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DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH

NEURO-DEVELOPMENTAL DELAY AND ASSOCIATED RISK FACTORS AMONG UNDER-FIVE CHILDREN WITH CONGENITAL HEART DISEASES ATTENDED AT JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA

By

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A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH

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CERTIFICATION

The undersigned certify that they have read and recommend for acceptance by Kairuki University a dissertation entitled **"**NEURO-DEVELOPMENTAL DELAY AND ASSOCIATED RISK FACTORS AMONG UNDER-FIVE CHILDREN WITH CONGENITAL HEART DISEASES ATTENDED AT JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA**"** in partial fulfillment of the requirements for the degree of Master of Medicine in Paediatrics and Child Health.

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ACKNOWLEDGEMENT AND DEDICATION

Glory and honor be to God, the almighty, who blessed and guided me throughout this work and my career at large.

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DEDICATION

I dedicate this work to my late parents; Awadh Mbarak and Salma Hassan, who provided me with good education and loving home.

ABSTRACT

Background: Significant advancements in medical and surgical care for children with congenital heart diseases have resulted in increased survival. However, they have increased risk of neuro-developmental delay which poses a risk for attainment of full developmental potential. The aim is to identify neuro-developmental delay and risk factors in under-five children that were attended at JKCI. Early detection and intervention for neuro-developmental disabilities can minimize their impact and enhance attainment of full developmental potential.

Objectives: To determine the proportion of neuro-development delay and associated risk factors among under-five children with congenital heart diseases attended at Jakaya Kikwete Cardiac Institute from January to April 2025.

Methodology: A hospital-based cross-sectional study was conducted among under-five children with congenital heart diseases at Jakaya Kikwete Cardiac Institute whose diagnoses were confirmed with echocardiography. Data was collected using a structured questionnaire that inquired about socio-demographic characteristics, risk factors, anthropometric measurements and oxygen saturations. Ages and Stages Questionnaire third edition (ASQ-3) was used to determine developmental status in relation to age. Data was recorded in excel sheet and on SPSS version 25. The mean and standard deviation, or median and inter-quartile range was used for numerical variables. Chi-square and Fisher's exact test was used to measure the

association between categorical variables. Factors associated with neuro-developmental delay were analyzed using binary logistic regression. A p-value of ≤ 0.05 was considered statistically significant.

Results: A total of 357 under-five children that were attended at JKCI were eligible for the study and were enrolled into the study. The mean age was 25.1 months and 120 (33%) study participants were below one year, with predominance of 191 (53.3%) of males. Among the 357 study participants, 153 (42.9%) had neuro-developmental delay. Children aged between 12 to 24 months (AOR=2.45; 95% CI 1.17-5.14, p-value =0.017); malnourished children (AOR=3.01; 95%CI 1.54-5.91, p-value =0.001)**;** those with cyanotic congenital heart disease (AOR=4.13; 95% CI 2.19-7.78, p-value <0.001); unmarried parents (AOR=2.78; 95%CI 1.18-6.55, p-value =0.02) and parity more than 1+ (AOR=2.96; 95%CI 1.44-6.09, p-value =0.003) were independently associated with neuro-developmental delay. The domain of neuro-developmental delay most affected was gross motor among 101 study participants (28.3%) and communication among 48 study participants (13.5%) was the least affected domain. Associated factors of neuro-development delay were age of the child below two years, malnutrition, unmarried parents and parity more than one.

Conclusions: The study demonstrates that neurodevelopmental delay is a significant public health concern among under-five children with congenital heart diseases at JKCI, with 42.8 percent affected. These delays are driven by a combination of medical and social factors, including low birth weight,

young age below two years, malnutrition, cyanotic congenital heart disease, lack of pre-primary education, single-mother care, multiparity, and low parental education. The findings highlight that neurodevelopmental outcomes are shaped by an interplay of biological vulnerability and socioeconomic conditions.

Recommendations: call for a fully integrated approach to the care of children with congenital heart disease. Management should extend beyond cardiac treatment to include nutrition support, growth monitoring, developmental surveillance, early child development services, and family counseling. Routine screening for neurodevelopmental delay should be incorporated into pediatric outpatient services at JKCI, with focused attention on high-risk groups. Parents and caregivers need clear counseling on developmental challenges, therapeutic options, psychosocial support, and educational interventions. Finally, future longitudinal studies are encouraged to better understand developmental trajectories and long-term quality of life.

Key words: *Congenital heart diseases, neuro-developmental delay, low birth weight, malnutrition.*

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS AND ACRONYMS

ACHD……Acyanotic congenital heart disease

ASQ-3……Ages and Stages Questionnaire third edition

CCHD……Cyanotic congenital heart disease

CHD……Congenital heart disease

HIV…… Human Immunodeficiency Virus

JKCI……Jakaya Kikwete Cardiac Institute

KU……Kairuki University

LBW……..Low birth weight

MUHAS……Muhimbili University of Health and Allied Sciences

MNH……Muhimbili National Hospital

NDD……Neuro-developmental delay

UNO……United Nations Organization

SD……Standard deviation

SPSS……Statistical Package for Social Sciences

WHO……World Health Organization

DEFINITION OF TERMS

Congenital Heart Disease (CHD): Is a heart structural and functional defect that develops in the foetus before birth. It can be cyanotic or acyanotic congenital heart disease (1).

Neuro-development delay (NDD): Is a term used to characterize developmental functioning that is a result of known or suspected central nervous system (CNS) malfunction, is well below age expectations (2).

CHAPTER ONE: INTRODUCTION

1.1 Background

Congenital heart diseases (CHD) can impact a child's heart's function and structure from birth (1-3). The child's hemodynamics may be affected by it (2- 4).). The defects of congenital heart diseases can be a small and may not affect hemodynamic status. However, major defects can significantly affect cardiovascular function. (3, 4). The brain may be impacted by CHD in various ways. Neurodevelopmental delay is now a common complication in children with congenital heart disease because more of these children are surviving than in the past. As survival improves, the long-term effects of the disease and its treatments become more visible, and developmental challenges are among the most frequent outcomes.

CHDs can be identified as early as before the child is born, after reaching maturity, or they can go undetected entirely (4). The likelihood of an early diagnosis increases with the severity of the condition (4, 5). The assessment of congenital heart defects can be aided by a variety of diagnostic techniques, such as electrocardiography, chest Computerized Tomography, echocardiogram, and prenatal ultrasound (5). If a health care professional suspects the infant has congenital heart disease, one or more of these diagnostic tests must be done (3). The level of oxygen in child's blood can be measured by pulse oximetry, which is utilized in the screening process for serious congenital heart diseases (6, 7). It is estimated that it has the potential to save the lives of 120 infants each year from critical congenital

heart disease (6, 7). In 2018, regulations were in place in the USA to undertake further investigations among neonates with low oxygen saturations in order to rule out congenital heart disease or other possible causes of low oxygen saturation (8).

Congenital heart defects are common, affecting 6 neonates for every 1,000 births and cyanotic CHD occurs in 1 in 1,000 live births (3). (5). It affects approximately 1 in 110 births, or nearly 1% of all births in the United States of America (3,9). The frequency of congenital heart diseases has remained largely unchanged worldwide. Africa has the lowest reported birth prevalence (1.9 per 1,000), whereas Asia has the highest (9.3 per 1,000) reported birth prevalence (10). In children, the most prevalent form of congenital heart disease is ventricular septal defect (3). A critical congenital heart defect affects about one in four neonates with CHDs, necessitating surgery or other therapies during the first year of life (9).

Approximately 20% of infant deaths are caused by birth defects (11). In 2014, CHDs were responsible for 23.5% of infant deaths as the most frequent reason why birth abnormalities result in newborn deaths (12). Throughout their first year of life, multiple-stage palliative surgical procedures are used for the most complicated defects, such as coarctation of the aorta, transposition of the great arteries, and Tetralogy of Fallot (2). Single-stage repairs of non-cyanotic lesions such as VSD are also performed (3, 4). Currently, there is a reduced death rate of 0.21% due to CHD in the

United States of America (13). People with CHDs are living longer lives as treatment improves, with more than 85% of American infants born with congenital heart defects surviving to adulthood. Reduced mortality has been demonstrated to improve lifespan, health, and quality of life when well-coordinated and continuing care recommendations are followed (14).

Most newborns with CHDs have an unknown aetiology. Due to chromosomal or genetic defects, some children are born with heart defects (15). The combination of environmental factors such as dietary habits, medical disorders, and medications used during pregnancy being implicated as causative factors (15.) For instance, a mother's previous Diabetes or obesity has been related to the baby's cardiac abnormalities. Pregnancy-related cardiac abnormalities have also been related to smoking and certain drug use (15). A minimum of 15% to 20% of CHD cases have been associated with recognized genetic disorders. Turner syndrome, DiGeorge syndrome, Trisomy 21 and other Trisomies are the most prevalent among them (16, 17). Stress and socio-economic status are two psychosocial factors that have been associated with an elevated risk of CHD (15).

According to World Health Organization projections, congenital heart disease affects 1% of all neonates born. Approximately 90% of these children, mostly in sub-Saharan Africa, are estimated by the WHO to have either no access to health care or insufficient access. Most of them are concentrated in low- and middle-income countries (18, 19).

In Tanzania there are relatively few studies that have been published regarding the prevalence of CHD. Congenital heart disease is the most frequent birth defect worldwide and the third leading cause of child death in Tanzania. According to estimates, there are 8 incidences of CHD for every 1,000 live births, which translate to 16,800 CHD births annually (22-25, 26). In a study done by D.M. Raphael et al more than a quarter of the children (34%) who had CHD were in the age group of less than 15 years (26).

In the year 2000 Tanzania made an effort to establish a cardiac unit at Muhimbili National Hospital. A Task Force from the Ministry of Health undertook feasibility studies on how to set up a cardiac unit and travelled to other counties that had cardiac units to learn from their experience (22). In 2008, the first facility was set up as part of Muhimbili National Hospital. More than 100 patients underwent surgery in its first year of existence; mainly supported by Chinese medical personnel by 35% (23). This effort has progressively helped Tanzania achieve independence in fundamental open heart and cardiac catheterization procedures for congenital heart defects (23).

Numerous estimates indicate that every year, more than 500,000 children in Africa are born with CHD (24). Over the past forty years, Tanzania has taken efforts to tackle this massive problem. Through the establishment of the CHD hub, it stands to follow in the footsteps of India and develop strong cardiac services. The economic expense of referring patients to Western nations can

be decreased by using these hubs to manage patients and improve training, thus advancing our own program (24).

Certain forms of CHD may lower blood oxygen content or the flow of blood during the foetal stage that reaches the brain. In fact, the brain maturity of full-term neonates with certain cardiac problems is around one month behind (27). Brain immaturity raises the risk of brain damage from stressful situations like childbirth, unstable blood pressure, or infection. White matter is especially prone to damage, which compromises the motor and cognitive systems necessary for the development of the child (28). Furthermore, the child's heart and brain may be impacted by their genes (29).

CHD has an impact on neuro-development, and developmental delays in infants are observed. These include persistent developmental impairments in numerous domains, such as language, social skills, and nutrition, as well as hypotonia in infancy (28). Although medical, environmental, and genetic factors all play a part, children with less severe cardiac disease experience fewer neuro-developmental sequelae than those with more complex abnormalities (28, 29).

The most common adverse outcome in children with CHD is neuro-developmental delay (29). Up to 50% of children who need cardiac intervention have neuro-developmental delay, which manifests as modest cognitive impairments, attention and hyperactivity disorders, motor functioning deficits, social interaction problems, language and

communication difficulties, and delayed executive function (30-32). Not only does neuro-developmental delay increase the burden of psychological distress and poor overall quality of life, but it also has a detrimental effect on later independence and relationships, educational achievement, and attainment of full developmental potential (33, 34). The neuro-developmental delay such as global developmental delay, attention deficit and hyperactivity disorder (ADHD), social and behavioural impairments, learning and intellectual disabilities, fine and gross motor delay, speech, language, and communication problems, are now currently seen in CHD children (35). In the long-term, it can impact educational achievements, employment attainment, independence, social and relationship difficulties, early-onset dementia, and reduced quality of life (35). Therefore, there is a need to know how big the problem is at JKCI, Dar es Salaam, Tanzania.

1.2 Problem statement

Neuro-developmental delay is a significant concern, affecting approximately 34.5% of children globally (26). It is well-documented that children with CHD are susceptible to a broad range of developmental delay, from cognitive and motor skill impairments to challenges with speech, attention, executive functioning, behavioral regulation, and socio-emotional development, all of which can hinder school readiness and overall well-being (2). Among children with congenital heart diseases, these developmental challenges are especially prevalent, as with increased survival rates for neonates and

children with CHD the focus is shifting towards reducing neuro-developmental risks within this vulnerable group (26, 35).

However, while the link between CHD and neuro-developmental delay has been established globally, there is limited knowledge about the extent of these delays and the specific risk factors involved among children with CHD in Tanzania (23, 26). The lack of data on the incidence and contributing factors of neuro-developmental delay within this population poses a critical gap in understanding and addressing these challenges locally. Given the established benefits of early intervention among young children, this study focused on identifying prenatal and postnatal factors associated with neuro-developmental delay in under-five children with congenital heart diseases (36 - 41).

1.3 Objectives

1.3.1 Broad objective

To determine the proportion and risk factors for neuro-developmental delay among under-five children with congenital heart disease attended at JKCI.

1.3.2 Specific objectives

1.3.2.1 To determine the proportion of children with neuro-developmental delay among under-five children with congenital heart disease attending JKCI.

1.3.2.2 To determine risk factors associated with neuro-development delay among under-five children with congenital heart disease attended JKCI.

1.4 Rationale of the study

The findings of this study will help physicians become more aware of the extent and kind of neuro-developmental delay in children under-five years of age who have congenital heart diseases. Additionally, a general emphasis will be placed on the significance of neuro-development screening in clinics utilizing the validated and accessible technologies to guarantee early detection of neuro-developmental delay and prompt referral of these high-risk children for appropriate treatment. The findings of the study will also help healthcare providers better understand the factors that contribute to neuro-development delay in children under-five years of age who have congenital heart disease. It identified the predictors of neuro-development delay, allowing for a more thorough approach in addressing the underlying cause of the problem.

1.5 Research questions

1.5.1 What is the magnitude of neuro-developmental delay among under-five children with congenital heart diseases attended at JKCI?

1.5.2 What are the risk factors associated with neuro-developmental delay among under-five children with congenital heart diseases attended at JKCI?

CHAPTER TWO: LITERATURE REVIEW

2.1 Magnitude of neuro-developmental delay among under-five children with congenital heart diseases

The prevalence of neuro-development delay in the general population varies greatly between research studies and nations. This the incidence of severe CHD requiring cardiologist review is about 2.5 to 3 per 1,000 live births, as documented by Hoffman and Kaplan in California, United States of America (4). This can be the result of using various study techniques and evaluation instruments. When comparing children with and without congenital heart diseases, those with CHD had greater risk of neuro-developmental delay (34).

According to data from the Australian "National Assessment Program—Literacy and Numeracy," 13.1% of children who had a heart procedure within their first year of life were classified as having "special needs" when they reached school age, compared to 4.4% of children who had not had a heart procedure. These children also had higher rates of overall learning disabilities and speech impairments (46). This shows that the bigger the heart lesion that needs surgical correction the higher the risk of neuro-developmental delay. Verall et al also stated that compared to children without a serious illness (~5%), abnormal brain development is a bigger concern for children with CHD (~20%) who require cardiac surgical intervention in infancy (35). This statement emphasizes the findings stated in the above paragraph (42 - 46).

Compared to other studies in developing countries, in India, Vagha et al concluded that in both types of CHDs, gross motor domain delays are more common than fine motor domain delay, language domain delay are the least common, and social domain delay are the least common (5). In another study which was also done in India by S. Shakya et al the prevalence of preoperative motor and mental delays was present in 32% and 26.9% of the children who were enrolled in their study (44).

Few studies have been done in Africa; for example in Egypt infants with cyanotic CHD (22%) had more statistically significant developmental delay than infants with acyanotic heart diseases in terms of receptive behaviour, personal behaviour, interpersonal relationships, socialization field, fine motor skills, and total motor skills (42). In Egypt, with more than three affected developmental domains, 69% of the infants were classified as having severe developmental delay and 30% as having moderate developmental delay, given that they had one or two affected developmental domains (42). Among the few studies conducted in Africa, this one revealed the highest prevalence of neuro-developmental delay. These results are consistent with the findings of Lata et al who showed that children with cyanotic congenital heart diseases were very susceptible to developmental delay as a result of prolonged hypoxaemia (43).

Children with CHD have different outcomes: some may have few to no neuro-developmental or neurocognitive defects, while others may have

severe life difficulties. There may be difficulties with neuro-development and academic achievement during childhood (38, 39). Therefore, it is imperative that children with CHD, especially those with the most severe variants, undergo screening for neuro-developmental and neuro-cognitive difficulties and be connected to resources that can be beneficial (40). With awareness, early identification, and management of the neuro-developmental, neuro-cognitive, and psychosocial problems, the quality of life as experienced by persons with CHD can be fairly good (41).

The percentage of neuro-developmental delays in CHD varies between industrialized and developing nations. According to Khalil et al a meta-analysis study, 42% of children had neuro-developmental delay. Since there is little information regarding the prevalence in Tanzania and East Africa, this study can help us to understand the situation.

2.2 Risk factors associated with neuro-development delay in CHD

The identification of the neuro-developmental delay predictors helps to address the underlying cause of the problem. Researchers from all around the world have examined the factors linked to neuro-developmental delay in under-five children who have congenital heart diseases, despite the lack of global studies in this area.

Neuro-developmental delay typically results from events that occur during the neonatal and perinatal stages, mainly maternal-related disorders such as to gestational diabetes, as demonstrated by Arcangeli et al in the United

Kingdom. Additionally, intra-uterine growth restriction and low birth weight are major contributors to neuro-developmental delay (6).

Other factors that have been shown to have a significant negative association with impaired developmental outcome included the presence of other medical co-morbidities, supplemental tube feeding, a birth weight of less than 2.5 kg, and a shorter time since last hospital discharge (7). Because the risk and prevalence of developmental delay change over time, health care professionals should support on-going screening of children with congenital heart diseases. Thus, this study used up-to-date data and emphasizes the need to conduct neuro-developmental screening on a regular basis.

Reduced cognitive, verbal, and motor function were substantially linked to growth failure and earlier age at first heart surgery, according to a study by Smith et al in South Africa (36). A study in Egypt by S. Sheta identified various risk factors, including underweight, cyanotic CHD, anaemia, prematurity, history of NICU stay, abnormal electroencephalogram and stunted growth (42).

According to a meta-analysis by Khalil et al the following factors contribute to neuro-developmental delay: seizures, feeding problems, cranial nerve abnormalities, motor abnormalities, and/or lethargy (48). In the absence of chromosomal or genetic abnormalities, children with CHD are more likely to experience neuro-developmental delays. Uncertainty surrounds the timing of

onset, whether prenatal or postnatal, but these findings are independent of surgical risk.

Preterm neonates frequently have a decrease in cortical gray and white matter volumes, as demonstrated in CHD. Additionally, there are localized areas that are vulnerable to the developing brain like the hippocampi and frontal-temporal lobes (49, 50). Additionally, based on a multivariate analysis of the secondary outcomes, living less than 200 miles from the Institution, being of Hispanic ethnicity, being older at motherhood, doing shorter drives, and having private health insurance were all linked to a higher number of visits (51 -53).

2.3 Conceptual framework for the study

Research has linked a number of factors to the frequency of neuro-developmental delay in children with congenital heart diseases. To find out how socio-demographic characteristics affect the frequency and severity of neuro-developmental delay, researchers looked at things like the age, gender, and level of educational of the child as well as the parents' ages and educational backgrounds. By researching on the risk factors linked to neuro-developmental delay in our context, we can reduce the prevalence of neuro-developmental delay in the future by early identifying such risks and potentially preventing them.

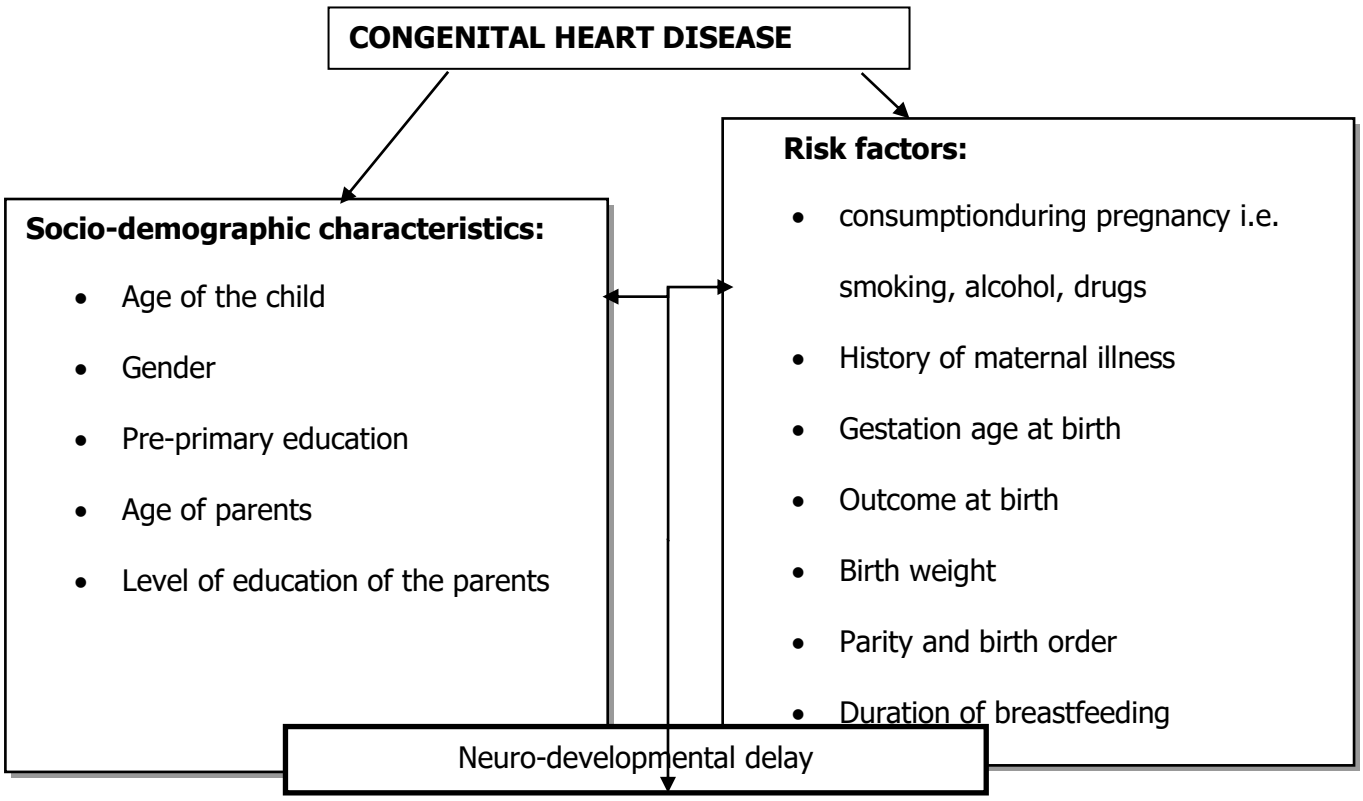

Figure 2. 1: Conceptual framework for the study

CHAPTER TWO: METHODOLOGY

3.1 Study area and population

The study was conducted at paediatric outpatient clinic at Jakaya Kikwete Cardiac Institute in Dar es Salaam. This public-owned facility is a University Teaching Hospital with specialists that provides cardiovascular care, education, and research services. JKCI was establishment in 2015. The Institute sees more than 150 outpatient and 50 inpatient children each week (unpublished report). The outpatient clinic has three consultation rooms equipped with echocardiogram machines, one resuscitation room, a reception area, and a spacious waiting area. There are three super specialists-paediatric cardiologists, three paediatricians, medical officers, and four nurses. As a public-owned facility, it provides highly specialized cardiovascular care to patients from all over Tanzania. In addition, patients from neighboring countries are admitted to the Institute. The Institute has patient rooms, an Intensive Care Unit, state-of-the-art theaters, and specialized laboratory. In carrying out its authorized duties, JKCI collaborates with many partners to achieve not only national and ministerial health objectives but also WHO-mandated targets.

The study population was under-five children with CHD who attended the paediatric outpatient clinic at JKCI in Dar-es-Salaam from January to April 2025.

3.2 Study design

This was a hospital-based cross-sectional study.

3.3 Sampling method

The study applied a systematic sampling technique to recruit eligible participants. All children attending the pediatric cardiology clinic on each data-collection day were first screened for eligibility based on the study criteria. To ensure equal probability of selection and maintain consistency across clinic days, a fixed target of approximately 20 participants per day was set, allowing the study to reach the required sample size within the planned four-month period.

On each clinic day, the sampling interval (k) was calculated by dividing the total number of eligible attendees by 20. Clinic registration numbers, which are assigned consecutively upon arrival (from the first to the last child), were used as the sampling frame. Beginning with the first eligible child, participants were selected at every kth interval until the daily quota of 20 children was reached. This approach minimized selection bias, ensured proportional representation of clinic attendees, and maintained a systematic and replicable sampling process across all clinic days.

3.3.1 Sample size estimation

The sample size was calculated using the Kish Leslie formula shown below (52).

$$n = \frac{Z^2 P (1-P)}{\varepsilon^2}$$

Whereby:

Z = Percentage point of normal distribution corresponding to the level of confidence. If the level of significance is 95% then Z is 1.96

P = Prevalence of neuro-development delay in CHD 44% (10).

ε = Maximum likely error/ margin of error 5% i.e. 0.05

Hence the minimum sample size is:

$$n = \frac{1.96 \times 1.96 \times 0.44 (1 - 0.44)}{0.05 \times 0.05} = 378 \text{ participants}$$

Then adjusting to 5% non-response n=n/1-0.05.

Hence n=378/ 1-0.05=397

Thus the minimum sample size is 397.

3.4 Procedures for data collection

3.4.1 Data collection tools

A structured questionnaire was used to collect data (socio- demographic characteristics and risk factors). The Principal Investigator and three research assistants collected the data. The research assistants were medical

officers and they were trained by the principal investigator on using ASQ-3 tool and the structured questionnaire for 3 days.

The structured questionnaire was used to collect the following information: the age of the child, gestation age at birth, birth weight, current body weight, sex, birth order, and outcome at birth, including birth asphyxia, history of illnesses and attendance at pre-primary education were recorded. Data was also collected on maternal age, level of education of the mother, duration of breastfeeding, smoking habit of the mother during pregnancy, paternal age and level of education and family size.

Screening for neuro-developmental delay

The third edition of the Ages and Stages Questionnaire (ASQ-3) was used in screening of each study participant for neuro-developmental delay. The communication, gross motor, fine motor, problem-solving, and interpersonal social components of this screening test were conducted. ASQ-3 has 21 age-specific questionnaires designed to measure child's growth from infancy to age five. Each survey is used for one month age group. Each developmental component comprises of six items that can be answered in one of three ways: "Yes," "Sometimes," or "Not yet," with corresponding scores of 10, 5, or 0. Different age-groups have different cut-off values (2 SD) for each component. Study conducted in United States reported that the specificity was 85%, the sensitivity was 86%, and the validity was 0.86 (18).

A caregiver who has a good understanding of the child provided answers to both the ASQ-3 and the structured questionnaire. Additionally, during the interview, the children were given specific tasks to complete. Each child underwent a 20–30 minute evaluation. The cut-off points (18) for different age groups are different, but the latter two groups were considered not to have delayed development. Children who scored below the cut-off score were considered to have developmental delays, necessitating further evaluation by professionals; those whose scores lie close to the cut-off score need close follow-up; and those scoring above the cut-offs were considered to be developing normally.

The ASQ-3 has been validated in low resourceful countries (53) and can be used in Tanzania. It has not been validated in Tanzania, but one study has been done in Tanzania using ASQ-3 (54).

3.4.2 Data collection methods

The sample size was 400 from January to April, 2025. Each month, 100 study participants were enrolled into the study. Every week, 25 study participants were obtained on all clinic days. Approximately 40-60 children attend the JKCI paediatric clinic; not all have confirmed congenial heart diseases and others have acquired heart diseases. The children who had CHD were given numbers and a randomly selected starting point was chosen. Then the eligible study participants were screened for eligibility criteria at regular intervals to get at least twenty study participants per day.

3.4.3 Eligibility criteria

Inclusion criteria: The inclusion criteria were children under-five years of age with confirmed CHD by echocardiography attending the paediatric outpatient clinic at JKCI in Dar es Salaam during the study period.

Exclusion criteria:

- Children with clinically recognizable syndromes like Trisomy 21, Turner's syndrome, or other co-morbid illnesses that could contribute to neuro-developmental delay.
- Children who have CHD and have other neurological diseases, such as cerebral palsy.
- Severely ill children on advanced acute care for example children coming in with acute heart failures

3.4.4 Study variables

3.4.4.1 Dependent variable: Neuro-developmental status.

3.4.4.2 Independent variables:

- Socio-demographic characteristics of the study participants and the parents - (age, gender, level of education of parents/caretakers, employment status, region of residence).
- Clinical parameters (gestational age, birth weight, birth outcome – respiratory distress, jaundice, sepsis; exclusive breastfeeding; anthropometric measurements, age at first diagnosis of CHD; pulse oximeter readings).

- Maternal-related factors – history of TORCHES, Diabetes mellitus, smoking during pregnancy, use of alcohol during pregnancy.

3.4.5 Ethical considerations

Parents/caretakers of eligible study participates were provided with a detailed explanation about the study and its purpose and assured that their acceptance or refusal to participate would not affect the care given to them at the hospital. The ones who were found to have delays were referred to pediatric neurologists for further investigations and physiotherapy/speech therapy and occupational therapy. When each parent/caretaker had understood the information given, then were asked to grant a written informed consent to allow the child to participate in the study.

3.4.6 Ethical clearance

Ethical clearance for the study was obtained from Kairuki University Institutional Research Ethics Committee (IREC), according to the Standard Operating Procedures (SOPs) of KU, and permission to conduct was granted by the Administration of Jakaya Kikwete Cardiac Institute. The clinic's regular activities were not hampered during data collection.

Participants' personal information were kept confidential. Identifiable patient information was not included in the questionnaire, and all established procedures for safeguarding participant confidentiality were rigorously observed. . The interviews were conducted at the corner of the waiting area to enhance privacy. The study participants were interviewed while waiting for

their consultation. This whole process did not interfere with clinic daily services. The hard copies of the questionnaire and ASQ-3 tools were kept in a locked cabinet by the PI and the data was kept in a password-protected in PI computer.

3.4.7 Reliability and Validity of the data collection tool

Validity is defined as the extent to which a concept is accurately measured in a quantitative study and whether the instrument covers all the content that it should with respect to the variable. Reliability refers to the consistency of a measure, that is, a participant should have approximately the same responses each time the test is completed or when different investigators yield consistent responses of participants during an interview. The structured questionnaire for data collection was reviewed by a Paediatrics cardiologist and before data collection it was pilot-tested.

3.5 Data management

3.5.1 Data collection

The Principal Investigator undertook data collection with the assistance of three research assistants, who are medical officers who were well trained by the PI at Kairuki University campus for three days on the study protocol. To ensure a thorough understanding of the study, research assistants received comprehensive pre-training on the entire data collection process. A pre-tested structured questionnaire was used in the study to determine the

frequency and risk factors of neuro-development delay among under-five children with congenital heart diseases.

Standard Operating Procedures for Anthropometric measurements

A child wore light clothing and no shoes while participants were weighed using a 50-kg scale (Weighing Equipment, High Holborn, London, United Kingdom), to weigh the newborns, a standard beam balance (SECA) was used. We recorded the readings to the closest 0.1 kilogram. Every day of recruitment, the weighing scale was calibrated to zero.

The length of the infants was measured using an infantometer (SECA - Germany). Parents or guardians helped their children take off their shoes and carefully put them supine on the board with their heads 90 degrees from the fixed head piece. The investigators made sure that the children's legs were straightened at the knees and that their feet were at a correct angle to the sliding foot piece that was placed in contact with their heels. The height of other children above 2 years was measured by a stadiometer (SECA - Germany). Children were instructed to stand with their feet together, their shoulders, buttocks, and heels in contact with the stadiometer's vertical surface, and their arms hanging loosely by the side. The parent or guardian assisted, so the children would not bend their knees, hold their heels off the ground, or overextend themselves; avoided errors to happen. The length and height was measured and recorded to the nearest 0.1 centimeter.

3.5.2 Data coding and cleaning

The accuracy of response to the questions was checked for accuracy and consistency at the end of each working day by the PI.

3.5.3 Data analysis

The information was analyzed using SPSS version 29 (IBM, Chicago, USA) after the data was entered into the computer for analysis. Data was summarized using descriptive statistics whereby continuous variables were described in means with respective standard deviations or median with respective inter-quartile ranges depending on the distribution of data. Categorical variables were summarized in frequency and respective percentages.

Factors associated with neuro-developmental delay were analyzed in two steps: Univariate analysis was conducted for each variable at a time to assess its association with neuro-developmental delay. Odds Ratios (OR) and respective 95% confidence intervals were calculated. Variables with significant association equal to p-value of 0.2 were included in multivariate binary regression model. Adjusted Odds Ratios (AOR) and respective 95% confidence interval were computed. Variables with p-value of less than or equal to 0.05 were considered to be independently associated with neuro-developmental delay.

3.6 Dissemination of the study findings

The findings of this study was compiled into a Dissertation to be submitted to the Department of Paediatrics and Child Health of Kairuki University and JKCI. Also, a draft manuscript of the study findings will be prepared for publication in a peer-reviewed journal for possible publication. Whenever possible the PI will present the study findings in scientific conferences.

CHAPTER FOUR: RESULTS

4.1 Study Participants

A total of 390 children with CHD were screened for eligibility to participate in the study for four months between January 2025 and April 2025. Out of them 33 (8.4%) were excluded - 22 had chromosomal syndromes, 4 were acutely ill and 7 parents did not consent to participate in the study. A total of 357 study participants were enrolled into the study this is shown in Figure 4.1 below.

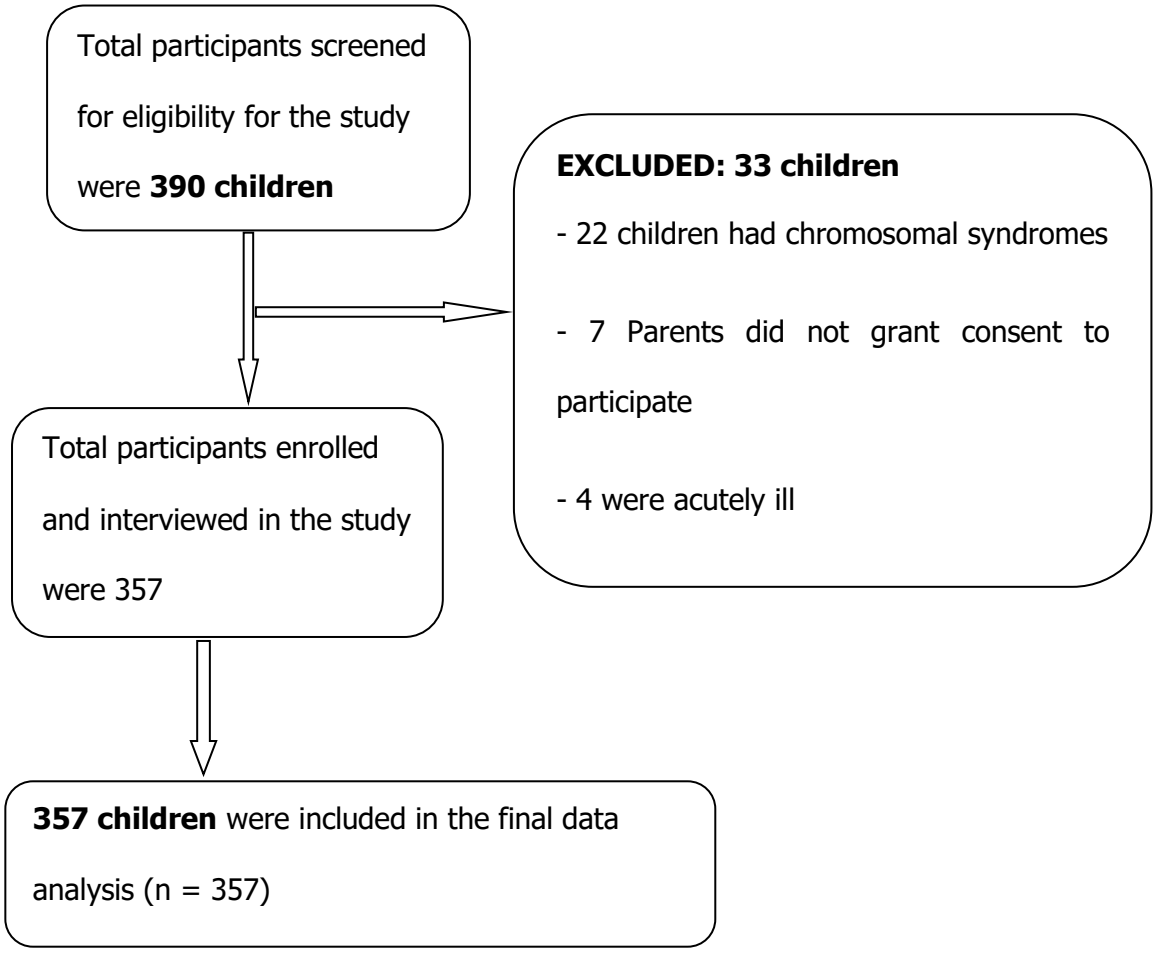

Figure 4.1: Flow chart of study participants

4.2 Baseline socio-demographic characteristics of study participants

More than a quarter 120 (33.6%) of the study participants were between ages of 0-12 months, with a male predominance 191 (53%). Most of the study participants were born at term 322 (90.2%) with normal birth weight of more than 2.5 kg 277 (77.6%), and they had no adverse birth outcome 280 (78.4%).

This is shown in Table 4.1 a below.

Table 4. 1a: Baseline socio-demographic characteristics of study participants

Variables		**Frequency, n = 357 (%)**
Study participants	0–12	120 (33.6)
Age-groups in months	13–24	95 (26.6)
	25–36	55 (15.4)
	37–48	35 (9.8)
	49–60	52 (14.6)
Gender	Male	191 (53.5)
	Female	166 (46.5)
Gestational age at delivery	Term (≥37 GA)	322 (90.2)
	Preterm(<37 GA)	35 (9.8)
Birth weight in kilograms	Normal (≥2.5)	277 (77.6)
	Low (<2.5)	80 (22.4)
Adverse outcome during delivery	No	280 (78.4)
	Yes	77 (21.6)

Exclusive breastfeeding for 6 months	≥6 months	152 (42.6)
	<6 months	205 (57.4)
Duration of breastfeeding	<6 months	89 (25.0)
	6-12 months	95 (26.6)
	13+ months	173 (48.4)
Type of congenital heart disease	Acyanotic	253 (70.9)
	Cyanotic	104 (29.1)
Oxygen saturation	Normal (≥90%)	255 (71.4)
	Severe hypoxia (<90%),	102 (28.6)
Nutritional status	Normal	209 (58.5)
	Moderate acute malnutrition	48 (13.5)
	Severe acute malnutrition	100 (28.0)
Attendance to pre-primary education	None	301 (84.3%)
	Attending ECD	56 (15.7%)

4.3 Baseline socio-demographic of parents/caretakers of study participants

Most mothers of study participants were aged 18-35 years 261 (73.1%), and the fathers 191 (53.5%). Most of the mothers had no formal education nor primary education 148 (41.4%), and fathers' education was one third of primary level, secondary and tertiary level. Most of the parents were married 321 (89.9%) and one third of mothers 113 (31.7%) were parity one. Most mothers had no history of any maternal illness 303 (84.9%).

Most were from the Eastern zone 217 (60.8%) and mostly from Dar es Salaam 167/217. This is shown in Table 4.1b below.

Table 4. 1b: Baseline socio-demographic characteristics of parents/caretakers of study participants (n= 357)

Variables		Frequency, n (%)
Mothers age group in years	18–35	261 (73.1)
	≥35	96 (26.9)
Fathers age groups in years	18–35	191 (53.5)
	≥35	166 (46.5)
Level of education of mothers	Informal/Primary education	148 (41.4)
	Secondary education	132 (37.0)
	Tertiary education	77 (21.6)
Level of education of fathers	Informal/Primary education	127 (35.6)
	Secondary education	121 (33.9)
	Tertiary education	109 (30.5)
Marital status	Married	321 (89.9)
	Unmarried	36 (10.1)
Parity	1	113 (31.7)
	2	104 (29.1)
	3	73 (20.4)
	4+	67 (18.8)
Residence zone	Central	22 (6.2)
	Eastern	217 (60.8)
	Lake	13 (3.6)
	Northern	54 (15.1)
	Southern	37 (10.4)
	Western	14 (3.9)

4.4 Primary outcome - Proportion of under-five children with neuro-developmental delay

Out of 357 study participants, 153 (42.8%) had neurodevelopment delay.

4.5 Distribution of neuro-development delay according to domains among study participants

Five domains of neuro-development were assessed among study participants. The most affected domain was gross motor in 101/153 (66 %) participants compared to other domains. Among children with neuro-developmental delay almost 83/153 (54.3 %) had more than one domain that was affected, while 70/153 (45.7 %) had only one domain that was affected. (Figure 4.2 below).

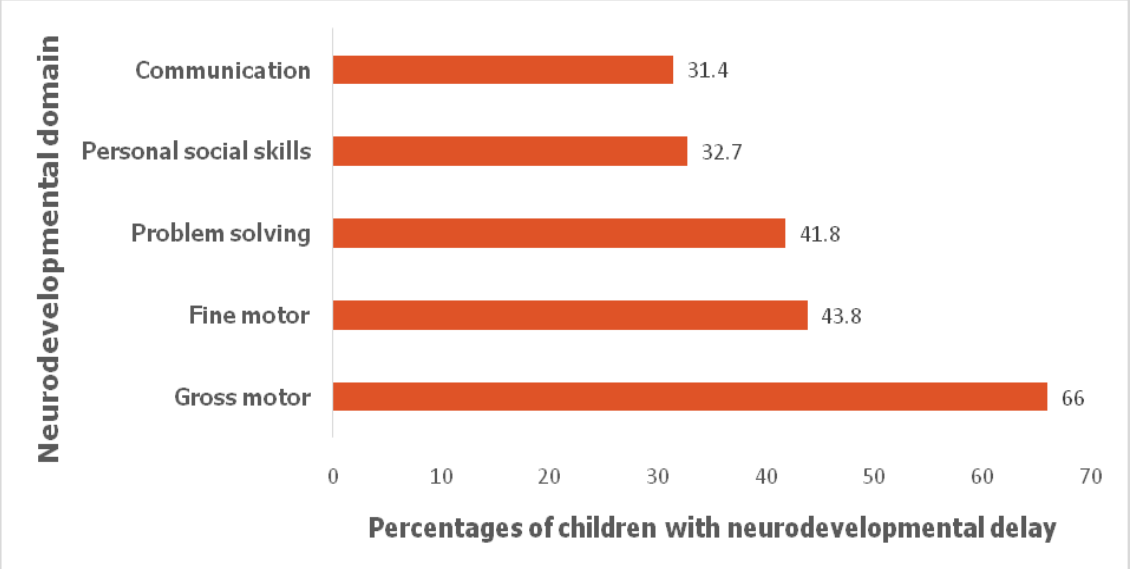

Figure 4.2: Percentage of each domain of neuro-developmental delay affected among study participants (n = 153)

4.6 Factors associated with neuro-developmental delay

In univariate analysis, the following socio-demographic and clinical characteristics of the study participants were associated with neuro-developmental delay: Type of congenital heart diseases (p-value = < 0.001), nutritional status (p-value = 0.024), level of oxygen saturation (p-value = < 0.001). This is shown in Table 2a below.

Table 4. 2a: Socio-demographic and clinical characteristics of study participants in association with neuro-developmental delay

Variables		**Neuro-developmental delay**		**Chi-square test**	**p-value**
		No	**Yes**		
Age-groups of study participants in months	0–12	71 (59.2)	49 (40.8)	5.70	0.222
	13–24	45 (47.4)	50 (52.6)		
	25–36	36 (65.5)	19 (34.5)		
	37–48	21 (60.0)	14 (40.0)		
	49–60	31 (59.6)	21 (40.4)		
Gestational age at birth	Term	183 (56.8)	139 (43.2)	0.13	0.719
	Preterm	21 (60.0)	14 (40.0)		
Birth weight in kilograms	Normal (≥2.5)	164 (59.2)	113 (40.8)	2.15	0.143
	Low (<2.5)	40 (50.0)	40 (50.0)		
Adverse outcome at delivery	No	158 (56.4)	122 (43.6)	0.27	0.603
	Yes	46 (59.7)	31 (40.3)		
Exclusive breastfeeding	≥6 months	78 (53.8)	67 (46.2)	2.72	0.099
	<6 months	118 (62.8)	70 (37.2)		
Total duration of	<6 months	56 (69.1)	25 (30.9)	5.39	0.067

breastfeeding	6-12 months	56 (58.9)	39 (41.1)		
	13+ months	84 (53.5)	73 (46.5)		
Type of congenital	Acyanotic	160 (63.2)	93 (36.8)	13.19	<0.001
heart disease	Cyanotic	44 (42.3)	60 (57.7)		
Oxygen saturation	Normal (≥90%)	170 (66.7)	85 (33.3)	33.06	<0.001
	Severe hypoxia (<90%),	34 (33.3)	68 (66.7)		
Nutritional status	Normal	132 (63.2)	77 (36.8)	7.46	0.024
	MAM	23 (47.9)	25 (52.1)		
	SAM	49 (49.0)	51 (51.0)		

MAM- moderate acute malnutrition, SAM- Severe acute malnutrition

With regard to parental socio-demographic characteristics -in univariate analysis, the following factors were associated with neuro-developmental delay: Level of education of parents (p-value =0.009); lower maternal level of education (p-value = 0.002) and lower paternal level of education (p-value = 0.009) was associated with increased risk of neuro-developmental delay in the offspring. Also children from unmarried households had a higher risk (p-value = 0.020); higher birth order (2 or more) was associated with greater risk (p-value = 0.005).This is shown in Table 4.2b below.

Table 4. 2b: The association of parental socio-demographic characteristics with neuro-developmental delay among study participants

Variables		Neuro-developmental delay		Chi-square test	p-value
		No	Yes		
Age group of mothers in years	18–35	148 (56.7)	113 (43.3)	0.08	0.783
	>35	56 (58.3)	40 (41.7)		
Age group of fathers in years	18–35	108 (56.5)	83 (43.5)	0.06	0.806
	>35	96 (57.8)	70 (42.2)		
Mothers level of education	Informal/Primary education	72 (48.6)	76 (51.4)	12.01	0.002
	Secondary education	76 (57.6)	56 (42.4)		
	Tertiary education	56 (72.7)	21 (27.3)		
Fathers level of education	Informal/Primary education	61 (48.0)	66 (52.0)	9.45	0.009
	Secondary education	69 (57.0)	52 (43.0)		
	Tertiary education	74 (67.9)	35 (32.1)		
Marital status	Married	190 (59.2)	131 (40.8)	5.45	0.020
	Unmarried	14 (38.9)	22 (61.1)		
Parity	1	79 (69.9)	34 (30.1)	12.72	0.005
	2	50 (48.1)	54 (51.9)		
	3	42 (57.5)	31 (42.5)		
	4+	33 (49.3)	34 (50.7)		

Maternal illness	No	176 (58.1)	127 (41.9)	0.73	0.394
	Yes	28 (51.9)	26 (48.1)		
Residence	Central	8 (36.4)	14 (63.6)	0.27	0.062
Zones	Eastern	127 (58.5)	90 (41.5)		
	Lake	11 (84.6)	2 (15.4)		
	Northern	26 (48.2)	28 (51.9)		
	Southern	23 (62.2)	14 (37.8)		
	Western	9 (64.3)	4 (35.7)		

4.7 Multivariate logistic regression of risk factors associated with neuro-developmental delay

On multivariate logistic regression of study participants' factors associated with neuro-developmental delay after adjusting for confounding variables; significant predictors of neuro-developmental delay were age of child, gender and attendance to pre-primary education. There were 2.4 increased odds to have neuro-developmental delay for children aged between 13-24 months; being female; while attendance to pre-primary education was found to be protective with odds 0.9 and 0.74 respectively. Also, moderate acute malnutrition has increased odds AOR = 2.87 (95% CI: 1.18–6.95), p-value = 0.020, with severe acute malnutrition AOR = 3.01 (95% CI: 1.54–5.91), p-value = 0.001; low birth weight (<2.5 kg) AOR = 2.57 (95% CI: 1.14–5.81), p-value = 0.023; cyanotic CHD AOR = 4.13 (95% CI: 2.19–7.78), p-value< 0.001. This is shown in Table 4.3a below.

**CI- Confidence Interval, COR- Crude Odds Ratio, AOR- Adjusted Odds Ratio,*

MAM- moderate acute malnutrition, SAM- Severe acute malnutrition

Table 4. 3a: **Multivariate logistic regression of study participants' characteristics in association with neuro-developmental delay**

Variable		COR (95% CI)	p-value	AOR (95% CI)	p-value
Age group of	0–12	1		1	
study participants in	13–24	1.61 (0.94-2.77)	0.086	2.45 (1.17-5.14)	0.017
months	25–36	0.76 (0.39-1.49)	0.429	0.79 (0.34-1.83)	0.583
	37–48	0.97 (0.45-2.08)	0.930	1.28 (0.42-3.88)	0.668
	49–60	0.98 (0.50-1.90)	0.956	1.80 (0.53-6.11)	0.347
Gender	Male	1		1	
	Female	0.83 (0.54-1.26)	0.375	0.91 (0.53-1.58)	0.750
Attendance to	None	1		1	
pre-primary education	Pre-primary	0.53 (0.29-0.98)	0.042	0.74 (0.23-2.37)	0.615
Gestational at	Term	1		1	
delivery	Preterm	0.88 (0.43-1.79)	0.719	0.56 (0.18-1.80)	0.334
Birth weight	Normal (≥2.5)	1		1	
	Low (<2.5)	1.45 (0.88-2.39)	0.144	2.57 (1.14-5.81)	0.023
Adverse outcome at	No	1		1	
delivery	Yes	0.87 (0.52-1.46)	0.603	1.31 (0.63-2.71)	0.474
Exclusive breastfeeding	≥6 months	1		1	
	<6 months	0.69 (0.44-1.07)	0.100	0.71 (0.38-1.32)	0.279
Total duration of	<6 months	1		1	
breastfeeding	6-12 months	1.56 (0.84-2.91)	0.162	1.26 (0.52-3.07)	0.615
	13+ months	1.95 (1.11-3.43)	0.021	2.21 (1.01-4.85)	0.047
Type of congenital heart	Acyanotic	1		1	
disease	Cyanotic	2.35 (1.47-3.74)	<0.001	4.13 (2.19-7.78)	<0.001
Oxygen saturation	Normal (≥90%)	1			

	Hypoxia (<90%),	4.00 (2.46-6.51)	<0.001		
Nutritional status	Normal	1		1	
	MAM	1.86 (0.99-3.51)	0.054	2.87 (1.18-6.95)	0.020
	SAM	1.78 (1.10-2.89)	0.019	3.01 (1.54-5.91)	0.001

Parental factors: Unmarried parents AOR = 2.78 (95% CI: 1.18–6.55), *p-value = 0.020* and parity = 2 AOR = 2.96 (95% CI: 1.44–6.09), *p-value = 0.003.* Table 4. 3b.

Table 4. 3b: Multivariable logistic regression of parental factors associated neuro-developmental delay

Variables		**COR (95% CI)**	**p-value**	**AOR (95% CI)**	**p-value**
Mothers age-groups in years	18–35	1		1	
	>35	0.94 (0.58-1.50)	0.738	0.85 (0.39-1.84)	0.678
Fathers age-groups in years	18–35	1		1	
	>35	0.95 (0.62-1.44)	0.806	1.16 (0.58-1.84)	0.670
Level of education of mothers	Informal/Primary education	1		1	
	Secondary education	0.70 (0.44-1.12)	0.136	0.67 (0.33-1.37)	0.277
	Tertiary education	0.36 (0.20-0.64)	0.001	0.33 (0.10-1.02)	0.054
Level of education of fathers	Informal/Primary education	1		1	
	Secondary education	0.70 (0.42-1.15)	0.157	0.66 (0.32-1.33)	0.242
	Tertiary education	0.44 (0.26-0.74)	0.002	0.74 (0.27-2.04)	0.561
Marital status	Married	1		1	
	Unmarried	2.28 (1.12-4.62)	0.022	2.78 (1.18-6.55)	0.020
Parity	1	1		1	
	2	2.51 (1.44-4.38)	0.001	2.96 (1.44-6.09)	0.003

	3	1.71 (0.93-3.17)	0.085	1.11 (0.46-2.67)	0.810
	4+	2.39 (1.28-4.47)	0.006	2.12 (0.82-5.46)	0.121
Maternal illness	No	1		1	
	Yes	1.29 (0.72-2.30)	0.395	0.86 (0.64-2.99)	0.408
Residence	Central	1		1	
Zones	Eastern	0.40 (0.94-2.77)	0.051	0.45 (0.16-1.31)	0.143
	Lake	0.10 (0.39-1.49)	0.011	0.12 (0.02-0.88)	0.037
	Northern	0.62 (0.45-2.08)	0.351	0.66 (0.20-2.26)	0.511
	Southern	0.34 (0.39-1.49)	0.058	0.37 (0.10-1.41)	0.144
	Western	0.32 (0.45-2.08)	0.107	0.18 (0.03-1.08)	0.061

CHAPTER FIVE: DISCUSSION

5.1 Overall prevalence of neuro-developmental among study participants

The overall prevalence of neuro-developmental delay among study participants with congenital heart diseases at JKCI is high particularly, among those with cyanotic CHD and those with malnutrition and low birth weight. Malnutrition, notably, tripled the odds of neuro-developmental delay, underscoring the critical role of appropriate infant and young child nutritional interventions. Similarly, young age (13–24 months), low birth weight, and longer breastfeeding period (possibly reflective of underlying socio-economic or health issues) were associated with higher odds of developmental delay. The association between cyanotic CHD and neuro-developmental delay is consistent with existing literature, likely due to chronic hypoxia's detrimental effects on brain development. Additionally, social determinants such as parental marital status and level of education highlight the importance of comprehensive approach to the management and care of children with congenital heart disease.

5.2 Proportion of neuro-developmental delay

In this study almost half of study participants had neuro-developmental delay. This is in keeping with the studies done in United Kingdom and United States of America which showed the proportion of neuro-development delay ranging between 42% - 44% (47, 54). In Asia, a study done in India by Maya et al showed that 32% had neuro-developmental delay (44), which is

lower compared to this study. This may be because the study had a smaller sample size of 100 participants and used a different tool.

In Africa data is scarce; however, risk may be higher due to limited access to early diagnosis, interventions and cardiac surgery. Studies suggest under-diagnosis of neuro-developmental delay in the region. (68, 69)

Studies done in India showed 22% more neuro-developmental delay in cyanotic CHD (44), which is in keeping with this study which had 20.9% more neuro-developmental delay in cyanotic CHD.

A study done in Ethiopia by Badawi et al showed 46% had neuro-developmental delay among children of the same age group with CHD; consisted with this study (42).

5.3 Neuro-developmental delays and its domains

A study done in India had the prevalence of pre-operative motor and mental delay in 32% and 26.9% of the children (44), this is in keeping with this study where gross motor delays were 28.3%, but mental delay was less (17.9%). This could be due to the facts the children enrolled in the study were in critical condition eligible for open heart surgery. Also results from a study done in Ethiopia is not in keeping with this study as motor domain was most affected by 42% and in this study it is only 28%; nonetheless it is the most affected domain. This could be due to the fact that different tools were used (42).

The same study in India had more than three affected developmental domains, 69% of the infants were classified as having severe developmental delay and 30% as having moderate developmental delay, given that they had one or two affected developmental domains; it is not the same in this study as more 19.6% had only one domain that is affected, and only a few study participants 2-4% had more than three domains that affected. This could be due to the fact the study in India involved critical CHD patients who were to be operated for open heart surgery.

5.4 Neuro-developmental delay and associated risk factors

In this study, the independent associated risk factors for neuro-developmental delay included child's age, malnutrition, low birth weight, low oxygen saturation and type of CHD. There was also higher risk of neuro-developmental delay among children aged 13-24 months, this is in keeping with studies done in USA (55, 56) where neuro-developmental delay prevalence in children with CHD varies with age, particularly in early childhood. Children in late childhood may be more vulnerable to neuro-developmental delay and hence the need for long-term follow-up and screening for neuro-developmental delay.

Being female was protective in this study which is consistent with study from Canada which showed among school-age children with CHD boys were significantly more likely to have fine motor delay (57 - 65). Also, a Danish study noted that compared to girls, boys with CHD had greater incidence

rates of mental health disorders (66). Although these studies had different study participants but they had the similar results. There are different hypothesis with gender difference in CHD, such as respond to stressors during foetal life, foetal stress factors, hormonal, genetic, epigenetic and environmental factors affecting heart development (67).

Malnutrition in this study showed significant higher risk of neuro-developmental delay, which is in keeping with a study in South Africa that found that malnutrition was strongly associated with poorer motor development, though they had used different tools used, but had same age-group of children which gave same results (56). Another study done in Ethiopia showed severe stunting to be a risk factor for neuro-developmental delay in children with CHD. Many studies did not show the relationship between malnutrition and neuro-developmental delay, but a several studies showed high prevalence of malnutrition in developed and developing countries among children with CHD (43, 60). Malnutrition impairs brain development through several mechanisms; micronutrient deficiency of iron, zinc, and iodine which disrupt myelination and neurotransmitter synthesis; inadequate caloric intake hampers synapse formation and overall brain growth and malnourished children are more susceptible to infections, which can further impede neurodevelopment (67).

Low birth weight had increased risk of neuro-developmental delay; this is in keeping with a study done in Washington, USA examining LBW infants with CHD found that nearly half had exhibited neuro-developmental delay by age

two years, particularly in language skills (61). Also another study done in Japan showed infants with CHD and very-low birth weight showed significant deficits in language, cognition, and motor skills compared to healthy controls, which is consistent with our findings; though our study had very few very low birth weight infants (67). Children with cyanotic CHD were more likely to have neuro-developmental delay. A study in Turkey showed cyanotic CHD 34.4% had moderate or mild mental retardation, and 41.6% had mild to severe psychomotor retardation compared to healthy controls (62). In India, a study found that children with cyanotic CHD had significantly lower motor development quotients compared to those with acyanotic CHD, indicating a higher risk for developmental delay (43). These studies are in keeping with this study due to the fact that less oxygenated blood gets into brain cells and results in neuro-developmental delay.

Traditionally, longer periods of breastfeeding is associated with improved neuro-developmental outcome**,** especially in the general paediatric population. Breast milk provides essential nutrients (e.g. DHA, ARA) critical for brain development (69). However, this study among children with CHD reveals the opposite trend, where longer periods of breastfeeding duration correlates with higher risk of neuro-developmental delay. This could possibly be explained by the fact that children who were sicker or had more severe forms of CHD (e.g. cyanotic CHD) might have been breastfed longer due to parental perception of vulnerability.

In fact, cyanotic CHD itself was strongly associated with neuro-developmental delay (AOR = 4.13, $p < 0.001$). Also it is possible that prolonged exclusive breastfeeding without adequate complementary feeding (common in low-resource settings) might lead to nutritional deficiencies**,** especially iron, zinc, and acute malnutrition - all linked to delayed neuro-development. While tertiary maternal education was protective (AOR = 0.33, $p = 0.054$), the adjustment may not fully eliminate all confounding. Longer breastfeeding in itself is not necessarily harmful, but in this population, it may be a proxy indicator of underlying medical, nutritional, or socio-economic vulnerabilities contributing to neuro-developmental delay.

5.5 Neuro-developmental delay and parental-associated risk factors

Low level of education of parents had increased risk of neuro-developmental delay among children with CHD. This is in keeping with a study done in India, which showed that maternal literacy was strongly linked to better cognitive and motor scores in children under-five years of age (64). Also a study that was done in Kenya among 2,000 children, low maternal education was one of the strongest predictors of developmental delay, even after adjusting for poverty and malnutrition (65). All the above two studies were not specifically done in children with CHD, as to the best of my ability I couldn't get similar studies done in similar population. Hence the need for further studies to understand the effect of the level of education of parents to neuro-development.

Children from unmarried households were nearly three times more likely to experience neuro-developmental delay. This is in keeping with National Survey in USA -NSCH 2016–2018) where children in single-parent households had higher rates of developmental delay and behavioural problems (66). Also UNICEF in 2020 showed single-parent status is a consistent risk factor for poor child development outcome when compounded by poverty and lack of social support (67). All the above were not specifically studied in CHD children. Hence further studies may be required to understand the marital status related factors. In the local context, unmarried parents would lead to single parenting whereby the mother might not have the financial resources and support from the father, which could explain neuro-developmental delay in the long run.

Parity of 2 or more remains a significant predictor of neuro-developmental delay in CHD children in this study. A study in India showed high parity was associated with lower developmental scores, particularly in language and motor skills (65), and a study done in Pakistan showed children of mothers with ≥3 children were more likely to experience delayed milestones, partly due to maternal exhaustion and financial constraints (67). Also, a study in Kenya showed children in households with higher birth order showed significantly increased risk of developmental delay (68). Again, all the above studies were not specifically done in CHD children; therefore further studies may be required to understand the birth order and parity related factors.

The Lake Zone has higher risk of neuro-developmental delay compared to all other zones in Tanzania, this could be due to its geographically remote location from specialized paediatric cardiac services (e.g. JKCI in Dar es Salaam). Delayed diagnosis and late surgical or medical intervention for CHD may lead to prolonged hypoxia, malnutrition, and poor developmental stimulation, all of which are risk factors for neuro-developmental delay (no published report). Cultural practices influencing child-rearing, nutrition, and health-seeking behavior may contribute to developmental outcomes. For instance, delayed initiation of complementary feeding or traditional beliefs that discourage seeking formal medical care early. The region has lower maternal education levels, poor caregiver knowledge of child development, and limited access to early childhood stimulation programs. The significantly higher prevalence of neuro-developmental delay among children from the Lake Zone suggests that geographical disparities play a major role in child health outcomes in Tanzania. This finding highlights the urgent need to reduce inequities in healthcare access, early diagnosis, and developmental support services, particularly in underserved regions.

5.6 Strengths and limitations

This study is among the first in Tanzania to examine the prevalence and risk factors of neuro-developmental delay in children with congenital heart disease. It addresses a critical knowledge gap in a vulnerable population, contributing valuable evidence to guide policy and clinical practice.

The use of an adequate sample size (n=357) and systematic sampling enhances the reliability of the findings and reduces selection bias. Study participants were drawn from diverse regions of Tanzania, increasing the generalizability of the results.

Neuro-developmental delay was assessed using the Ages and Stages Questionnaire, third edition (ASQ-3), a widely used and validated screening tool. This enhances the validity of the developmental assessments and allows comparability with global literature. The study employed both univariate and multivariate logistic regression analyses to identify independent risk factors for neuro-developmental delay. This analytical approach increases the accuracy of identifying predictors while adjusting for confounders. The study collected detailed socio-demographic, nutritional and clinical data, providing a wide range of the multiple risk factors influencing neuro-development in CHD patients.

Limitations

The Study was conducted at a single tertiary care facility (JKCI) in Dar es Salaam. While JKCI serves as a referral center for the entire country, the findings may not fully represent the broader population, especially rural communities with limited access to specialized care.

The use of a cross-sectional study design limits the ability to establish causality between identified risk factors and neuro-developmental delay.

Longitudinal follow-up provided better insight into developmental trajectories.

Information on maternal health, birth history, and breastfeeding duration relied on caregiver recall, which may be subject to memory errors or social desirability bias.

5.7 Conclusions

The study highlights a significant public health concern: neuro-developmental delay among under-five children with congenital heart diseases in Tanzania conducted at Jakaya Kikwete Cardiac Institute. The study showed that nearly half of children with congenital heart diseases had neuro-developmental delay.

The main risk factors independently associated with neuro-developmental delay include low birth weight, young age of children less than two years, malnutrition, cyanotic congenital heart diseases, single mothers, multi-parity and low level of education of parents.

The findings emphasize that neuro-developmental delay among children with congenital heart diseases is a result of complex interaction between medical and social determinants.

5.8 Recommendations

The following are recommendations to address the problem of neuro-developmental delay among children with congenital heart diseases:

1) Screening for neuro-developmental delay among children with congenital heart disease should be routinely done at paediatric outpatient clinic at JKCI in order to identify affected children very early and to initiate timely intervention and long-term monitoring. Special emphasis should be given to care of low birth weight children; children aged less than two years of age; those with cyanotic congenital heart disease; with malnutrition and living with a single mother.
2) Parents and caretakers should be counseled about neuro-developmental delay and options for therapeutic interventions as well as psychosocial support and educational support programs to enhance development of children that have congenital heart diseases and neuro-developmental delay.
3) Further longitudinal studies should be planned to identify in-depth the development trajectory and long term quality of life in children having CHD with neurodevelopmental delay

In conclusion, neuro-developmental delay is a substantial but modifiable burden among children with congenital heart diseases in Tanzania. With strategic, evidence-based interventions and policy support, early detection and appropriate care can significantly enhance developmental trajectories and long-term quality of life for these children. The study provides a foundation for national strategies aimed at integrating neuro-developmental care into paediatric cardiology services and calls for further research to

explore long-term outcomes of neurodevelopmental delays and intervention effectiveness in this population.

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APPENDICES

APPENDIX 1: INFORMED CONSENT

FOR STUDY "NEURO-DEVELOPMENTAL DELAY AND ASSOCIATED RISK FACTORS AMONG UNDER FIVES WITH CONGENITAL HEART DISEASE ATTENDING JAKAYA

KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA."

Introduction: I'm Ahlam Awadh Mbarak, a medical doctor pursuing degree in Master of Pediatrics and Child Health at Kairuki University. I am conducting research on NEURODEVELOPMENTAL DELAY AND ASSOCIATED RISK FACTORS AMONG UNDER-FIVE CHILDREN WITH CONGENITAL HEART DISEASE AT THE JAKAYA KIKWETE CARDIAC INSTITUTE, DAR ES SALAAM, TANZANIA. This study will provide the proportion and understanding of the risk factors of neuro-developmental delays among under-five with congenital heart disease and also provide general emphasis on the importance of screening for neurodevelopment in clinics using available and validated tools. Confidentiality will be maintained, and only study numbers (rather than names) will be used in questionnaires in order to safeguard your privacy. I will appreciate it if you agree to participate in this research because your response and views are very important.

Purpose of the Study: This study aims to determine the prevalence and understand the associated factors of neuro-developmental delays in under-five children with congenital heart disease. If you accept to take part in the study, you will be asked some questions on demographic information,

assessing the neurodevelopment delay, and also associated factors with neurodevelopment. The information that you will provide will be confidentially handled and protected in such a way that nobody will be able to access it, but only the general information that will be used purposefully for health-related issues.

How to participate: Parents or guardians who will be ready to allow their children to participate will sign an assent and consent form to approve his or her willingness.

Possible benefits: Your involvement in this study will be helpful in making an evaluation and assisting in planning for health care improvement of neurodevelopment delay in under-5 children with congenital heart disease in Tanzania.

Possible Risks: There are no physical risks or discomforts expected to happen to your child during or even after participation in this study because the study only involves collecting information and taking anthropometric measurements.

Financial benefit: There is no financial benefit that you will receive or pay for by participating in the study.

Confidentiality: Your child's information will be kept confidential. Questionnaires will be marked with a special number without involving registration numbers or names. Nobody will be able to access the information you provide in the questionnaire. Your child's information will remain confidential during and after study work.

Voluntary Participation and Rights to Withdraw: Your child's participation is voluntary, and you have the right to withdraw your child's information during the study. Your decision will be respected, and no right to health services will be denied to you by denying your participation.

Whom to Contact: In case of any question or query concerning this study, please contact the principal investigator, Dr. Ahlam Awadh Mbarak, from the Department of Pediatrics and Child Health, KU, P.O. Box 65300, Dar es Salaam, mobile number 0788230314. If you have any questions about your rights as a participant, you may contact Ms. A. Pallangyo, IREC secretary, KU, P.O. Box 65300, Dar es Salaam, Tanzania, Tel. 0682074620

Participation agreement: I have read the contents of this form and understand them, and my questions have been adequately answered. I agree with my child's participation in this study.

Signature of parent or guardian's

participant……..Date……

Signature of researcher …… Date……

APPENDIX 2: INFORMED CONSENT (Swahili version)

FOMU YA RIDHAA KUSHIRIKI KATIKA UTAFITI WA "UCHELEWEFU WA MAENDELEO YA MISHIPA NEVA HUSIKA MIONGONI MWA WATOTO CHINI YA MIAKA MITANO WENYE UGONJWA WA MOYO WANAOHUDHURIA TAASISI YA MOYO YA JAKAYA KIKWETE, DAR ES SALAAM, TANZANIA."

Utambulisho: Habari, mimi ni daktari Ahlam AwadhMbarak, mwanafunzi wa shahadaya uzamili wa Udaktari wa watoto katika Chuo Kikuu cha Kairuki (KU). Kwaniaba ya Chuo Kikuu cha Kairuki (KU), ninafanya utafiti juu ya ukubwa wa uchelewefu wa maendeleo ya mishipa neva miongoni mwa watoto chini ya miaka mitano wenye ugonjwa wa moyo wanaohudhuria taasisi ya moyo ya Jakaya Kikwete, Dar es Salaam, Tanzania.

Kusudi la Tafiti: Tafiti hii ina lengo la kugundua ukubwa wa tatizo la uchelewefu wa maendeleo mishipa neva miongoni mwa watoto chini ya miaka mitano wenye ugonjwa wa moyo. Ikiwa utakubali mtoto wako kua sehemu ya tafiti hii, utaulizwa maswali katika dodoso juu ya taarifa zake binafsi, kutathmini ucheleweshaji wa maendeleo ya neva na pia mambo yanayohusiana na ucheleweshaji wa maendeleo ya. Taarifa utakazotoa za motto wako zitatunzwa kwa usiri na zitalindwa na hamna mtu atakayeweza kupata taarifa zako.

Jinsi ya kushiriki: mzazi au mlezi wa mhusika atakaekua tayari kushirikI katika tafiti hii atasaini fomu hii ya makubaliano kama ushahidi wa ukubali wake.

Faida: Kushiriki kwako katika tafiti hii itasaidia kufanya maamuzi na kusaidia kupanga namna ya kuongeza uwazi juu ya ugonjwa wa uchelewefu wa maendeleo mishipa neva miongoni mwa watoto chini ya miaka mitano wenye ugonjwa wa moyo ili kuona ukubwa wa tatizo lake na kuondokana na tatizo hili nchini Tanzania

Athari: Hakuna athari yoyote utakayopata kwa kushiriki katika tafiti hii. Una hakiya kukubali au kukataa kushiriki katika tafiti hii baada ya kuwa umesoma na kuelewa fomu hii. Uchaguzi wa kukataa hauto adhiri kwa namna yoyote ile haki yako ya upatikanaji ya huduma za afya. Maamuzi yako yataheshimiwa na kuzingatiwa.

Faida kifedha: Hakuna faida yoyote utakayo ipata kifedha kwa kukubali kushiriki katika tafiti.

Usiri: Taarifa zote zitakazo kusanywa katika utafiti huu zitatunzwa kwa usiri mkubwa. Taarifa hizi hazitawekwa wazi, namba maalumu zitatumika kuhifadhi taarifa hizo ambazo zitawakilisha jina lako. Mtu yeyote hatoweza kupata taarifa zako binafsi utakazo toa katika utafiti huu. Taarifa zote utakazo toa zitahifadhiwa kwa siri.

Utayari wakushiriki au kujitoa: Kushiriki kwako ni hiyari na unaweza kujitoa kwenye Usajili wakati wowote. Unaweza kuamua kushiriki katika tafiti hii baada ya kusoma na kuelewa fomu hii. Maamuzi yako yata heshimiwa na haita kunyima haki yako yoyote kwa kujitoa kwako.

Mawasiliano: Ili kuhojiwa au swali lolote kuhusu utafiti huu, tafadhali wasiliana na mtafiti mkuu, Ahlam Awadh Mbarak, kutoka katika idara ya

Watoto, Chuo kikuu cha Kairuki, P.O.BOX 65300, Dar es Salaam, namba ya simu 0788230314. Ikiwa una swali lolote kuhusu haki yako kama mshiriki unaweza kuwasiliana na Bibi A. Pallangyo, Katibu wa tafiti, Chuo Kikuu cha Kairuki, P.O. Box 65300, Dar es Salaam, Tanzania, Namba ya simu 0682074620.

Ridhaa kushiriki katika utafiti: Mimi …… nimeelezwa/ nimesoma yaliyomo katika fomu hii na nimeelewa maana yake. Nakubali kushiriki katika utafiti huu.

Saini yamzazi/mlezi wa mshiriki …….. Tarehe…….

Saini ya mtafiti ……..... Tarehe……

APPENDIX 3: QUESTIONAIRE

QUESTIONNAIRE FOR STUDY "NEURO-DEVELOPMENT DELAY AND ASSOCIATED RISK FACTORS AMONG UNDER FIVE WITH CONGENITAL HEART DISEASE AT JKCI, DAR ES SALAAM, TANZANIA."

PART 1A- Child's demographic characteristics.

ID number: ……..

1. Age: …….
2. Gender a) Male b) Female
3. Education level a) None b)Nursery/KG
4. Residential Region: ……
5. Anthropometric measurements: a) Weight (kg)……b) Length/Height (cm) ……..
6. Pulse oximeter readings %: ……..
7. Birth outcomes at birth; a) uneventful b) birth asphyxia c) jaundice d) infections e)respiratory distress f) others …….
8. Child gestation age at birth; a) preterm b) term c) post-term
9. Birth weight: ……kg
10. Duration of breastfeeding: a) exclusive BF ……months
    b) Total duration of BF……months c) not BF.
11. Specific CHD type per echocardiogram.....
12. Type of CHD a. cyanotic b. acyanotic

PART 1B- <u>Parent's/Caretaker's demographic characteristics</u>

1. Age: Mother's age…….. Father's age ……..
2. Level of education: Mother……Father……
3. Occupation: Mother……Father……
4. Marital status:……
5. Parity:……
6. History of maternal illness:
    a) TORCH'S disease if yes which one? .....
    b) DM
    c) Obesity
    d) Others…..
7. Mother smoked while pregnant? a)Yes b)No

    If yes, how many cigarettes per day……
8. History of alcohol intake during pregnancy? a)Yes b)No

    If yes how many glasses/ bottles per day……..
9. Any drugs taken during pregnancy for chronic illness? a)Yes b)No

        If yes……..

Appendix 4: Questionnaire in Swahili

DODOSO LA KUJIFUNZA "UCHELEWEFU KWA MAENDELEO YA MISHIPA NEVA NA MAMBO YA HATARI MIONGONI MWA MIAKA CHINI YA TANO WENYE UGONJWA WA MOYO WANAOHUDHURIA TAASISI YA MOYO YA JAKAYA KIKWETE, DAR ES

SALAAM, TANZANIA."

SEHEMU 1A : Taarifa za mtoto

Nambari ya Utambulisho: ……..

1. Umri: ……..

2. Jinsia a) Mwanaume b) Mwanamke

3. Kiwango cha elimu a) Hakuna b)Nursery/KG

4. Eneo la Makazi: ……

5. Vipimo vya kianthropometriki: a) Uzito (kg)……. b) Urefu (cm) ……..

6. Usomaji wa 'pulse oximeter' % : ……..

7. Matokeo ya wakati wa kuzaliwa; a) hamna tukio b) kukosa hewa wakati wa kuzaliwa c) manjano d) maambukizo ya bakteria e) shida ya kupumua f) vengine …….

8. Umri wa ujauzito wa mtoto wakati wa kuzaliwa; a) kabla ya muda b) wakati timilifu c) baada ya muda……..wiki

9. Uzito wa kuzaliwa: ……kg

10. Muda wa kunyonyesha: a)ziwa pekee …… miezi b) Jumla ya muda wa kunyoyesha……. c) kutonyonyeshwa.

11. maraadhi ya moyo iligunduliwa lini? ..... wiki/miezi/miaka.

12. Aina maalum ya maradhi ya moyo kwa kipimo cha 'echocardiogram'.....

13. Aina ya maradhi ya moyo a. ubuluu b. Bila ubuluuu

SEHEMU YA 1B- Sifa za demografia za Mzazi/Mlezi

Umri: Umri wa mama…… Umri wa baba …….

2. Kiwango cha elimu: Mama……Baba……

3. Kazi: Mama……

4. Hali ya ndoa: ……

5. Mimba ya ngapi:……

6. Historia ya ugonjwa wakati wa mimba.

a)Magonjwa ya 'TORCH' kama ndiyo upi au yepi? .....

b) kisukari

c) Unene kupita kiasi

d) venginevyo.....

7. Mama alivuta sigara akiwa mjamzito? A. Ndiyo B. Hapana

Kama ndiyo, ni sigara ngapi kwa siku ……

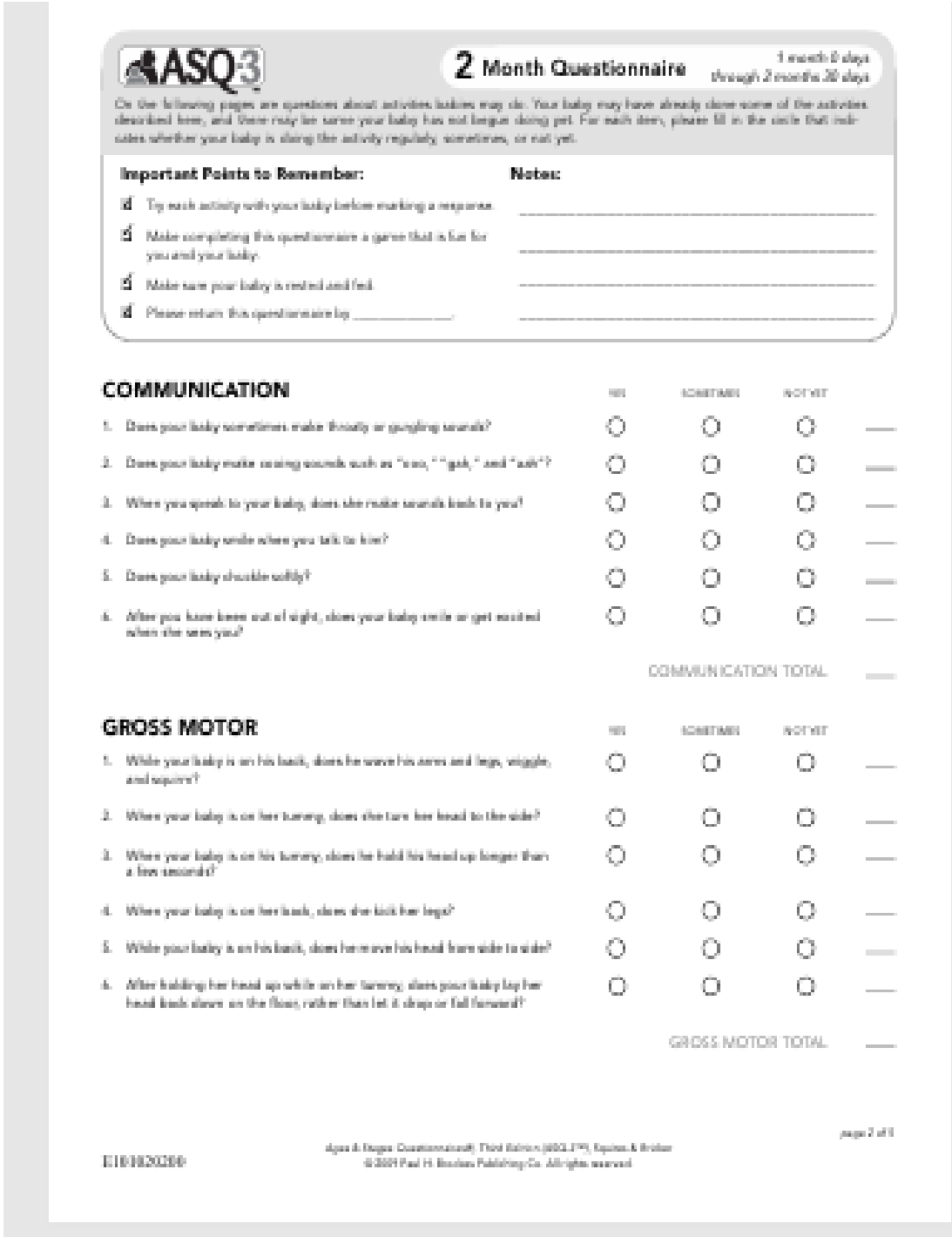
8. Historia ya unywaji wa pombe wakati wa ujauzito? A. Ndiyo B. Hapana

Kama ndio glasi/chupa ngapi kwa siku ……..

9. Dawa yoyote iliyochukuliwa wakati wa ujauzito kwa ugonjwa wa muda mrefu? A. Ndiyo B. Hapana

Kama ndiyo……..

Appendix 5: ASQ Questionnaire SAMPLE



ASQ-3

2 Month Questionnaire

1 month 0 days through 2 months 30 days

On the following pages are questions about activities babies may do. Your baby may have already done some of the activities described here, and there may be some your baby has not begun doing yet. For each item, please fill in the circle that indicates whether your baby is doing the activity regularly, sometimes, or not yet.

Important Points to Remember:

- Try each activity with your baby before marking a response.
- Make completing this questionnaire a game that is fun for you and your baby.
- Make sure your baby is rested and fed.
- Please return this questionnaire by _____.

Notes:

_____

_____

_____

_____

COMMUNICATION

	YES	SOMETIMES	NOT YET	
1. Does your baby sometimes make throaty or gurgling sounds?	○	○	○	___
2. Does your baby make cooing sounds such as "coo," "gah," and "ooh"?	○	○	○	___
3. When you speak to your baby, does she make sounds back to you?	○	○	○	___
4. Does your baby smile when you talk to him?	○	○	○	___
5. Does your baby chuckle softly?	○	○	○	___
6. After you have been out of sight, does your baby smile or get excited when she sees you?	○	○	○	___

COMMUNICATION TOTAL ___

GROSS MOTOR

	YES	SOMETIMES	NOT YET	
1. While your baby is on his back, does he wave his arms and legs, wiggle, and squirm?	○	○	○	___
2. When your baby is on her tummy, does she turn her head to the side?	○	○	○	___
3. When your baby is on his tummy, does he hold his head up longer than a few seconds?	○	○	○	___
4. When your baby is on her back, does she kick her legs?	○	○	○	___
5. While your baby is on his back, does he move his head from side to side?	○	○	○	___
6. After holding her head up while on her tummy, does your baby lay her head back down on the floor, rather than let it drop or fall forward?	○	○	○	___

GROSS MOTOR TOTAL ___

page 2 of 5

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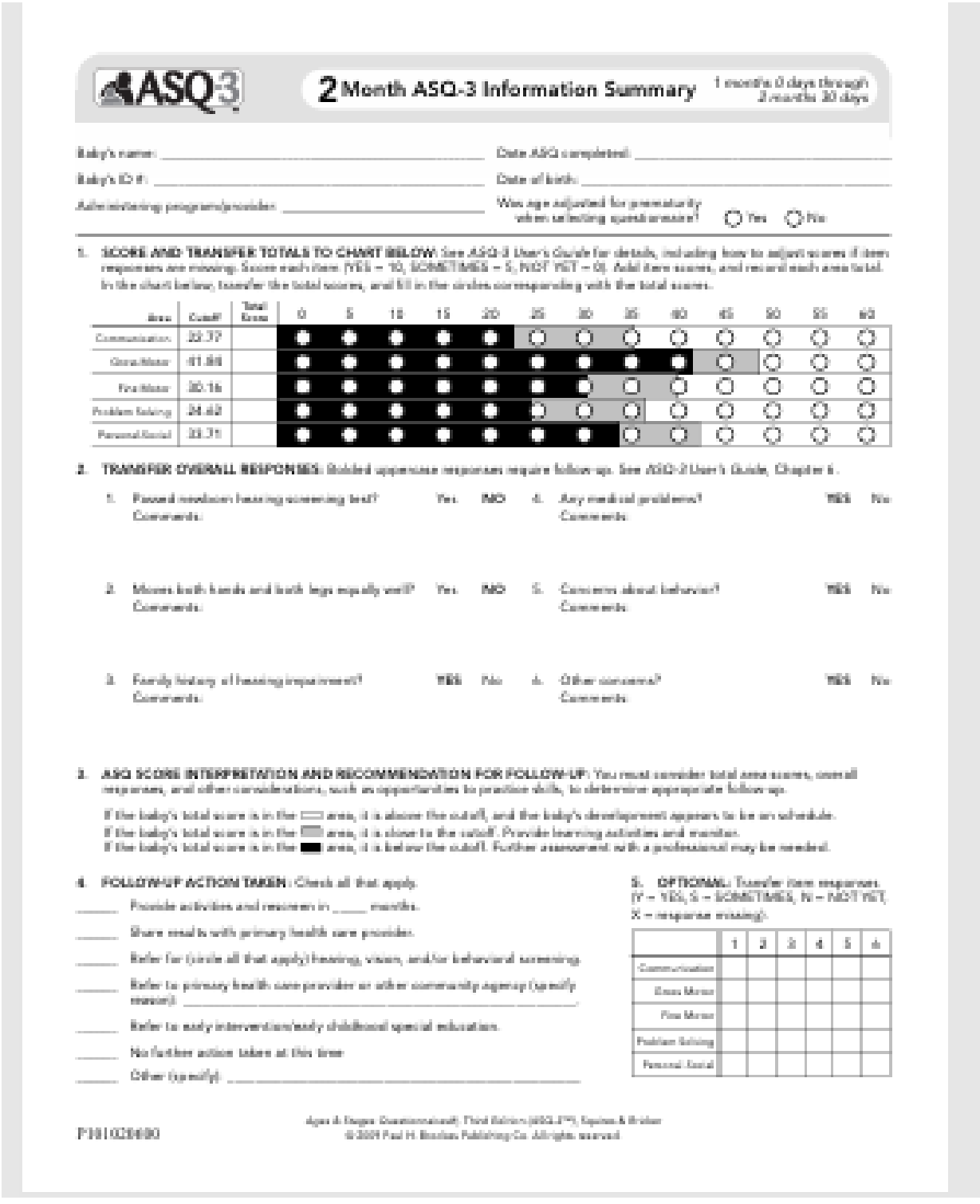
Appendix 6: ASQ-3 SAMPLE SCORE AND INTERPRETATION



ASQ-3

2 Month ASQ-3 Information Summary

1 months 0 days through 3 months 30 days

Baby's name: _____ Date ASQ completed: _____

Baby's ID #: _____ Date of birth: _____

Administering program/provider: _____ Was age adjusted for prematurity when selecting questionnaire? ◯ Yes ◯ No

1. **SCORE AND TRANSFER TOTALS TO CHART BELOW:** See *ASQ-3 User's Guide* for details, including how to adjust scores if item responses are missing. Score each item: YES = 10, SOMETIMES = 5, NOT YET = 0. Add item scores, and record each area total. In the chart below, transfer the total scores, and fill in the circles corresponding with the total scores.

Area	Cutoff	Total Score	0	5	10	15	20	25	30	35	40	45	50	55	60
Communication	22.37		●	●	●	●	●	○	○	○	○	○	○	○	○
Gross Motor	41.88		●	●	●	●	●	●	●	●	●	○	○	○	○
Fine Motor	30.16		●	●	●	●	●	●	●	○	○	○	○	○	○
Problem Solving	24.62		●	●	●	●	●	○	○	○	○	○	○	○	○
Personal-Social	33.31		●	●	●	●	●	●	●	○	○	○	○	○	○

2. **TRANSFER OVERALL RESPONSES:** Bolded uppercase responses require follow-up. See *ASQ-3 User's Guide*, Chapter 6.

1. Passed newborn hearing screening test? Yes **NO** — Comments:
2. Moves both hands and both legs equally well? Yes **NO** — Comments:
3. Family history of hearing impairment? **YES** No — Comments:
4. Any medical problems? **YES** No — Comments:
5. Concerns about behavior? **YES** No — Comments:
6. Other concerns? **YES** No — Comments:

3. **ASQ SCORE INTERPRETATION AND RECOMMENDATION FOR FOLLOW-UP:** You must consider total area scores, overall responses, and other considerations, such as opportunities to practice skills, to determine appropriate follow-up.

If the baby's total score is in the ▭ area, it is above the cutoff, and the baby's development appears to be on schedule.
If the baby's total score is in the ▨ area, it is close to the cutoff. Provide learning activities and monitor.
If the baby's total score is in the ■ area, it is below the cutoff. Further assessment with a professional may be needed.

4. **FOLLOW-UP ACTION TAKEN:** Check all that apply.

_____ Provide activities and reassess in _____ months.
_____ Share results with primary health care provider.
_____ Refer for (circle all that apply) hearing, vision, and/or behavioral screening.
_____ Refer to primary health care provider or other community agency (specify reason): _____
_____ Refer to early intervention/early childhood special education.
_____ No further action taken at this time.
_____ Other (specify): _____

5. **OPTIONAL:** Transfer item responses. (Y = YES, S = SOMETIMES, N = NOT YET, X = response missing).

	1	2	3	4	5	6
Communication						
Gross Motor						
Fine Motor						
Problem Solving						
Personal-Social						

P101020690

Ages & Stages Questionnaires®, Third Edition (ASQ-3™), Squires & Bricker

APPENDIX 7: ETHICAL CLEARANCE

KAIRUKI UNIVERSITY (KU)

70 Chwaku Street,
Mikocheni,
P.O BOX 65300,
Dar es Salaam,
Tanzania.

Tel: +255-22-2700021/4
Fax: +255-22-2775591
Email: inec@ku.ac.tz
Website: www.ku.ac.tz

Ref. No. KU/IREC/27.10/490

7th January, 2025

Dr. Ahlam Awadh Mbarak,
Kairuki University,
70 Chwaku Street,
Mikocheni,
P. O. Box 65300,
Dar es Salaam, Tanzania.

RE: ETHICAL CLEARANCE CERTIFICATE FOR CONDUCTING HEALTH RESEARCH

I am pleased to inform you that the research titled: **Neurodevelopmental Delay and Associated Risk Factors among under five Children with Congenital Heart Disease Attending Jakaya Kikwete Cardiac Institute, Dar es Salaam, Tanzania (Mbarak A. A., 2024)** has been granted ethical approval.

This approval is in effect for one year from the above date. Any changes in the procedures should be reported to the Institutional Research Ethics Committee. Significant changes will require the submission of a revised request for ethical approval. You will be required to submit **a study progress report** every six months.

Permission to publish your findings should be sought from the National Institute for Medical Research (NIMR) before submission to a publisher and not concurrently.

CHAIR PERSON
Name: Prof. Frederick Kajage
Signature:

SECRETARY
Name: Prof. Columba Mbekenga
Signature:

DIRECTOR POSTGRADUATE STUDIES AND RESEARCH INSTITUTE
KAIRUKI UNIVERSITY
P. O. Box [illegible], DSM

APPENDIX 8: PERMISSION LETTER

UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

JAKAYA KIKWETE CARDIAC INSTITUTE
(JKCI)

JAKAYA KIKWETE CARDIAC INSTITUTE

In reply please quote;
Ref No: AB.123/307/01L/40

15/01/2025

Dr. Ahlam A. Mbarak
MMED in Paediatrics and Child Health
Kairuki University (KU)

RE: PERMISSION TO CONDUCT RESEARCH AT JKCI

Reference is made to your letter requesting to do a research study entitled **"Neurodevelopment Delay and Associated Risk Factors Among Under Five with Congenital Heart Disease at JKCI, 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. However, the institution also requires you to have JKCI local co-supervisor.

It is our sincere hope that you will adhere strictly to the rules and regulations governing good clinical practice. Your compliance with these standards will ensure the integrity and ethical conduct of your study.

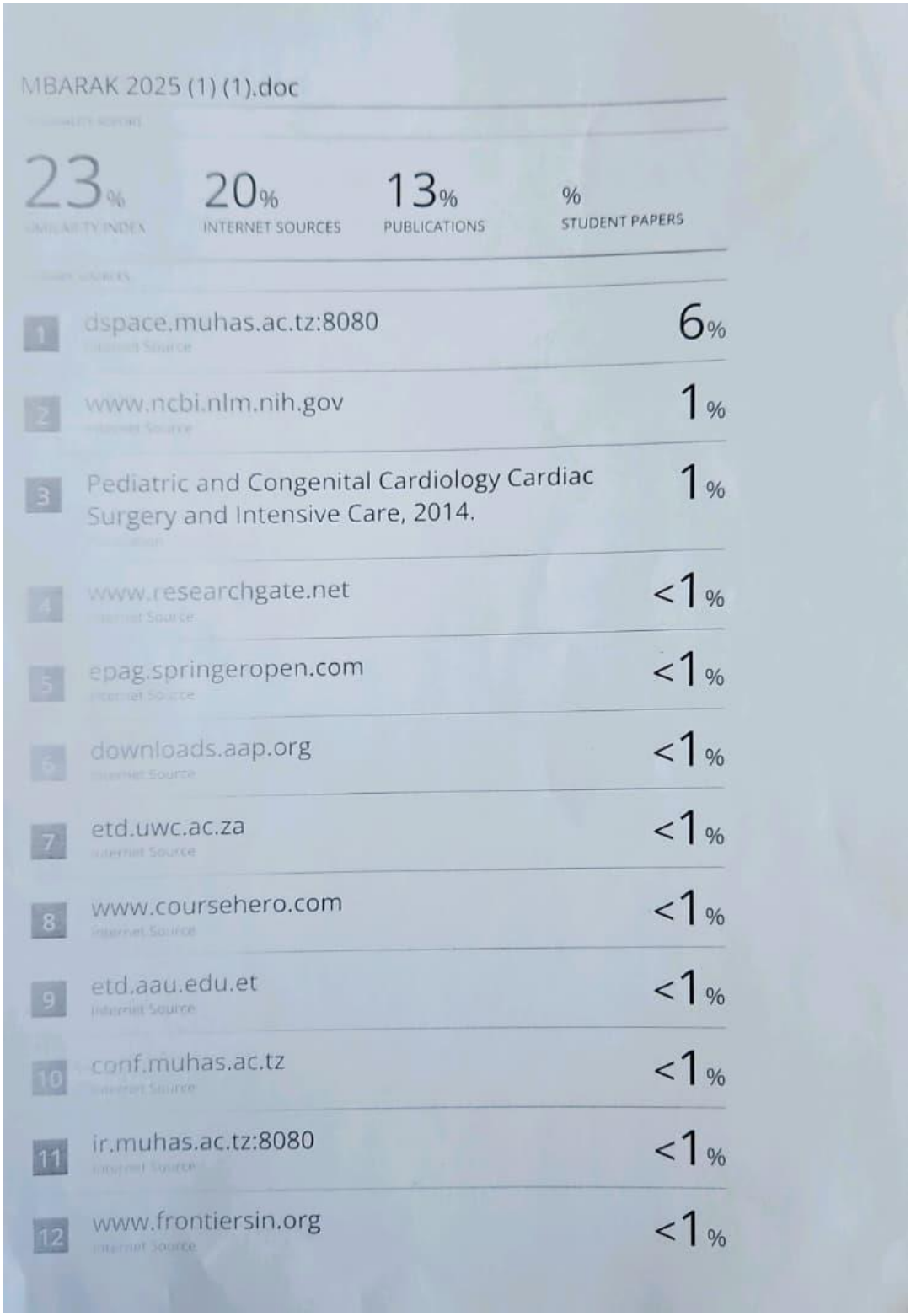
Best Regards,

JAKAYA KIKWETE CARDIAC INSTITUTE
P. O Box 65141
Dar-es-Salaam
JKCI

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

APPENDIX 9: PLAGIARISM REPOR



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