subjects assesesd using a face-to-face interview |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | |
| | Overall risk of Bias | 4- moderate risk | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Bezaye et al. (2019) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | only children aged 2 months to 14 years were included |
| 2 | Was the sampling frame a true or close representation of the target population? | 0 | It accounts all pediatric individuals recorded in the hospital |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | Censu was done |
| 4 | Was the likelihood of non-response bias minimal? | 0 | It was secondary data and complete census |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 1 | It is from secondary data |
| 6 | Was an acceptable case definition used in the study? | 0 | All cause are well defined |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 0 | New York Heart Association (NYHA)classification were used |
| 8 | Was the same mode of data collection used for all subjects? | 0 | data were collected using structured record review checklist |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | |
| | Overall risk of Bias | 2-low risk | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Oli K et al. (1999) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 1 | Only Grade seven and eight students are included in the study. |
| 2 | Was the sampling frame a true or close representation of the target population? | 0 | The sampling from was a list of all populations in that target population |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | Random selection is used to select both Government and private school |
| 4 | Was the likelihood of non-response biasminimal? | 0 | The response rate was 93% |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | Data was collected directly from students |
| 6 | Was an acceptable case definition used in the study? | 0 | There was clear case defination |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 0 | The questionare were tested to assess the prevalence of RHD among Addis Ababa School children . |
| 8 | Was the same mode of data collection used for all subjects? | 0 | Information was collected through questioner that asess difrent parmeters like socio economic status |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Appropriate numerator and denominator were used to calculate prevalence |
| | Overall risk of Bias | 1 (low risk) | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Yadeta et al. (2016) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 0 | Includes all regions of Ethiopia with relevant variables |
| 2 | Was the sampling frame a true or close representation of the target population? | 0 | a list of almost every individual within the target population are included in the sampling frame |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | The study try to sample every individual with in the target population |
| 4 | Was the likelihood of non-response bias minimal? | 0 | The response rate was 98.1% |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | Data were collected directly from the study subjects |
| 6 | Was an acceptable case definition used in the study? | 0 | Used standard case definitions |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 1 | Instrument was not validated or reliability test were not done |
| 8 | Was the same mode of data collection used for all subjects? | 0 | same mode of data collection used for all subjects |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Appropriate numerator and denominator was used to calculate prevalence |
| | Overall risk of Bias | 1 (low risk) | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Oli K et al. (1992) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 0 | All age group and both sex founed in Butajira elementery school were included |
| 2 | Was the sampling frame a true or close representation of the target population? | 1 | Not clear |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 0 | Census was under take |
| 4 | Was the likelihood of non-response bias minimal? | 0 | The response rate was 92.8% |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 0 | The data was taken from school children |
| 6 | Was an acceptable case definition used in the study? | 1 | There is no clear statement of case defination for RHD |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? | 1 | There was no clear report on reliability and validity of the nstrument |
| 8 | Was the same mode of data collection used for all subjects? | 1 | Initial screening was done with a high index of suspicion. |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Appropriate numrator and denominator were used |
| | Overall risk of Bias | 4( moderate risk) | |

| First Author (year) | ENTRY | JUDGEMENT | DESCRIPTION |
|---|---|---|---|
| Gebremariam et al (2016) | External Validity | | |
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation? | 0 | It adress pediatrics age group who come from diffrent corner of Ethiopia . |
| 2 | Was the sampling frame a true or close representation of the target population? | 1 | Not clearly indicated |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? | 1 | The study samples were purposivelly selected |
| 4 | Was the likelihood of non-response biasminimal? | 1 | Unclear |
| | Internal Validity | | |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? | 1 | Discharge recordes was taken |
| 6 | Was an acceptable case definition used in the study? | 0 | There was clear case defination |
| 7 | Was the study instrument that measured the parameter of interest shown to have reliability and validity (if necessary)? | 0 | Data were extracted from the patient charts and were filled into the questionnaire format by the investigators. |
| 8 | Was the same mode of data collection used for all subjects? | 0 | Similar modeof datacollection were used |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate? | 0 | Yes,approperate parameters used |
| | Overall risk of Bias | 4- moderate risk | |

## 10.7 Declaration

I, hereby declare that this dissertation titled "**Rheumatic heart disease in Southwestern Ethiopia: Burden, Severity and Self-Management Education Effectiveness"** is the bona fide record of my original research. It has not been submitted to any other university or institution for the award of any degree. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

Name: _____

Signature: _____

Date: _____