BURDEN OF COGNITIVE IMPAIRMENT AND ASSOCIATED FACTORS AMONG RHEUMATIC HEART DISEASE PATIENTS AT JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA

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Department of Internal Medicine

BURDEN OF COGNITIVE IMPAIRMENT AND ASSOCIATED FACTORS AMONG RHEUMATIC HEART DISEASE PATIENTS AT JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA

By

Moses Mlawa Lazaro, MD

A dissertation Submitted in (partial) Fulfillment of the Requirements for the Degree of Master of Medicine (Internal Medicine) at

Muhimbili University of Health and Allied Sciences.

October, 2024

CERTIFICATION

The undersigned certifies that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled:" **Burden of cognitive impairment *and associated factors among patients with rheumatic heart disease at Jakaya Kikwete Cardiac Institute*"** in partial fulfillment requirement for the degree of Master of Medicine in Internal Medicine of the Muhimbili University of Health and Allied Sciences.

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Date: _____

DECLARATION AND COPYRIGHT

I, **Moses Mlawa Lazaro** declare that this dissertation is my original work and that it has not been presented and will not be presented to any other University for a similar or any other degree award.

Signature: …… Date: …….....

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Finally, I thank my lovely wife Carole, my son Brayden, and my daughter Eliana-Wendo whose presence and calmness soothed me during my study.

DEDICATION

I dedicate this dissertation to my supervisor Prof. Reuben Mutagaywa and my co-supervisor Dr. Peter Kisenge.

ABSTRACT

Background: Globally rheumatic heart disease (RHD) affects an estimated thirty to seventy million people. Despite a drop in the incidence of RHD fatalities around the world, 90% of them still live in developing nations. The burden of RHD in Tanzania is around 1-3% of the population. In patients with RHD neuropsychiatric manifestation has been observed such as cognitive impairment (CI). However, there is a noticeable research gap concerning CI, in RHD patients, particularly in Tanzania. This study is aiming at addressing this gap.

Objective: We aimed to determine the burden of CI and its associated factors among RHD patients at Jakaya Kikwete Cardiac Institute (JKCI), Tanzania.

Methodology: Hospital-based cross-sectional study was conducted from November 2023 to February 2024 at the JKCI. A sample size of 216 RHD patients aged ≥ 14 years was provided with informed consent/assent. We excluded patients with mental illness before being diagnosed with RHD. Recruitment was done by a consecutive sampling technique. A face-to-face interviewer-based questionnaire was used to obtain the socio-demographic and clinical characteristics of the study participants. The general practitioner assessment of cognition (GPCOG) tool is used to diagnose and assess the severity of CI.

Data entry and cleaning were done using the REDcap tool, then data was analyzed using STATA version 15.1. Descriptive statistics was summarized using frequencies and proportions for categorical variables and a measure of central tendencies with respective measures of dispersion for numerical variables. Bivariable and multivariable logistic regression was used to assess associated factors of CI among patients with rheumatic heart disease. Ethical approval was sought from the MUHAS and JKCI Research and Ethics Committee.

Results A total of 216 patients with a diagnosis of RHD were studied. Above three-quarters were outpatient, with a median age of 27 years, and female predominance (51.4%). More than half 123 (56.9%) participants attained a secondary level of education or higher, nearly two-thirds 127 (58.8%) were insured and less than half 88 (40.7%) were employed. In substance use, less than a quarter 12 (5.6%) were cigarette smokers but more than a quarter 61 (28.2%) were alcohol drinkers. Prevalence of cognitive impairment was 44 (20.4%); old

age (aPR=1.04; 95% CI: 1.02-1.05, p<0.0001), positive HIV status (aPR= 5.00; 95%CI:1.85-13.53, p=0.02), undernutrition (aPR=2.44; 95%CI:39-4.29, p<0.002), History of atrial fibrillation (aPR=3.16; 95%CI:1.08-9.30, p=0.036), and history of stroke (aPR=2.58; 95%CI:1.43-4.68, p =0.002) were independently associated with CI.

Conclusion and Recommendations: We recommend all patients with RHD to be screened for cognitive impairment, specifically in patients with atrial fibrillation, positive HIV status, old age, undernutrition, and stroke.

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LIST OF ABBREVIATIONS

ARF	Acute Rheumatic fever
BMI	Body Mass Index
BP	Blood pressure
CI	Cognitive Impairment
CKD	Chronic Kidney Disease
DM	Diabetes Mellitus
GAS	Group A Streptococci
HIV	Human immunodeficiency Virus
HTN	Hypertension
JKCI	Jakaya Kikwete Cardiac Institute
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
NCDs	Non-Communicable Diseases
RHD	Rheumatic Heart Disease
SC	Sydenham Chorea
VCI	Vascular cognitive impairment
WHO	World Health Organization

DEFINITION OF TERMS

Acute rheumatic fever (ARF) is an acute illness caused by an autoimmune response to infection with group A *Streptococcus*, leading to a range of possible symptoms and signs affecting any or all of the following organs: heart, joints, brain, skin, and subcutaneous tissues.(1)

Cognitive impairment (CI) refers to the distortion of high-level intellectual functions and processes like memory, planning, visuospatial function, reasoning, judgment, knowledge, decision-making, perception, comprehension, and language.(2)

Rheumatic heart disease (RHD) is a life-threatening heart condition that results from damage to heart valves caused by one or several episodes of rheumatic fever, an autoimmune inflammatory reaction to infection with streptococcal bacteria (streptococcal pharyngitis or strep throat). (3)

History of atrial fibrillation in this study, means those patients who either were previously/currently diagnosed to have atrial fibrillation after being diagnosed to have RHD or are on treatment of atrial fibrillation.

History of heart failure in this study, means those patients who either were previously/currently diagnosed with heart failure after being diagnosed to have RHD or are on treatment of heart failure.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background

Rheumatic heart disease (RHD) is a non-transmissible disease characterized by valvular damage. (4, 5) Globally RHD affects an estimated thirty to seventy million people. (6) Despite a drop in the incidence of RHD fatalities around the world, 90% of them still live in developing nations. (11, 12) A systematic analysis of the global occurrence and fatal consequences of RHD over 25 years estimated that, in 2015, approximately 10 out of every 1,000 individuals in South Asia and central Sub-Saharan Africa were afflicted by RHD. (6) In Tanzania, the prevalence of RHD is approximately 17.9% over 1000 cases and it is the third most common cause of heart failure. (9)

Aside from the heart, the brain and other bodily parts may be involved. When the heart is involved, it usually affects cardiac valves, which are better understood than the brain. For the brain, cognitive impairment (CI) is among the neuropsychiatric manifestations including severe depression, generalized anxiety disorder, migraine, and seizures. (10) CI refers to the distortion of high-level intellectual functions and processes like memory, planning, reasoning, judgment, knowledge, decision-making, and language. (11) Most of the patients tend to be diagnosed with an advanced form of CI like Alzheimer's disease or Dementia as compared with mild to moderate CI form. (8, 9)

Cardiovascular causes rank as the second leading contributor to CI. (10) RHD stands out as one of the most prevalent among those cardiovascular diseases. (9) Apart from this, other factors leading to CI include neurodegenerative diseases, traumatic brain injury, infections, inflammation, metabolic and nutritional imbalances, psychiatric disorders, genetic factors, medication and substance-related issues, hormonal imbalances, and sleep disorders. (10)

Cognitive impairment due to various causes affects an estimated 40 million individuals worldwide, accounting for nearly 5% of the global population. It is one of the new emerging non-communicable disease epidemics, with an estimated eighty-two million cases by 2030 and one hundred fifty-two million cases by 2050. (17) The prevalence of CI in the African

elderly population has been identified within a wide range, varying from 6.3% to 25%, (14) as reported in a meta-analysis encompassing 11 cross-sectional studies across different countries.

The proposed pathophysiological mechanisms for CI in RHD due to valvular dysfunction which may result in cerebral hypo-perfusion and multiple cardiogenic emboli. (15) Another pathophysiological mechanism is a direct distortion of brain circuits by the autoimmune mechanisms. (16) Complications associated with CI among RHD patients include poor quality of life, higher death rate, hospitalization as well as an economic burden to individuals, relatives, and the government. (17) Globally, RHD is associated with over 10 million disability-adjusted life-years. (18)

Worldwide, and particularly in Africa, there remains a scarcity of data regarding CI specifically among RHD patients. To the best of our knowledge, In Tanzania, there is no available data on CI. Therefore, it is crucial to study CI in RHD patients as they are a high-risk population. Early diagnosis and effective channeling of patients towards specific treatment is a valuable battling approach in the arena of neuropsychiatric complications of RHD, as the delay has various human, societal, and economic consequences.

1.2 Problem Statement

Cognitive impairment is a rising non-communicable disease epidemic, affecting approximately 40 million people globally, with projections of 82 million by 2030 and 152 million by 2050. The first WHO global action against cognitive impairment took place in Geneva, Switzerland, in 2015. Key challenges identified include a lack of data on the burden of cognitive impairment, evidence for risk reduction strategies, and insufficient prioritization in health policies. (19)

In African countries, RHD is still a major cause of mortality and morbidity especially in children and young adults; the prevalence of CI was found to range from 6.3% to 25%. (20) This is by the meta-analysis study done to include 11 cross-sectional studies in different countries, with these few results from the search, still, none of them was done specifically in patients with RHD. (20)

In Tanzania, the burden of RHD is prevalent at around 1-3% (21) most of the patients have a late presentation with already developed complications, and the CI prevalence in this population is unknown.

RHD is a disease of public health concern, especially because it is an avoidable disease, and the role of primary and secondary preventive strategies following a diagnosis of acute rheumatic fever is well implemented. Despite all this effort, the burden of poor quality of life and high cost of life to the patient and family members is high as a consequence of RHD complications such as CI. (22)

To our knowledge, there are no studies that have been done in Tanzania on the burden of CI and factors associated with it among patients with RHD. This study, therefore, targets to determine the prevalence of CI and its associated factors at JKCI, in Dar es Salaam, Tanzania.

1.3 Conceptual Framework

This is a self-developed conceptual framework.

The degree of CI in RHD patients is influenced by several different factors include social demographic, and clinical factors. Age, sex, economic, economic status, health insurance status, substance use, and education level are among the sociodemographic variables. Clinical factors are previous or current history of heart failure, nutritional status, history of atrial fibrillation, stroke, HIV status, history of Sydenham chorea, and history of previous cardiac surgery. (23) See *Figure 1*.

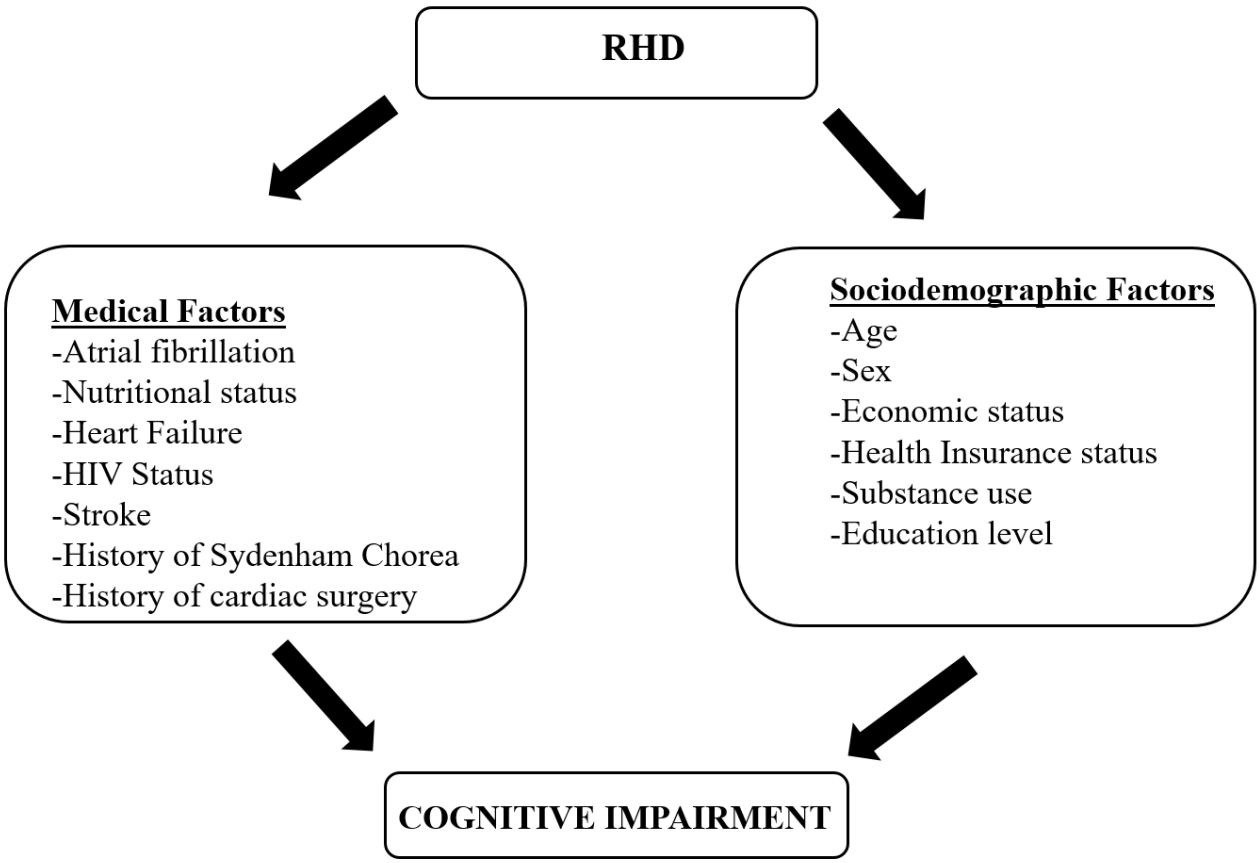


Figure 1: An illustrative conceptual framework showing different factors that are associated with the presence of cognitive impairment (CI) and its impact, among patients with rheumatic heart disease (RHD); HIV = human immunodeficiency virus.

1.4 Rationale

This study aimed to address the current knowledge gap regarding the burden of CI and its associated factors among RHD patients in Tanzania. To date, there are no documented studies available, which highlight the importance and novelty of this research. This study was the first in Tanzania to provide baseline data on the burden and associated factors of CI in RHD patients.

The primary objective of this study was to determine the prevalence, severity, and associated factors of CI in patients with RHD, at JKCI in Tanzania. By collecting comprehensive data on CI in this patient group, we can gain crucial insights into the burden of CI and its impact on these individuals.

It is thus expected that the results of this study will help provide valuable insights and raise awareness about the prevalence, severity, associated factors and raise awareness about CI in RHD patients in Tanzania; this will influence clinician's practice of enquiring about CI in routine clinics among patients at risk but again help policymakers and other specialties involved in providing care to RHD patients to make effective combating strategies and policies.

1.5 Research Questions

1.5.1 Overall Question

What is the burden of cognitive impairment and its associated factors among patients with RHD attending JKCI?

1.5.2 Specific Questions

1. What is the prevalence of cognitive impairment among patients with RHD at JKCI?
2. What are the sociodemographic factors associated with cognitive impairment in RHD patients at JKCI?
3. What are the clinical factors associated with cognitive impairment among RHD patients at JKCI?

1.6 Objectives

1.6.1 Broad Objective

To determine the burden of cognitive impairment and its associated factors among RHD patients at JKCI, Dar es Salaam, Tanzania, from November 2023 to February 2024.

1.6.2 Specific Objectives

1. To determine the prevalence of CI among patients with RHD at JKCI from November 2023 to February 2024.
2. To determine the sociodemographic factors (age, gender, marital status, education level, economic status, and health insurance status) associated with CI among patients with RHD at JKCI from November 2023 to February 2024.
3. To determine the clinical factors (atrial fibrillation, nutrition status, heart failure, HIV status, stroke, Sydenham chorea, and previous history of cardiac surgery) associated with CI among patients with RHD at JKCI from November 2023 to February 2024.

1.7 Study Hypothesis

There is a high prevalence of cognitive impairment among patients with RHD.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Prevalence of ci among rhd patients

According to the WHO report on the burden of disease; globally, around 40 million people have CI, which is approximately 0.5% of the world population. It is among the new rising non-communicable disease epidemics, with an estimation of eighty-two million cases by the year 2030, and one hundred and fifty-two million cases by the year 2050. (19) Cardiovascular factors including RHD are the second largest cause of CI worldwide. (13) Another hospital-based cross-sectional research was carried out in South America (Brazil) on RHD patients who were sent to a tertiary centre specialized in cardiac diseases. The study comprised fifty patients, with a mean age of 43.2 years and a predominance of females (84%), validated questionnaires for assessing cognitive function were used, and a worrying tendency emerged from the study, with 66% of patients experiencing cognitive difficulties. (16) This is similar to the cross-sectional study done in Macau the presence of CI was 44.35% which is high. (24) None of the studies has reported the prevalence of CI in RHD in Europe due to declining prevalence in developed countries.

In Africa, the prevalence of cognitive impairment (CI) ranges from 6.3% to 25%, particularly among older adults, with higher rates observed in individuals with comorbidities such as hypertension, diabetes, and cardiovascular diseases. This finding aligns with a meta-analysis of 11 cross-sectional studies conducted across various countries; however, none of these studies specifically focused on the cognitive impairment prevalence in patients with rheumatic heart disease (RHD), including those in Tanzania**.** (20)

2.2 Factors associated with ci among rhd patients

Social demographic factors

a) Age

The global senior citizen population is on the rise, according to United Nations projections. This increase is primarily due to the growing average life expectancy. It is estimated that the number of people aged sixty and above will rise by 56% in the next 15 years. Additionally,

those classified as the "oldest old," aged 80 years and above, will triple compared to the current figure by the year 2050. (25) The swift demographic aging trend is anticipated to raise the incidence of diseases and disabilities, with a specific focus on the CI.

A worldwide review was conducted, examining the incidence and prevalence of cognitive impairment in adults over 50 years of age residing in different communities. The findings indicated that the prevalence of CI varied significantly, falling within the range of 5.1 to 41 percent. (26)

With senescence, the expectation is a significant number of people may succumb to cognitive impairment of mild severity; Dementia becomes notably more prevalent with age, impacting more than 13% of individuals aged seventy-two and above. By the time individuals reach 85 years and older, about 32% of them may develop Alzheimer's disease, which constitutes the most common form of dementia, affecting approximately 70% of patients. Interestingly, in individuals with RHD, the manifestation of CI tends to occur at an earlier age and progresses until complete dependence on others and care is required. (27) Findings were similar to one comparison study that examined the frequency and age at onset of psychiatric disorders among children with a history of rheumatic fever, Sydenham’s chorea, or both, and a comparison group, found psychiatric manifestation can occur as early as 10 years of age. (28)

b) Sex

In a systematic review of the Global, Regional, and National burden of RHD, it was observed RHD is more prevalent among female individuals than male individuals. (13) In a meta-analysis study looking at CI in the general population, it has been observed that CI is more prevalent in females compared to males. (9) This is similar to another study done in China looking at the prevalence and mortality of CI in the general population, the findings were females had a higher prevalence than males. (29) No studies have been done looking at sex as a CI determinant in patients with RHD per se.

c) Education level

Cognitive impairment is also known as a distortion of previously acquired cognitive level in the form of education. (30) One prospective cohort study discovered that poorly educated persons have a greater risk of CI than better-educated ones. (31) these findings were opposite

to another study in which it was found greater education levels frequently correspond to higher cognitive ability. (32) However, a common study done in school-aged children with RHD found that persons with RHD have difficulty in attaining comparable levels of competence as their peers of the same age. (33)

d) Economic parameter and health insurance status

Low economic status has been associated with an increased risk of developing RHD (34), Additionally, RHD can substantially raise living costs for patients and their caregivers. A cross-sectional study involving 1,593 older adults utilized the Mini-Mental State Examination (MMSE) to assess cognitive impairment (CI) and found that individuals from lower economic classes and with limited access to health insurance were more likely to experience CI. (35) This is similar to the cross-sectional study done in China, where they found the prevalence of CI to be high in low socioeconomic populations. (24) The financial and health insurance aspects of RHD management are crucial considerations in addressing the holistic well-being of affected individuals and their support systems. (19)

e) Substance use

Alcohol use

Alcohol use not only has detrimental effects on social and personal life but also negatively impacts brain development and cognitive functions. (36) A study done by Fu-Shun Yen et al, in Taiwan, was carried out to look into the impact of alcohol use on the risk of developing CI in older adults with long-standing ailments. They used the Digit Symbol Substitution Test (DSST) to assess cognitive function in individuals aged sixty years and older in the National Health and Nutrition Examination Survey. Study candidates were grouped as heavy drinkers, moderate drinkers, or light drinkers. They used logistic regression analyses to investigate the relationship between CI and alcohol drinking in patients with or without chronic kidney disease (CKD), high blood pressure, and diabetes mellitus. Their analysis showed that heavy drinking of alcohol was significantly associated with a higher risk of cognition impairment in patients who had high blood pressure with OR 6.089, and 95% CI 1.318–28.13; and CKD patients with OR 6.324, and a 95% Confidence interval of 1.158 to 34.52 in comparison to those who were categorized as light drinkers. This is similar to another study done to examine

dose-response exploration showed that moderate alcohol consumption and heavy alcohol consumption resulted in a higher risk of cognition impairment in patients with diabetes and CKD; and heavy alcohol drinking escalated the risk of cognition impairment in participants who had high blood pressure. They concluded that the impact of drinking alcohol on the impairment of cognition significantly varied in patients who had different coexisting ailments. (37)

Overall, there is a paucity of data in Tanzania, East Africa, and globally on the impact of alcohol use among individuals who have RHD. This study will be able to add knowledge to this gap.

Cigarette smoking

Smoking cigarettes has often been related to dementia. This association has been thought to be mediated by brain hypo-perfusion. Martine Elbejjani et al, used information obtained from the CARDIA study group, with a mean age of fifty, which examines the development of coronary artery risk in young adults; they were able to evaluate the relation between smoking behavior such as status, cumulative pack years, age at initiation of cigarette smoking, and years since discontinuation and Cerebral blood flow in different lobes of the brain and areas connected to dementia. Compared to those who never smoked, former smokers had lower cerebral blood flow in the putamen, occipital lobe, and parietal lobe, cuneus, precuneus, and insula. The association between cigarette pack years and cerebral blood flow was disparate between former cigarette smokers and current cigarette smokers and this difference was statistically significant. The study was able to show a relationship between the development of cognitive functions and cigarette smoking among middle-aged adults. (38) In the CARDIA study, it was noted that there was a huge extensive association between smoking and smaller grey matter volume in middle age; accounting for vascular, respiratory, and substance use or psychological factors, and this association was found to be same in the study conducted in concomitant alcohol consumers. Regions recognized to be most vulnerable were those where addiction and cognitive activities overlapped. (39)

CLINICAL FACTORS

a) Atrial fibrillations

Most patients in developing countries tend to present late with complicated RHD, and atrial fibrillation is one of the complications, it was observed in one study that 20 to 40% of the patients presented with atrial fibrillation. (40) A systematic review of 15 prospective studies found that atrial fibrillation was associated with an increased risk of dementia in people with stroke, but the association was only of borderline significance in people without stroke. (41) A subsequent post hoc analysis of 2 randomized controlled trials involving 31,506 participants found that atrial fibrillation was associated with an increased risk of cognitive decline and dementia in both people with and without stroke. (42)

b) Heart failure

In western the prevalence of mild impairment in cognition (MCI) exceeded the occurrence of dementia, ranging from fifty three percent to fifty eight percent in older patients with moderate and mild Heart failure. (43) One comprehensive literature review examines the relationship between cognitive decline and heart failure. This review pooled analysis demonstrates that HF patients had worse cognitive performance than control others. The odds ratio CI was 1.62 (95% confidence interval: 1.48-1.79 (p-value of 0.0001) among subjects with HF in a pooled sample of 2937 heart-failure patients and 14,848 control subjects. The results of this review indicate that HF is associated with a pattern of generalized CI that includes primarily memory, attention, mental flexibility, and global cognitive deficits. (44) In the study done in South Africa, it was observed that most of the patients presented with RHD – mitral stenosis, had heart failure NYHA class II or III, this indicates the risk of CI in this population is high. (45)

c) HIV

In the study done in the US, HIV-associated dementia occurred in 10% to 15% of Human Immunodeficient Virus-positive individuals with advanced infection. (46) Prospective study meta-analysis sixteen studies with quality data from seven countries in Sub-Saharan Africa were included to assess the burden of HIV neurocognitive impairment among adult patients on and off antiretroviral medication (ART) in Sub-Saharan Africa. Pre-ART, the prevalence of Neurocognitive Impairment was 42.37% among HIV patients, and 30.39% among those

on ART for 6 months. Estimates of Neurocognitive Impairment in Uganda were 46.49% and 28.50%, respectively. The conclusion was that HIV substantially predisposes to CI, resulting in a massive specifically in areas with high HIV prevalence. (47)

d) Poor nutritional status

In one cross-sectional study looking on neuropsychiatric manifestation in malnourished senior citizens, about 35.0% were at risk of malnutrition and 11.3% were under-nourished, while 34.4% of the participants had impaired cognitive functioning, and about 32.3% showed symptoms consistent with depression. Malnutrition was more frequently noticed in individuals presenting with CI, and depressive symptoms, in multiple regression analysis, nutritional status was independently associated with cognitive and psychological status. (48) In another cross-sectional study involving 2365 individuals aged 60 and above was conducted. The nutritional status of the participants was evaluated using the Mini Nutritional Assessment Short Form (MNA-SF), while cognitive function was assessed through the Mini-Mental State Examination (MMSE). The study revealed that 5.54% of the participants suffered from malnutrition, 33.45% were at risk of malnutrition, and 36.74% displayed CI. These results underscore the notable prevalence of malnutrition and CI, with a clear association between malnutrition and the heightened risk of cognitive decline in malnutrition.

e) Stroke

Stroke is one of the complications of RHD; with both ischaemic stroke and haemorrhagic stroke, the risk of Vascular CI increases with the aggregate of cerebrovascular events that occur over time. In one of the prevalence study conducted in the United States aimed to determine the prevalence and incidence of Mild Cognitive Impairment (MCI), eligible participants without documented dementia or any other neurocognitive issues were invited to take part, results revealed 1640 subjects with normal cognitive function and 329 subjects diagnosed with MCI, out of which 241 had amnestic MCI, and 88 had no amnestic MCI. In fully adjusted models, considering only subjects without dementia, the study found that a history of stroke was linked to a higher odds ratio (OR) of non-amnestic MCI. (49) These results were similar to a review study done in Africa in which 5 to 15% of stroke patients were found to have CI. (50) again another cohort study done in Tanzania - Dodoma region, its was

hospital based among patients with first stroke at 3 months it was found that the prevalence of CI in patients with first stroke is 80.4% (51) this high prevalence is alarming.

f) History of Sydenham chorea

Sydenham Chorea (SC) is one of the late presentations of the RHD. (52) Isolative occurs within weeks to months, as a result of different pathological mechanisms of basal ganglia cell destruction. A retrospective study based on file reviews found that 46% of the children with RHD examined exhibited behavioral changes associated with cognitive function impairment. (53) In another hospital-based cross-sectional study done in adults showed 48% of individuals with a previous history of Sydenham chorea as presentation of ARF, had CI later on in life. (16) The results were in comparison to case-control study done in Brazil in which three groups of patients were assessed: adults who had rheumatic fever with SC during childhood, adults who had rheumatic fever without SC during childhood and controls in which the rate of CI was observed to be more in rheumatic fever with SC during childhood. (54)

g) Previous history of cardiac surgery

Fixing of heart with protection of mind is still a challenge. Observational study done in china in RHD patient underwent valvular repair, showed the prevalence of cognitive impairment post-operative was around 47%, with various perioperative factors linked included aortic cross clamp time, cardiopulmonary bypass time and total surgical time. (55) This has been observed even in post Coronary Artery Bypass Surgery (CABG) patients, where the prevalence was observed to be from baseline of 19% to around 40% with prevalence of around 20 to 30% after 1 year of follow up. (54, 55) Aortic cross cramp time has been observed in a retrospective study of 8 years to the patients underwent cardiac surgery to be an independent determinant of mortality and morbidities including low cardiac output, renal complication, prolonged ventilation, blood transfusion and prolonged hospital stay. These observations were made when the aortic cross cramp time exceeds 60 minutes (58) same as for total surgical time and cardiopulmonary bypass time.

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study Design

A hospital-based analytical cross sectional study.

3.2 Study Area

The Jakaya Kikwete Cardiac Institute is a prominent national cardiac hospital that offers extensive in- and out-patient cardiovascular care. It is located in Dar es Salaam and serves patients not only from Tanzania but also from other nations**.** JKCI has a bed capacity of 104 and provides a broad range of cardiac care, including surgical and medical situations. Additionally, every Wednesday, the institution hosts an RHD clinic with an enrolment of more than 400 patients.

3.3 Study Duration

The study was scheduled to take place in a period of four months, starting in November 2023 and concluding in February 2024.

3.4 Study Population

The study involved patients, who were already diagnosed to have RHD, by echocardiography, and attended clinic at JKCI.

3.5 Inclusion Criteria

All patients with RHD attending JKCI clinic aged 14 years and above and who were providedG informed consent or assent if below 18 years of age.

3.6 Exclusion Criteria

All patients with RHD with prior history of confirmed mental illness before diagnosis of RHD, medications that may cause CI, or with moderate to severe Multisystem organ damage.

3.7 Sample Size

$n = Z^2P (100-P)/ \varepsilon^2$

Whereby:

n = needed minimum sample size

Z = set at 1.96 (equivalent to a 95% confidence level), the typical standard deviation

ε = 5.0% as the appropriate marginal error

P = prevalence of patients CI was estimated to be 50% (since no study done on CI in RHD patients in Africa)

Therefore, the proposed sample (n) initial was 384.

However since our population was a finite population and data was collected for five months, the formula **(Cochran's adjustment formula)** for sample size calculation was:

N= n/(1+((n-1)/population)))

N= Adjusted sample size for a finite population

n= Calculated sample size from above

Population: Population from which the study participants was obtained

N= 384/(1+((384-1)/400)))

N= 196

The final sample size required was 196 study participants**.**

3.8 Study Variables

3.8.1 Dependent Variables

Cognitive impairment among RHD patients

3.8.2 Independent Variable

In this study it included the following factors divided into social demographic and clinical factors:-

Social demographic variables

Age in years, sex (whether male or female), education level (No formal education/Primary school education/Secondary school education/College or University education), income level (Self-employment or Employed in the informal sector/Government employment/

Unemployed), health insurance status (insured/not insured), substance use like alcohol and smoking (yes or no even single sip or cigarette within six months).

Clinical variables

History of being diagnosed or treated for Heart failure, Nutrition status by using BMI (Undernutrition/Over nutrition/Normal), history of being diagnosed or treated for atrial fibrillation, stroke, HIV status (positive/negative/unknown), and history of previous or current Sydenham chorea, any history of cardiac surgery (yes/no).

3.9 Sampling Technique

All patients aged 14 years and above with a confirmed diagnosis of RHD who received care at JKCI in Dar es Salaam, Tanzania were considered for inclusion. It was anticipated that around 80 RHD patients seek care at the institute per month (approximately 4 patients per day) in outpatient clinic and 7 to 8 admissions per week. The sampling was encompassed all eligible patients registered at JKCI, from November 2023 to February 2024. The basis of the study was that all RHD patients they are at increased risk of getting CI. The sequential number for recruiting patients to the study was determined by this calculation; it was obtained each day, and the expected number of patients attending (4 patients per day) was divided by the number of participants expected to be recruited (2 participants per day). For instance, if 4 patients attended and 2 need to be recruited, they were numbered sequentially (1, 2, 3, 4), and every second patient (in this example, patients 1 and 3) was invited to participate in the study; it's the same for the patients in the ward they were given numbers then divided by two and every second patient was assessed for eligibility. By using this sequential numbering method, it ensured that each eligible patient attending the institute on any given day had an equal chance of being selected for inclusion in the study. A record of patients attending the institute daily was maintained to track the sequential numbering process for recruitment. Any fluctuations or variations in the number of patients attending the institute daily were taken into account when calculating the sequential numbering for participant recruitment to maintain fairness in selection.

3.10 Study Procedure

Participants were recruited from Monday to Friday. The IPD comprises three distinct wards, with wards 1 and 2 designated for medical cases and ward 3 specifically for surgical cases. Meanwhile, the OPD operates within a single building housing seven consultation rooms, a nursing station, and a designated waiting area at the nursing station, patients were efficiently assessed and directed to their respective areas for clinic visits and consultation. This particular zone is where the study station was established for OPD, while those in wards were followed in their respective wards. At this particular allocated area, the principal investigator was identifying potential participants from the pool of RHD patients attending JKCI. The patients attending the RHD clinic with the established diagnosis of RHD by echocardiograph findings which were confirmed by assessing RHD registry or documented echocardiographic results as hard/soft copy were eligible for the study. Similarly, For IPD patients with confirmed RHD by documented results of echocardiogram they were also eligible. By using a systematic sampling technique, the sequential number and number of participants to be recruited were identified. The selected participant was approached, details about the study and consent was sought. Participants who consented were interviewed in consultation room 7 to ensure privacy. A thorough physical examination was done starting with a general and then systemic examination. Participants were given a questionnaire comprised of 16 questions, with part one (consisting of 6 questions) querying about social demographic factors. Part 2 consists of 7 questions querying about clinical factors and lastly, part 3 asks about the history of previous cardiac surgery. After completing a questionnaire principal investigator tested cognition by instituting a Swahili or English validated tool to the patient, the tool is containing two parts: part 1 of which the patient himself/herself will be asked, consists of 9 questions, and the maximum score is 9 each question scoring one point, for question no.2 of the tool which is for visual-spatial functioning a paper with a printed circle was instituted (for the patient to draw a watch with correct labeled hours), those scoring between 5 to 8 (1 to 4 is cognitive impairment, 9 means no cognitive impairment) results will be inconclusive then the informant who knows patient 5 years back was asked to complete the second part, which consists of 6 questions, in this second part if patient scored 0 to 3 then the patient was termed to have cognitive impairment. In case the informant who knows the patient is not around then a

scheduled meeting or telephone with the one who knows the patient was sought. By completing the questionnaire and cognition assessment tool the collected data was taken for data cleaning and analysis. Those who were found to have cognitive impairment they referred to their respective unit for proper management**.**

3.11 Data Collection Methods and Tools

A total of 216 participants confirmed to have RHD who were attending JKCI outpatient clinic and those admitted to the wards were asked to provide informed written consent from November 2023 to February 2024. A systematic random sampling method was utilized to recruit consented participants until the desired sample was achieved. Data collection was conducted by the principal investigator except during working hours it was done by the research assistant, who is a certified medical doctor under close supervision and monitoring by the principal investigator.

For social demographic and Clinical parameters; Clinical and social demographic data that includes age, sex, economic status, health insurance status, education level, and history of cigarette a questionnaire was used; the questionnaire was also used to gather information on clinical factors such as history of atrial fibrillation, HIV status, history of Sydenham chorea, and previous cardiac surgery. Furthermore, documented complications associated with RHD in patients, including atrial fibrillation, stroke, and heart failure were obtained through the same questionnaire.

In Physical examination; all patients underwent a thorough physical examination. For the current history of heart failure, clinical signs tarrying with Framingham criteria they were examined such as posture on sitting/lying, bilateral lower limb edema, ascites, raised Jugular venous distension, and bilateral and bibasal fine crackles. For the history of current atrial fibrillation patient was examined by taking the rhythm of pulse rate if its irregular with a difference between heart rate and pulse rate of more than 10 then atrial fibrillation was considered positive. Vital signs including heart rate were obtained using a pulse oximeter, and blood pressure measurement using an automated digital sphygmomanometer. The patient's blood pressure was determined as the average of two readings taken with at least a two-minute

interval. Additionally, body weight (in kilograms) was measured using a calibrated weighing scale, and Height (in cm) was measured using a stadiometer. Using the weight (kg) and height (cm) the body mass index (BMI) was calculated whereby a BMI < 18.5 kg/m^2 signified underweight, a BMI of 18.5-24.9 kg/m^2 was normal, a BMI of 25-29.9kg/m^2 is overweight and BMI ≥ 30 kg/m^2 as obese.

For Cognitive assessment; GPCOG (The General Practitioner Assessment of Cognition). This is the tool used for the assessment of CI, which is copyrighted by the New South Wales University, with specificity and sensitivity for English versions ranging from 0.72 to 0.95 and 0.81 to 0.98 respectively. It is validated and used in a wide number of populations, including patients with heart diseases. It has also been validated for use in Tanzania. (59) It was found to be superior compared to other screening tools like the Abbreviated Mental Test (AMT) or the Mini-Mental State Examination (MMSE) for assessment of CI. (58, 59, 60)

There are two components to the GPCOG: (i) A cognitive assessment of the patient consisting of nine questions that assess time orientation, visuospatial functioning, and information recall ability, and this was filled by the researcher/research assistant except for question number 2 of which a paper with drawn circle was given for participant to draw a watch and correct labeling arrows. A score of 0–4 indicated CI; a score of 5-8 indicated inconclusive results; and a score of 9 indicates no significant CI and no need for additional testing. (ii) An informant questionnaire consisting of six questions is only completed if the results of the cognitive assessment above are inconclusive informant should know the patient 5 years back, if the informant is not available at the moment the one who knows the patient 5 years ago called and reschedule for meeting. CI is indicated if the patient receives 0–3 on the 6-point rating scale.

3.12 Validity And Reliability

The structured questionnaire was subjected to a pilot test before the study officially begins in order to evaluate its validity and reliability.

3.13 Data Management And Data Analysis

Data entry and cleaning were done using the REDcap tool, then data was analyzed using STATA version 15.1. Where descriptive statistics were summarized as median and Interquartile range (IQR) for continuous variables and proportions for categorical variables. Group differences for categorical and continuous variables with Cognitive Impairment (CI) were examined using the Chi-square/Fisher exact test Kruskal Wallis test, and then all factors with $p<0.2$ were subjected to Bivariable and Multivariable Robust Poisson regression analysis. Bivariable Robust Poisson regression analysis was performed to identify factors associated with Cognitive Impairment among rheumatic heart disease patients depending on the crude prevalence ratio (cPR) with 95% CI. Finally, Multivariable Robust Poisson regression analysis was performed to examine the associations between the outcome variable and independent variables after adjustment for other variables. Associations in the Multivariable Robust Poisson regression analysis models were presented as adjusted prevalence ratios (aPR) with 95% CI. A two-sided *p*-value <0.05 was considered significant.

3.14 Ethical Clearance

For ethical approval before conducting this research, the MUHAS Directorate of Research and Publication Committee was consulted (Appendix VI). A JKCI permission request was made (Appendix VII). Participants were asked for their written informed consent before being enrolled in the study. Patients less than 14 years of age were given assent forms and parents/legal guardians signed written consent forms on their behalf. The study's objectives and the rights of participants to take part, stop taking part at any time, or not take part at all were explained to those who were recruited for the study. Confidentiality and privacy were protected at all times. Patients identified to have CI were referred to the specific departments including Psychiatry, Neurology, and Occupational therapy for proper management.

3.15 Data Dissemination

The results of the study is presented at both scientific conferences and the Department of internal medicine; JKCI has received a presentation of the study's findings. The dissertation is available at the MUHAS library. A manuscript is also written for peer-reviewed medical journals.

CHAPTER FOUR

4.0 RESULTS

4.1 Flow Diagram Of Patients

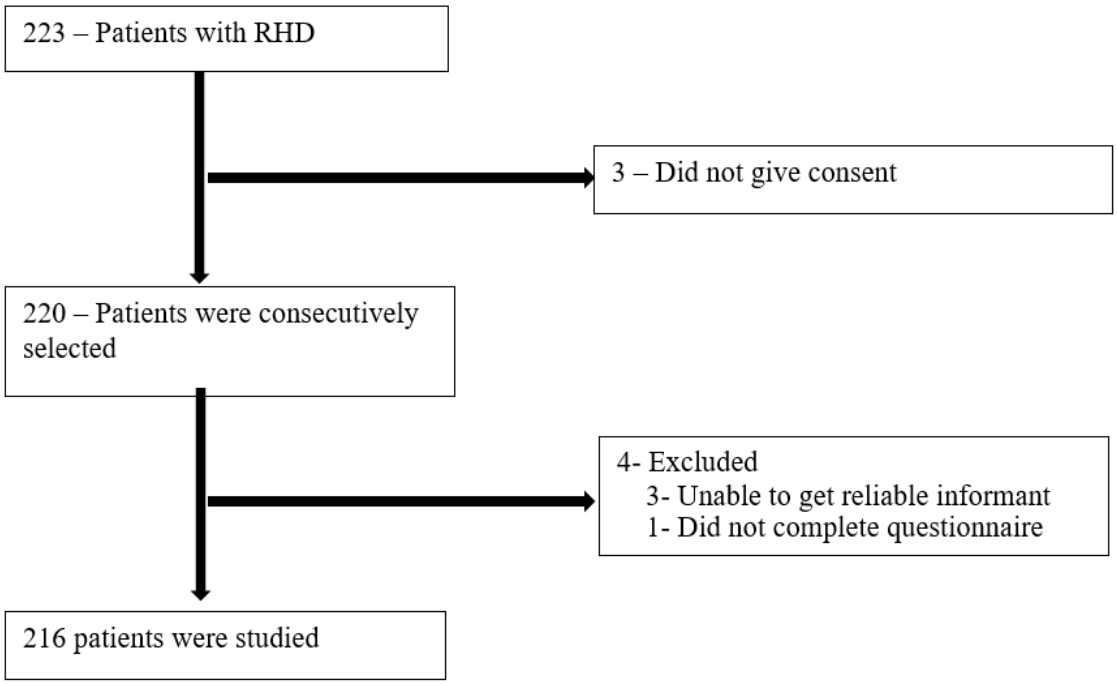


Figure 2: Flow diagram of patients enrolled in the study

4.2 Socio-Demographic Characteristics Of The Study Participants

A study of 216 patients diagnosed with RHD revealed a median age of 27 years. Females constituted the majority, accounting for 111 individuals (51.4%). A significant portion, over three-quarters, were treated as outpatients. Among the participants, 123 (56.9%) attained a secondary level of education or higher, 127 (58.8%) were insured, and 88 (40.7%) were employed. Regarding substance use, 12 (5.6%) were cigarette smokers, and 61 (28.2%) were alcohol drinker as shown in Table 1.

Table 1: Social-demographic characteristics of rheumatic heart disease patients, N =216

VARIABLE	FREQUENCY, N	PERCENT (%)
Median age in Years	**27.0 IQR [16.0-45.5]**	
Sex		
Female	111	51.4
Male	105	48.6
Education level		
Primary and below	56	25.9
Secondary	123	56.9
College/University	37	17.2
Occupation		
Unemployed	128	40.7
Employed	88	59.3
Health insurance status		
Not insured	89	41.2
Insured	127	58.8
Smoking		
No	204	94.4
Yes	12	5.6
Alcohol drinking		
No	155	71.8
Yes	61	28.2

4.3 Clinical Characteristics Of The Study Participants

Among the 216 patients diagnosed with RHD studied at JKCI, the majority, 184 (85.2%), were reported to be HIV negative. More than a quarter, 67 (31%), were undernourished. A history of atrial fibrillation was positive in 73 (33.8%) patients, while 135 (62.5%) had a history of heart failure. Few participants had a history of stroke 11 (5.1%) or Sydenham chorea 17, (7.9%). Additionally, more than half had a history of cardiac surgery 127, (58.8%) as shown in Table 2.

Table 2: Clinical characteristics of rheumatic heart disease patients, N=216

VARIABLE	FREQUENCY, N	PERCENT (%)
HIV status		
No	184	85.2
Yes	4	1.9
Unknown	28	12.9
Nutrition status		
Undernutrition	67	31.0
Normal	98	45.4
Overnutrition	51	23.6
History of having/being treated of Afib		
No	73	33.8
Yes	143	66.2
Diagnosed (currently/previously) with Heart failure		
No	81	37.5
Yes	135	62.5
Previous or current history of stroke		
No	205	94.9
Yes	11	5.1
Previous or current history of Sydenham Chorea		
No	199	92.1
Yes	17	7.9
History of any cardiac surgery		
No	127	58.8
Yes	89	41.2
TOTAL	**216**	**100**

4.4 Prevalence Of Cognitive Impairment Among Rheumatic Heart Disease Patients

Out of 216 patients studied, 44 (20.4%) had cognitive impairment as shown in figure 3. GPCOG tool was used of which in the first part (patient part) only 14 (6.5%) patients were found to have CI, 72 (33.3%) had no CI, while 130 (62.5%) were an intermediate score of 5 to 8, taken to the second part (informant part) were 23.1% were found have cognitive impairment as shown in figure 4 and 5.

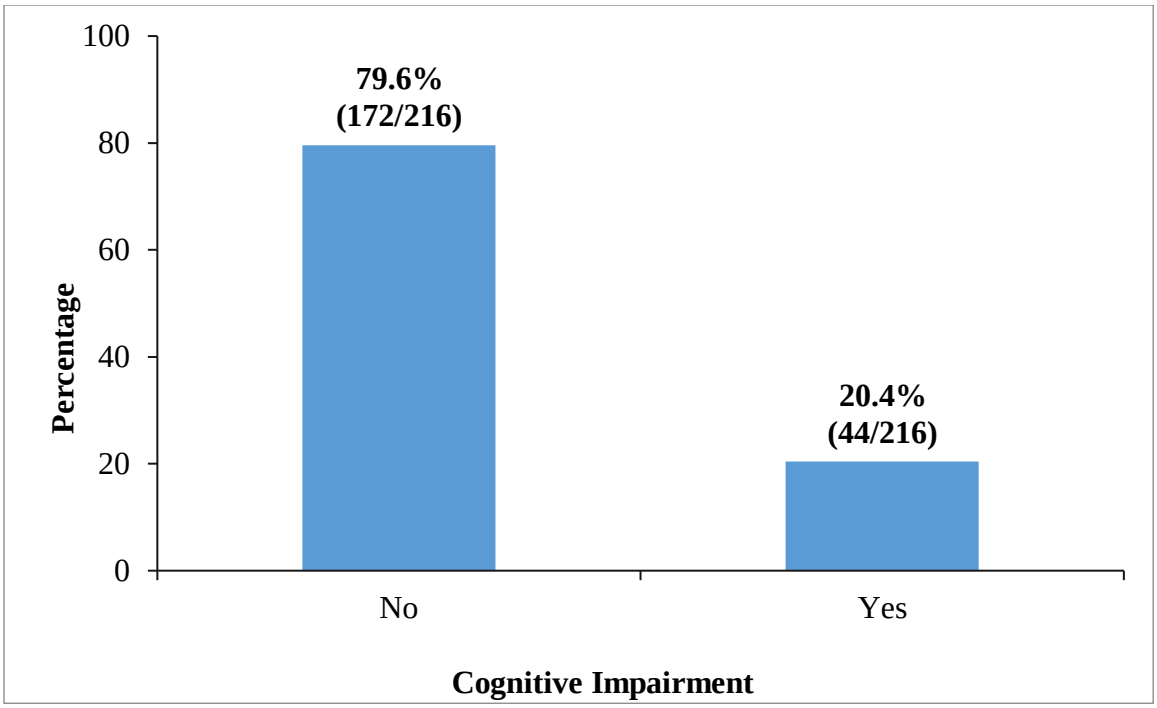


Figure 3: Prevalence of Cognitive Impairment among rheumatic heart disease patients

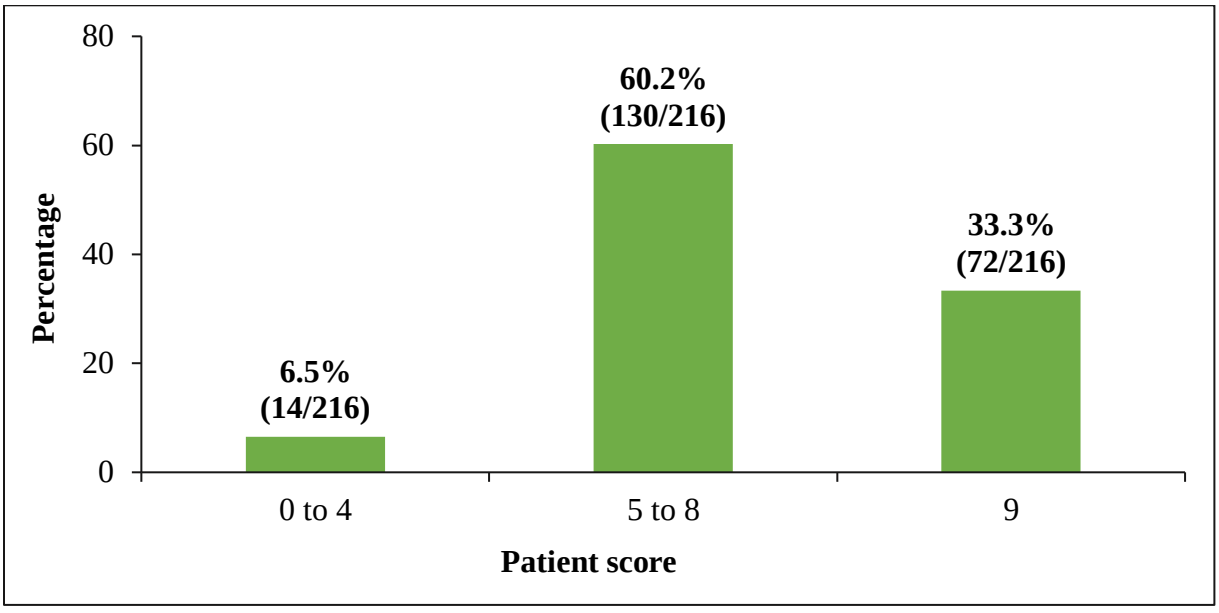


Figure 4: Patient score for GPCOG – tool of assessing Cognitive Impairment among rheumatic heart disease patients

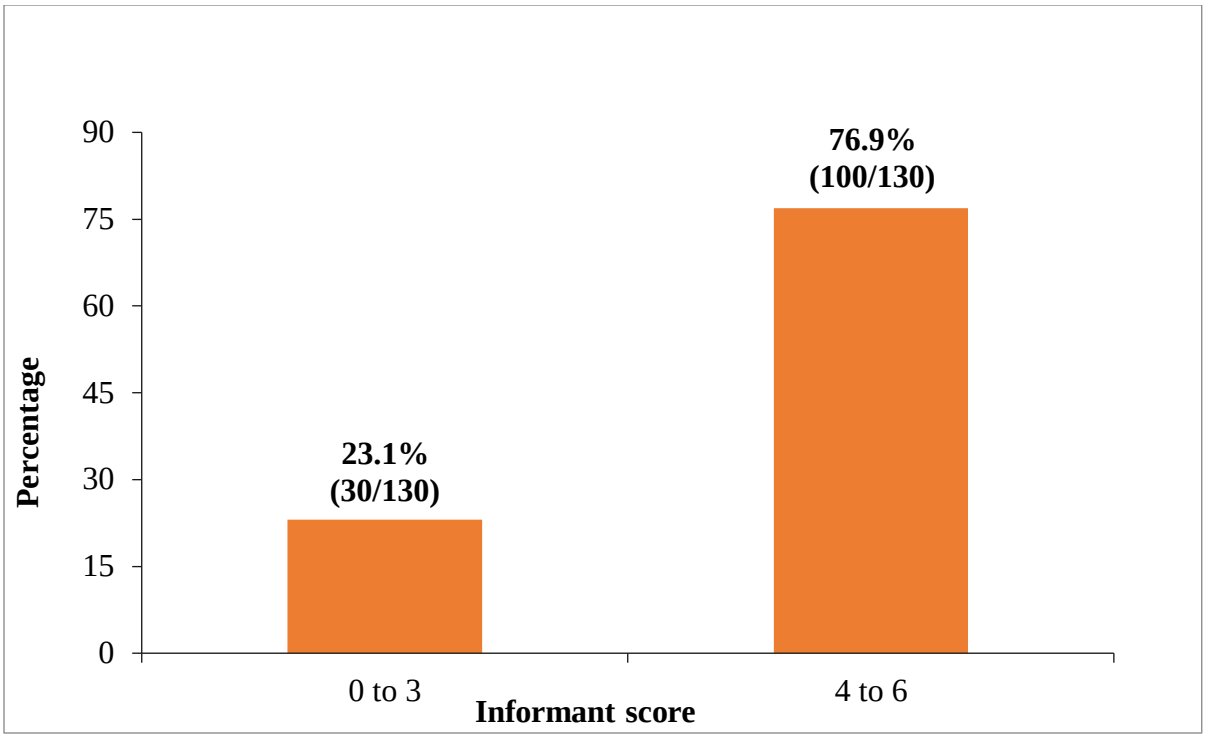


Figure 5: Informant part score for GPCOG – tool of assessing Cognitive Impairment among rheumatic heart disease patients

4.5 Distribution Of Factors Associated With Cognitive Impairment

The distribution of factors associated with or without cognitive impairment is presented in Table 3. The results show that among patients with RHD, CI was significantly associated with those median age of 47.5 years (81.8%) compared to those with median age 20 years ($p<0.0001$)), positive HIV status (100%) compared to negative HIV status ($p<0.0001$), undernutrition (35.8%) compared to normal and over nutrition ($p<0.001$), history of atrial fibrillation (28.7%) compared to those who had no history atrial fibrillation ($p<0.0001$), stroke (81.8%, $p<0.0001$) compared to those who had no history of stroke.

Other factors were not significantly associated with CI as shown in Tables 3A, and 3B below.

Table 3A: Cognitive Impairment by social-demographic and clinical characteristics among rheumatic heart disease patients

VARIABLE	Total, n	Cognitive Impairment		*p*-value
		No, n (%)	Yes, n (%)	
Median Age in Years	Median=27.0 IQR [16.0-45.5]	20.0, IQR [16.0-37.0]	47.5, IQR [30-60]	**0.0001**
Sex				0.895
Female	111	88 (79.3)	23 (20.7)	
Male	105	84 (80.0)	21 (20.0)	
Education level				0.380
Primary and below	56	41 (73.2)	15 (26.8)	
Secondary	123	101 (82.1)	22 (17.9)	
College/University	37	30 (81.1)	7 (18.9)	
Occupation				0.980
Unemployed	128	102 (79.7)	26 (20.3)	
Employed	88	70 (79.6)	18 (20.5)	
Health insurance status				0.965
Not insured	89	71 (79.8)	18 (20.2)	
Insured	127	101 (79.5)	26 (20.5)	
Smoking				0.059
No	204	165 (80.9)	39 (19.1)	
Yes	12	7 (58.3)	5 (41.7)	
Alcohol drinking				0.086
No	155	128 (82.6)	27 (17.1)	
Yes	61	44 (72.1)	17 (27.9)	

Table 3B: Cognitive Impairment by social-demographic and clinical characteristics among rheumatic heart disease patients

VARIABLE	Total, n	Cognitive Impairment		*p*-value
		No, n (%)	Yes, n (%)	
HIV status				
No	184	154 (83.7)	30 (16.3)	**<0.0001**
Yes	4	0 (0)	4 (100)	
Unknown	28	18 (64.3)	10 (35.7)	
Nutrition status				
Undernutrition	67	43 (64.2)	24 (35.8)	**<0.001**
Normal	98	85 (86.7)	13 (13.3)	
Overnutrition	51	44 (86.3)	7 (13.7)	**<0.0001**
History of having/being treated of Afib				
No	73	70 (95.9)	3 (4.1)	
Yes	143	102 (71.3)	41 (28.7)	0.861
Diagnosed (currently/previously) with Heart failure				
No	81	64 (79.0)	17 (21.0)	
Yes	135	108 (80.0)	27 (20.0)	**<0.0001**
Previous or current history of stroke				
No	205	170 (82.9)	35 (17.1)	
Yes	11	2 (18.2)	9 (81.8)	0.111
Previous or current history of Sydenham Chorea				
No	199	161 (80.9)	38 (19.1)	
Yes	17	11 (64.7)	6 (35.3)	0.465
History of any cardiac surgery				
No	127	99 (78.0)	28 (22.1)	
Yes	89	73 (82.0)	16 (18.0)	
OVERALL	**216**	**172 (79.6)**	**44 (20.4)**	

BIVARIABLE AND MULTIVARIABLE ROBUST POISSON REGRESSION ANALYSIS OF THE SOCIO-DEMOGRAPHIC AND CLINICAL FACTORS ASSOCIATED WITH COGNITIVE IMPAIRMENT AMONG RHEUMATIC HEART DISEASE PATIENTS

Bivariate and multivariate analysis using modified poison regression was done to identify factors independently associated with CI in patients with RHD (Table 4). In bivariate analysis, a total of six factors were significantly associated with CI. After adjusting for confounders, five factors were found to be independently associated with CI, old age (aPR=1.04; 95% CI: 1.02-1.05, p<0.0001), positive HIV status (aPR= 5.00; 95%CI:1.85-13.53, p=0.02), undernutrition (aPR=2.44; 95%CI:39-4.29, p<0.002), History of atrial fibrillation (aPR=3.16; 95%CI:1.08-9.30, p=0.036), and history of stroke (aPR=2.58; 95%CI:1.43-4.68, p =0.002).

Table 4: Bivariable and Multivariable Robust Poisson regression analysis of the socio-demographic and clinical factors associated with Cognitive Impairment among rheumatic heart disease patients.

	Bivariable Robust Poisson regression analysis		Multivariable Robust Poisson regression analysis	
VARIABLE	**cPR (95% CI)**	***p*-value**	**aPR (95% CI)**	***p*-value**
Age in Years	1.04 (1.03-1.05)	**<0.0001**	1.04 (1.02-1.05)	**<0.0001**
Smoking				
No	Ref		Ref	
Yes	2.18 (1.05-4.51)	**0.036**	1.10 (0.49-2.47)	0.814
Alcohol drinking				
No	Ref		Ref	
Yes	1.60 (0.94-2.72)	0.083	0.86 (0.49-1.47)	0.574
HIV status				
No	Ref		Ref	
Yes	6.13 (4.41-8.52)	**<0.0001**	5.00 (1.85-13.53)	**0.002**
Unknown	2.19 (1.21-3.98)	**0.010**	0.93 (0.44-1.96)	0.858
Nutrition status				
Under nutrition	2.70 (1.48-4.92)	**0.001**	2.44 (1.39-4.29)	**0.002**
Normal	Ref		Ref	
Over nutrition	1.03 (0.44-2.44)	0.938	0.75 (0.36-1.60)	0.462
History of having / being treated of Afib				
No	Ref		Ref	
Yes	6.98 (2.23-21.83)	**0.001**	3.16 (1.08-9.30)	**0.036**
Previous or current history of stroke				
No	Ref		Ref	
Yes	4.79 (3.18-7.23)	**<0.0001**	2.58 (1.43-4.68)	**0.002**
Previous or current history of Sydenham chorea				
No	Ref		Ref	
Yes	1.85 (0.91-3.74)	0.088	1.32 (0.53-3.28)	0.550

*__cPR__ and __aPR__ stand for crude prevalence ratio and adjusted prevalence ratio

CHAPTER FIVE

5.0 DISCUSSION

5.1 Discussion

Acknowledging the significant morbidity and mortality associated with cognitive impairment (CI), including that caused by rheumatic heart disease (RHD), the WHO Global Action Plan on the Public Health Response to Dementia 2017-2025 emphasizes the need for research on the burden and risk factors of CI as an early form of dementia across different populations to ensure comprehensive management of dementia patients. The primary focus of this study was to understand the relationship between RHD and CI. By addressing questions related to prevalence and associated factors, it was aimed to be the foundation for further studies but also contribute valuable insights to the holistic care of RHD patients. In this study, 44 (20.4%) of the RHD patients included in the study were found to have CI.

This high burden of CI 44 (20.4%) in RHD patients is similar to the range observed in a meta-analysis of the studies on the prevalence of CI in Africa which is 6.3 to 25%, with this prevalence being close to the upper limit of the observed prevalence range, signifies there is a high burden of cognitive impairment in RHD patients; (20) Our finding was also significantly lower than that found by Vasconcelos LPB et al. in Brazil, (16) Zhang Z et al. in Macau. (24) prevalence was 66% and 44.4% respectively.

The variability in the prevalence of CI observed in our study compared to other areas may be attributed to several factors, including differences in ethnicity, individual study designs, variations in tools used in assessing CI, and differences in sample sizes. For example, a study by Zhang Z in Macau (24) used data sets from two readily available large population surveys with a sample size of 2592 while that of Brazil by Vasconcelos LPB (16) had a smaller sample size of only 50 participants; WAIS-III a digital coding tool for assessing CI and a well-structured questionnaire were used respectively to assess CI. Black population presentation which is similar population to our study is only 14% in a study by Zhang Z in Macau (24) while none in the study by Vasconcelos LPB in Brazil. (16) However, both studies used the same design, cross-sectional study design.

In addition, our study identified five factors that showed a significant association with CI, one is a social demographic factor of a unit increase in age from the age of 14 increses the risk of CI ($p<0.0001$), and the remaining others are clinical factors which are positive HIV status ($p=0.02$), undernutrition ($p<0.0001$), History of atrial fibrillation ($p=0.045$), and history of stroke ($p =0.001$).

In our study, we found that a unit increase in age , a median age of 47 years was independently associated with CI in RHD; a prevalence ratio of 1.04 higher in a unit increase of age in years as compared to those with a median age of 20 years. It is similar to a study done by José C. Millán-Calenti et al in Spanish elderly population (63) which also found that in the general population, a unit increase in age is associated with an increased probability of CI, the odds ratio was 1.11 unit increase in age, mean age of 80 years as compared to the mean age of 73 in those with no CI. The difference in cut point of age as compared to our study is due to differences in the study population and tool for assessment of CI, in this study they used the Mini-Mental Status Examination score while in our study we used GPCOG, both studies have the same cross-sectional study design.

A study by RK Mutagaywa et al in Tanzaina, found that a history of atrial fibrillation was independently associated with CI (39) in RHD patients, these findings were similar to what we have found in our study, atrial fibrillation has been one of the major cardiovascular causes of cognitive impairment. In our study, we found that patients who had history of atrial fibrillation had prevalence of 3 times higher than to comparison group with no history of atrial fibrillation and this was statistically significant. Pathophysiological mechanisms for CI in RHD due to valvular dysfunction which may result in cerebral hypo-perfusion and multiple cardiogenic emboli. (15) Another pathophysiological mechanism is a direct distortion of brain circuits by the autoimmune mechanisms. (16) Early detection and treatment is the corner stone in reducing the prevalence of CI.

Positive HIV status is one of the independent factors found in our study to associate with CI similar to Abdulrazaq G. et al a meta-analysis involving sub-Saharan African countries (46) in which positive HIV status patients were 6.49 likely to have CI compared to HIV-negative patients with RHD, these findings were similar to another study done in Uganda (64) as we

have found in our study. The presence of low number of individuals with positive HIV status in our study, compared to the studies done in meta-analysis by Abdulrazaq G. et al, (64) may have influenced the results, potentially leading to skewed outcomes. This could pose challenges in drawing definitive conclusions about the impact of positive HIV status on cognitive impairment in patients with RHD.

Undernutrition is independently associated with CI in RHD patients in this study; where by patients with low BMI prevalence ratio was 2.4 more as compared to those with a normal BMI. Most studies have assessed BMI as a measure of nutritional status and its association with CI. This finding is comparable to a study done by Benjamin B. Cronk et al a systematic review across globe (65) and a study in Greek by Maria Mantzorou et al. (64) This common finding between undernutrition and CI can be attributed to lack of important nutrients and vitamins for proper cognitive functions in the brain; RHD patients may find it challenging to be financially stable to have a balanced diet regularly, (66) Additionally, healthcare providers can employ strategies to minimize the risk of CI in RHD patients by linking nutrition clinics and cardiology as a one-stop shop.

Stroke is another independent factor found to be associated with CI, in our study similar to a study done by H J Jokinen et al in Finland and Alphonce et al at Dodoma, in which CI impairment in stroke patients is prevalent in about 83% and 80.4% respectively, the difference in the magnitude of prevalence as compared to our study in which CI was prevalent by 20.4% is due to differences in the mean age of the sample population, study design and variability in the study population; in which a study by H J Jokinen et al in Finland mean age was 70 years and Alphonce et al at Dodoma mean age was 58 years and tools used for assessment of CI are Mean Mental Status Examination tool (MMSE) and Montreal Cognitive Assessment (MoCA) respectively. The study design were a Prospective cohort in both H J Jokinen et al in Finland and Alphonce et al at Dodoma while ours is cross-section.

However, the study did not show any independent associations between cigarette smoking, alcohol use and over nutrition. This could be because these variables might have been potential confounding factors. Further studies are needed to look into the associations for these variables.

5.2 Study Strength and Limitation

To the best of our knowledge, this is the first study to evaluate the Burden of CI and its associated factors among RHD patients in Tanzania, it will act as a stepping stone for further studies. The identification of both social and clinical factors associated with CI provides valuable insights. Understanding these factors is crucial for designing interventions and strategies to improve care among patients with ARF and RHD.

Our study has some limitations; first, Since this is the first study on the topic, there aren't many review papers available for comparison, which has limited our discussion. Second, JKCI is a single centre available with comprehensive cardiological services in Tanzania, with a fixed population of patients used in this study may be questionable to generalize the results. Third, we relied on patient's self-reported and informant data for calculating CI which has the possibility of subjectivity and recall bias. Patient's or guardian's responses may be influenced by their perceptions, experiences, or current feelings at the time of the interview, lastly Cross-sectional study design: The cross-sectional nature of our study limits the ability to establish cause-and-effect relationships. It provides a snapshot of CI and associated factors at a specific point in time but does not allow for assessing changes in CI over time or establishing temporal relationships between factors and CI. Longitudinal studies or intervention studies would provide stronger evidence of causality.

CHAPTER SIX

6.0 CONCLUSION AND RECOMMENDATION

6.1 Conclusion

We have found a high prevalence of cognitive impairment among patients with RHD. The independent associated factors of cognitive impairment were older age, positive HIV status, undernutrition, history of atrial fibrillation and history of stroke.

6.2 Recommendation

We recommend all patients with RHD should be screened for cognitive impairment by using the GPCOG tool which is a cost-effective and noninvasive method, specifically in patients with Atrial fibrillation, positive HIV status, older age, undernutrition, and stroke.

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APPENDICES

Appendix I: Informed Consent Form (ENGLISH)

CONSENT TO PARTICIPATE IN THE STUDY BURDEN OF COGNITIVE IMPAIRMENT AND ASSOCIATED FACTORS AMONG RHEUMATIC HEART DISEASE PATIENTS AT JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA.

NAME_____

MRN ----------

AGE ----------

Dear Sir/Madam,

My Name is Dr. Moses Mlawa Lazaro, a resident doctor in the department of Internal Medicine at Muhimbili University of Health and Allied Sciences (MUHAS). Am conducting study on burden of cognitive impairment and associated factors among rheumatic heart disease patients at Jakaya Kikwete Cardiac Institute**.**

I would like to conduct this study as a requirement for fulfilment of my postgraduate studies.

Purpose of the study:

This study aims to determine burden of cognitive impairment and associated factors among rheumatic heart disease patients at Jakaya Kikwete Cardiac Institute, this will help in change in the management and follow-up of patients who has RHD.

How to participate:

Participants who are willing to participate in this study will have to sign a consent form.

Short interview will be done and blood sample for investigation be taken.

Confidentiality:

No findings obtained will be disclosed to anybody except the attending doctors and patient him/herself.

The information shall be very helpful in this study as well as creating awareness of the burden of cognitive impairment and associated factors among rheumatic heart disease patients at Jakaya Kikwete Cardiac Institute.

Costs:

You will not pay any amount for your participation in this study.

Voluntary participation and the right to withdraw from the study:

Your participation is voluntary, and you have the right to withdraw from participating in this study at any time. Whatever your decision may be, it will have no effect in any way to your rights to care and treatment.

Risks:

There are no risks associated in participating in this study.

Benefits:

Your participation in this study will help you know about if you have cognitive impairment; you will as well get the benefit of getting appropriate treatment as per need.

I hope that the information from this research will be useful in contributing to improve the quality of care of Rheumatic heart disease patients.

I will be grateful if you willingly agree to participate in this study.

INVESTIGATOR'S STATEMENT

I the investigator have educated the research participant on the purpose and applications of this study.

Signed…… Date…….

PARTICIPANT'S STATEMENT

I am willingly agreeing to take part in this study on burden of cognitive impairment and associated factors among rheumatic heart disease patients at Jakaya Kikwete Cardiac Institute; I do this with full understanding of the purposes of the study and the procedures involved which include filling out a study questionnaire and having examined, all of which have been explained to me by Dr. Moses Mlawa Lazaro

Signature of patient----------

Signature of witness----------

Date----------

If you have questions during the study, you may contact the following:

Dr. Moses Mlawa Lazaro
Principal Investigator
Muhimbili University of Health and Allied Sciences (MUHAS)
Department of Internal Medicine
P.O. Box 65001 Dar es Salaam.
Mobile phone: 0746329728

OR

Prof. Reuben Mutagaywa
Supervisor for this research.
Muhimbili University of Health and Allied Sciences (MUHAS)
Department of Internal Medicine
P.O. Box 65001 Dar es Salaam.

In case of any information about your rights as a participant in this study please contact:

The Chairperson of Research and Publication Committee
Muhimbili University of Health and Allied Sciences (MUHAS)
P.O. Box 65001 Dar es Salaam
Tel. 022-2152489

Appendix II: (Informed Consent Swahili Version)

KIAMBATISHO II: FOMU YA OMBI LA RIDHAA

RIDHAA YA KUSHIRIKI KATIKA UTAFITI KUHUSU HALI YA UHARIBIFU WA UTAMBUZI NA MAMBO YANAYOHUSIANA NA UHARIBIFU WA UTAMBUZI KWA WAGONJWA WA RUMATIZIMU WANAOTIBIWA KATIKA HOSPITALI YA MOYO YA JAKAYA KIKWETE

JINA_____

NAMBARI YA HOSPITALI_____

UMRI_____

Kwa Bibi/Bwana,

Jina langu Dkt.Moses Mlawa Lazaro, mwanafunzi wa shahada ya uzamili katika chuo cha afya na sayansi shirikishi cha Muhimbili, nafanya utafiti juu ya hali ya uharibifu wa utambuzi na mambo yanahusiana na uharibifu wa utambuzi, kwa wagonjwa Rumatizimu wanaotibiwa Hospitali ya moyo ya Jakaya Kikwete

Nia ya utafiti:

Utafii huu unalenga kuangalia hali ya hali ya uharibifu wa utambuzi na mambo yanahusiana na uharibifu wa utambuzi, kwa wagonjwa Rumatizimu ili kusaidia uboreshaji wa matibabu yake.

Jinsi ya kushiriki:

Unaweza kushiriki katika utafiti kwa kujaza kwa hiyari yako fomu ya kuridhia kushiriki. Utafiti huu utakuwa na mahojiano kwa kutumia dodoso na kufanyiwa uchunguzi wa mwili.

Utunzaji wa siri:

Taarifa zote zitakazochukuliwa katika utafiti huu zitakuwa ni siri na zitatunzwa kwa usiri na zitatumika katika utafiti huu ili ziweze kusaidia katika kuboresha huduma kwa wagonjwa watakaokuwa wamefanyiwa uzibuaji wa mishipa ya damu kwenye moyo.

Gharama za Ushiriki:

Ushiriki katika utafiti huu ni bure yaani hakuna gharama yeyote kwa mshiriki

Hiyari ya kushiriki na kujitoa katika utafiti huu

Ushiriki katika utafiti huu ni wa hiyari na pia ni haki yako kujitoa katika utafiti huu muda wowote unapohisi kufanya hivyo. Maamuzi yako ya kuamua kutoshiriki au kujitoa katika utafiti huu hayataathiri haki yako ya kupata huduma na matibabu.

Madhara ya Kushiriki Utafiti:

Hakuna madhara yeyote yatakayompata mshiriki wa utafiti huu

Manufaa ya kushiriki utafiti huu:

Ushiriki wako katika utafiti huu utakuwa na faida kwako kwa kuweza kujua hali hali ya uharibifu wa utambuzi. Pia utapatiwa matibabu sahihi kadri itakavyo hitajika.

Ni matumaini yangu matokeo ya utafiti huu yatasaidia kushauri katika matibabu sahihi hali ya uharibifu wa utambuzi na mambo yanahusiana na uharibifu wa utambuzi, kwa wagonjwa Rumatizimu.

Nitashukuru sana kama kwa hiyari yako utaamua kushiriki katika utafiti huu.

KAULI YA MTAFITI

Mimi mtafiti, nakiri nimemuelewesha mshiriki wa utafiti huu kuhusu huu utafiti.

Sahihi…… Tarehe…….

KAULI YA MSHIRIKI

Natoa idhini mwenyewe bila aina yoyote ya kushurutishwa au kulazimishwa kushiriki katika utafiti uliotajwa hapa kuhusu utafiti wa kuangalia hali ya uharibifu wa utambuzi na mambo yanahusiana na uharibifu wa utambuzi, kwa wagonjwa Rumatizimu wanaotibiwa Hospitali ya moyo ya Jakaya Kikwete

Nafanya hivi baada ya kuelewa taarifa zote nilizoelezwa na mtafiti, Dkt Moses Mlawa Lazaro, na pia amenijibu na kunielewesha zaidi maswali niliyomuuliza.

Nimeelezewa kikamilifu kuhusu madhumuni na hali yake na naelewa kuwa nitaulizwa maswali kadhaa na kufanyiwa uchunguzi mwilini.

Pia naelewa kuwa naweza kujiondoa wakati wowote iwapo nitabadilisha mawazo.

Sahihi ya Mshiriki……

Saini ya Shahidi…….

Tarehe ……..

Mawasiliano kwa wahusika:

Kwa maswali au maoni kuhusiana na utafiti huu tafadhali wasiliana na wafuatao:

Dkt. Moses Mlawa Lazaro

Mtafiti mkuu

Chuo kikuu cha afya na tiba shirikishi Muhimbili

Idara ya Magonjwa ya ndani

S.L.P 65001 Dar es Salaam

Nambari ya simu: 0746329728

AU

Prof. Reuben Mutagaywa

Msimamizi wa utafiti huu.

Chuo kikuu cha afya na tiba shirikishi Muhimbili

Idara ya Magonjwa ya ndani

S.L.P 65001 Dar es Salaam**.**

Kwa mawasiliano zaidi kuhusiana na haki zako kwenye utafiti huu kama mshiriki, tafadhali wasiliana na:

Mwenyekiti wa tume ya tafiti na uchapishaji wa tafiti.

Chuo kikuu cha afya na tiba shirikishi Muhimbili

S.L.P 65001 Dar es Salaam

Nambari ya simu: 022-2152489

Appendix III (Clinical Research Form - English Version)

STUDY QUESTIONNAIRE ON BURDEN OF COGNITIVE IMPAIRMENT AND ASSOCIATED FACTORS AMONG RHEUMATIC HEART DISEASE PATIENTS AT JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA

PATIENT RECORD FORM

GENERAL DATA

Study number _____

Study Date DD/MM/YYYY_____

Hospital Registration Number _____

Physical address: (District / ward/ Location) _____

Telephone Number: _____

Next of Kin _____ type of relation with patient _____

Anthropometrics and vitals measured

Weight _____

Height _____

Blood pressure _____

Positive findings in general and cardiovascular examination _____

Part 1: Socio-Demographic characteristic of respondent

1. Age _____
2. Gender
    a. Male
    b. Female
3. Marital Status
    a. Single
    b. Married
    c. Divorce
    d. Separated
    e. Widow
4. Education Level
    a. No formal education
    b. Primary school education

c. Secondary school education

d. College/University education

5. Health insurance status

a. Insured

b. Not insured

6. Economic parameter

a. Self-employment/Employed in the informal sector

b. Government employment

c. Unemployed

Part 2: clinical factors associated with cognitive impairment among patients.

7. History of having / being treated of Afib
   a. Yes
   b. No
8. Have you ever taken alcohol? (even single sip within 6 months)
   a. Yes
   b. No
9. History of smoking (even single cigarette within 6 months)

a. Yes

b. No

10. Positive Seroconversion status

a. Yes
b. No
c. unknown

11. Nutrition status BMI (To be calculated by the researcher)

a. Under nutrition
b. Over nutrition
c. Normal BMI

12. Have you ever been diagnosed (currently/previously) with Heart failure

a. Yes, if yes current NYHA class_____

b. No

13. Any previous or current history of stroke
    a. yes
    b. No
14. Any previous or current history of Sydenham chorea
    a. Yes
    b. No

Part 3: surgical factors associated with cognitive impairment

15. History of any cardiac surgery
    a. Yes
    b. No

If yes in question 15 then continue with these questions;-

16. a.What type of surgery_____
    b. When was it _____
    c.Where was it _____

Appendix IV: Clinical Research Form - Swahili Version

UTAFITI KUHUSU HALI YA UHARIBIFU WA UTAMBUZI NA MAMBO YANAYOHUSIANA NA UHARIBIFU WA UTAMBUZI KWA WAGONJWA WA RUMATIZIMU WANAOTIBIWA KATIKA HOSPITALI YA MOYO YA JAKAYA KIKWETE

FOMU YA REKODI YA UTAFITI

Taarifa za awali

Namba ya dodoso_____
Tarehe ya tafiti DD/MM/YYYY_____
Jina _____
Makazi: (Wilaya/ Kata) _____
Namba ya simu: _____
Ndugu wa karibu _____

Vipimo vya awali

Uzito _____
Urefu _____
Msukumo wa damu _____

Sehemu ya Kwanza: Taarifa binafsi na za kijamii

1. Umri……..
2. Jinsia
    a) Kiume
    b) Kike
3. Hali ya ndoa
    a) Mpweke
    b) Nipo kwenye ndoa
    c) Nimeacha/Kuachika
    d) Tumetengana
    e) Mwenza alifariki
4. Kiwango cha elimu
    a) Sina elimu rasmi
    b) Shule ya msingi
    c) Shule ya sekondari

d) Chuo

5. Je una Bima ya Afya
   a) Ndiyo
   b) Hapana
6. Hali ya uchumi
   a) Nimejiajiri/ nimeajiriwa sekta isiyo rasmi
   b) Nimeajiriwa serikalini
   c) Sina ajira

Sehemu ya 2: Vitu vinavyochangia uharibifu wa utambuzi

7. Ulishawahi kutibiwa kuwa na historia ya shida ya mapigo ya moyo
   a) Ndio
   b) Hapana
8. Ulishawahi kunywa pombe (hata kwa kuonja ndani ya miezi 6 iliyopita)
   a) Ndio
   b) Hapana
9. Ulishawahi kuvuta sigara (hata sigara moja ndani ya miezi 6)
   a) Ndio
   b) Hapana
10. Hali ya maambukizi ya VVU
    a) Nimegundulika kuwa na maambukizi
    b) Sijagundulika kuwa na maambukizi
11. Hali ya utapia mlo kwa kutumia (BMI); itajazwa na mtafiti
    a) Unene uliopitiliza
    b) Chini ya kiwango kinachotakiwa
    c) Hali ya kawaida
12. Ulishawahi kuwa na historia ya moyo kufeli
    a) Ndiyo, NYHA ngapi…….
    b) Hapana
13. Ulishawahi kutibiwa/ au kuwa na historia ya kiharusi
    a) Ndio
    b) Hapana
14. Ulishawahi kuwa na ugonjwa wa miguu na mikono kujinyongorosha
    a) Ndio
    b) Hapana

Sehemu ya Tatu: mambo ya upasuaji yanayohusiana na uharibifu wa utambuzi

15. je ulishawahi kufanyiwa aina yeyote ya upasuaji wa moyo
    a) Ndio
    b) Hapana

Kama jibu swali la (15) ni Ndio, jibu maswali yafuatayo

16. a) Aina gani ya upasuaji_____

    b) Ilifanyika lini_____

    c) Ilifanyikia wapi _____

Appendix V Tool Swahili Version

Step 1: Patient Examination.

Name and Address for subsequent recall test.

1. Nitakutajia jina na anwani na ninahitaji uvikumbuke maana nitakuuliza baada ya dakika chache: Juma Ali, Kariakoo namba 45, Dar es Salaam.

	Correct	Incorrect
Time orientation.		
2. Leo ni tarehe gani ya mwezi upi?	☐	☐
Clock drawing.		
3. Tafadhali chora saa ya ukutani na uonyeshe namba kama zinavyotakiwa kuwepo.	☐	☐
4. Weka mishale ya saa kuonyesha muda wa saa kumi na moja na dakika kumi.	☐	☐
Information.		
5. Je waweza kuniambia kuna jambo gani kubwa limeripotiwa kwenye habari siku za karibuni? **(Only specific answer scores)**	☐	☐
Recall.		
6. Nitajie jina na anwani niliyokupa awali na kukwambia ukumbuke. **(Allow a maximum of 4 attempts)**		
Juma	☐	☐
Ali	☐	☐
Kariakoo	☐	☐
Namba 45	☐	☐
Dar es Salaam	☐	☐

To get total score, add items answered correctly: Total correct ___ / 9.

☐ **0-4: cognitive impairment.** ☐ **5-8: Proceed with step 2.** ☐ **9: Normal cognition**

Step 2: Informant Interview.

Uhusiano na mgonjwa: _____

Maswali yafuatayo yanataka kufahamu jinsi mgonjwa alivyo sasa ukilinganisha na miaka kadhaa iliyopita.

	Yes	No	N/A
Sijui			
1. Je mgonjwa anapata ugumu kukumbuka vitu vilivyotokea siku za karibuni ukilinganisha na kipindi cha nyuma?	☐	☐	☐
2. Je mgonjwa anapata ugumu kukumbuka maongezi baada ya siku chache kupita?	☐	☐	☐
3. Wakati wa kuzungumza, je mgonjwa anapata ugumu kuchagua maneno sahihi au anatumia maneno yasiyo sahihi mara kwa mara?	☐	☐	☐
4. Je uwezo wa mgonjwa kushughulika na mambo ya fedha umepungua?	☐	☐	☐ ☐
5. Je uwezo wa mgonjwa kumudu matumizi ya dawa zake mwenyewe umepungua?	☐	☐	☐ ☐
6. Je mgonjwa anahitaji kusaidiwa kutoka eneo moja hadi lingine?	☐	☐	☐ ☐

To get total score, add items answered "NO", "SIJUI" or "NA": Total score ___ / 6

☐ **0-3: cognitive impairment.** ☐ **4-6: no significant impairment**

Appendix Vi: Ethical Clearance

UNITED REPUBLIC OF TANZANIA

MINISTRY OF EDUCATION, SCIENCE AND TECHNOLOGY

MUHIMBILI UNIVERSITY OF HEALTH AND ALLIED SCIENCES

OFFICE OF THE DIRECTOR – RESEARCH, PUBLICATIONS AND INNOVATION

Ref. No.DA.282/298/01.C/1992 Date: 19/12/2023

MUHAS-REC-12-2023-1992
DR. MOSES MLAWA LAZARO
COLLEGE OF MEDICINE
MUHAS

RE: APPROVAL FOR ETHICAL CLEARANCE FOR A STUDY TITLED: BURDEN OF COGNITIVE IMPAIRMENT AND ASSOCIATED FACTORS AMONG RHEUMATIC HEART DISEASE PATIENTS AT JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA

Reference is made to the above heading.

I am pleased to inform you that the Chairman has on behalf of the University Senate, approved ethical clearance of the above-mentioned study, on recommendations of the Senate Research and Publications Committee meeting in accordance with MUHAS research policy and Tanzania regulations governing human and animal subjects research.

APPROVAL DATE: 19/12/2023
EXPIRATION DATE OF APPROVAL: 19/12/2024

STUDY DESCRIPTION:
Purpose:

The purpose of this cross-sectional study is to determine the burden of cognitive impairment, and its associated factors among rheumatic heart disease patients at JKCI, Dar es salaam, Tanzania.

The approved protocol and procedures for this study is attached and stamped with this letter, and can be found in the link provided: https://irb.muhas.ac.tz/storage/Certificates/Certificate%20-%2014801.pdf and in the MUHAS archives.

The PI is required to:

1. Submit bi-annual progress reports and final report upon completion of the study.
2. Report to the IRB any unanticipated problem involving risks to subjects or others including adverse events where applicable.
3. Apply for renewal of approval of ethical clearance one (1) month prior its expiration if the study is not completed at the end of this ethical approval. You may not continue with any research activity beyond the expiration date without the approval of the IRB. Failure to receive approval for continuation before the expiration date will result in automatic termination of the approval for this study on the expiration date.
4. Obtain IRB amendment (s) approval for any changes to any aspect of this study before they can be implemented.
5. Data security is ultimately the responsibility of the investigator.
6. Apply for and obtain Data Transfer Agreement (DTA) from NIMR if data will be transferred to a foreign country.
7. Apply for and obtain Material Transfer Agreement (MTA) from NIMR, if research materials (samples) will be shipped to a foreign country.
8. Apply for and obtain permission to publish the results from National Institute for Medical Research. The application should be before submitting to a publisher and not concurrently through the email publications@nimr.or.tz.
9. Any researcher, who contravenes or fail to comply with these conditions, shall be guilty of an offence and shall be liable on conviction to a fine as per NIMR Act No. 23 of 1979, PART III section 10 (2)
10. The PI is required to ensure that the findings of the study are disseminated to relevant stake holders.
11. PI is required to be versed with necessary laws and regulatory policies that govern research in Tanzania. Some guidance is available on our website https://drp.muhas.ac.tz/.



Dr. Nahya Salim Masoud,
Chairperson, MUHAS Research and Ethics Committee

Appendix Vii: Permission Letter JKCI

UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

JAKAYA KIKWETE CARDIAC INSTITUTE (JKCI)

JAKAYA KIKWETE CARDIAC INSTITUTE

In reply please quote;
Ref No: AB.123/307/01K/15

10/01/2024

Moses Mlawa Lazaro
HD/MUH/T.73/2021
MUHAS

RE: PERMISSION TO CONDUCT RESEARCH AT JKCI

Reference is made to your letter request to do a research study entitled **"Burden of Cognitive Impairment and Associated Factors among Rheumatic Heart Disease Patients at Jakaya Kikwete Cardiac Institute, Dar es Salaam, Tanzania."** here at JKCI.

This letter serves as an official document that permits you to do the above-mentioned task as requested.

It is our sincere hope that you will abide by the rules and regulations of good clinical practice. We wish you the best and hope your stay at JKCI will be fruitful.

Best Regards,

Dr. Pedro Pallangyo
Head of Research, Training and Consultancy.
CC: ALL DIRECTORATES & Head of Units

Jakaya Kikwete Cardiac Institute (JKCI); Upanga East Plot No. 1048, Kalenga Street, Malik Road, P. O. Box 65141 - Dar es Salaam; Telephone Number + 255 -22- 2152392Email:info@jkci.or.tz, Website: ww.jkci.or.tz.