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PATTERNS OF CARDIAC DISEASES AND RISK FACTORS FOR IN-HOSPITAL MORTALITY AMONG CHILDREN ADMITTED TO MULAGO NATIONAL REFERRAL HOSPITAL

BY

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DECLARATION AND APPROVAL

I, **Akol Christine**, declare that this dissertation titled "***Patterns of Cardiac Diseases and Risk Factors for In-Hospital Mortality among Children Admitted to Mulago National Referral Hospital***" is my work except where specific acknowledgement is given. This work has neither been submitted in whole or in part to any other university for the award of a degree nor has it been offered anywhere for publication.

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DEDICATION

I dedicate this work to my husband, whose unwavering support and encouragement sustained me throughout this MMED journey; to my parents and brothers, for their constant love, and belief in me; and to my children, who remain my greatest source of motivation and strength. Above all, I dedicate this study to the children living with cardiac disease, whose courage and resilience inspired me to undertake this work and continue striving for better care and outcomes for them.

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LIST OF ACRONYMS

AHD – Acquired Heart Disease

CHD – Congenital Heart Disease

CVD – Cardiovascular Disease

ECG – Electrocardiogram

HIV – Human Immunodeficiency Virus

MNRH – Mulago National Referral Hospital

MOH – Ministry of Health

RHD – Rheumatic Heart Disease

SOMREC – School of Medicine Research and Ethics Committee

SPSS – Statistical Package for the Social Sciences

TB– Tuberculosis

UNHRO – Uganda National Health Research Organization

UNST – Uganda National Council for Science and Technology

WHO – World Health Organization

OPERATIONAL DEFINITIONS

Cardiac Diseases: Medical conditions affecting the structure or function of the heart, including congenital heart defects and acquired heart diseases.

Congenital Heart Defects (CHDs): Heart abnormalities present at birth that may affect blood flow, including conditions such as ventricular septal defects and tetralogy of Fallot.

Acquired Cardiac Diseases: Heart conditions that develop after birth due to infections, inflammation, or other factors, such as rheumatic heart disease or cardiomyopathy.

Patterns of Cardiac Diseases: Refers to the types, frequency, and distribution of heart conditions within a specific population over a defined period.

Hospital Admission: The formal process of admitting a patient to a healthcare facility for treatment or observation.

Cardiopulmonary ward (Firm C): A paediatric medical unit within Mulago National Referral Hospital specializing in the care and treatment of children with heart and respiratory diseases. This ward was selected as the study setting because it serves as the primary inpatient facility for all children with confirmed or suspected cardiac disease at Mulago Hospital, making it the appropriate location to capture the target population for this study. All children admitted with cardiac conditions during the study period were managed on this ward, and their medical records were archived from this unit.

Paediatric Patients: Individuals aged 0 to less than 18 years receiving medical care.

Rheumatic Heart Disease (RHD): A chronic heart condition resulting from untreated streptococcal throat infections, leading to damage to heart valves.

In-hospital mortality in this study means the occurrence of death during admission among children aged 0 to 17 years with a confirmed diagnosis of cardiac disease at Mulago National Referral Hospital.

Heart failure was defined as a documented clinical diagnosis by the treating paediatrician or paediatric cardiologist based on symptoms and signs consistent with cardiac failure, including tachypnoea, feeding difficulty, hepatomegaly, cardiomegaly, pulmonary oedema, or requirement for anti-failure therapy.

Severe pneumonia was defined according to World Health Organization criteria as pneumonia accompanied by at least one danger sign including hypoxaemia, severe respiratory distress, inability to feed, altered consciousness, central cyanosis, or requirement for oxygen therapy.

Malnutrition was defined as severe acute malnutrition documented in the medical record, characterized by weight-for-height Z-score below −3 SD, MUAC less than 11.5 cm in children aged 6–59 months, bilateral pitting oedema, or clinician diagnosis of severe acute malnutrition.

Arrhythmia was defined as any abnormal cardiac rhythm documented on electrocardiography and confirmed by the attending physician or paediatric cardiologist.

Severe anaemia was defined as haemoglobin concentration below 7 g/dL.

Thrombocytopenia was defined as platelet count below 150×10^9/L.

ABSTRACT

Background: Paediatric cardiac diseases, including congenital and acquired heart conditions, are a major cause of morbidity and mortality in low-resource settings such as Uganda. Despite the dual burden of congenital heart disease (CHD) and preventable acquired conditions like rheumatic heart disease, local evidence on disease patterns and determinants of in-hospital mortality remains limited.

Objective: To describe the patterns of cardiac diseases, estimate the in-hospital mortality, and identify risk factors for mortality among children admitted to Mulago National Referral Hospital.

Methods: A retrospective cohort study was conducted using medical records of children aged 0–17 years admitted to the cardiopulmonary ward (Firm C) with confirmed cardiac disease from January 2015 to January 2025. Demographic, clinical, laboratory, and echocardiographic data were extracted. Disease patterns were summarized descriptively. In-hospital mortality was expressed as a proportion and incidence density with 95% confidence intervals (CI). Cox proportional hazards regression and Kaplan-Meier curves were used for survival analysis.

Results: A total of 521 children were included, with a mean age was 3.0 ± 4.2 years; 41.8% were infants aged 1-12 months and 50.3% were male. Congenital heart disease accounted for 81.6% of admissions, predominantly ventricular septal defect (32.2%), tetralogy of Fallot (17.1%), and atrial septal defect (11.9%). Acquired heart disease comprised 18.4% of admissions, mainly rheumatic heart disease (8.8%) and dilated cardiomyopathy (5.4%). The overall in-hospital mortality was 21.1% (110/521; 95% CI: 17.6–24.9). The incidence density of mortality was 25.2 deaths per 1000 person-days (95% CI 20.7-30.4), with median hospital stay of 6.0 days (IQR: 3.0–11.0). Independent predictors of mortality were malnutrition (aHR 2.38, 95% CI: 1.28-4.42), heart failure (aHR 2.61, 95% CI: 1.41-4.83), severe pneumonia (aHR 2.89, 95% CI: 1.48-5.64), and lower platelet count (aHR 0.75 per 100×10^9/L increase, 95% CI: 0.60-0.94). Cardiac diagnosis was not independently associated with mortality.

Conclusion: Children admitted with cardiac disease at Mulago National Referral Hospital experience substantial in-hospital mortality. Mortality was primarily associated with potentially modifiable clinical conditions including malnutrition, heart failure and severe pneumonia rather than the underlying cardiac diagnosis itself. Strengthening early recognition and integrated management of these comorbidities offers an immediate opportunity to improve inpatient survival even within current resource constraints.

Keywords: congenital heart disease, acquired heart disease, rheumatic heart disease, paediatric cardiology, mortality, heart failure, Uganda.

CHAPTER ONE: INTRODUCTION

1.1 Background

Paediatric cardiac diseases encompass a range of heart-related conditions affecting children from birth to 18 years, including congenital heart diseases (CHDs) and acquired cardiac diseases (AHDs). CHDs are birth defects involving the heart's structure, such as ventricular septal defects or tetralogy of Fallot. In contrast, AHDs like rheumatic heart disease (RHD), myocarditis, and cardiomyopathies typically arise from infections or inflammation [1, 2]. Understanding the patterns and outcomes of these diseases is vital for improving interventions.

On a global scale, CHDs are the most frequently occurring congenital anomalies, with a reported prevalence ranging from 8–12 per 1,000 live births[1]. In high-income countries, early detection and advanced treatment have led to survival rates exceeding 90% in children with CHDs and mortality rates falling below 5% even for complex conditions [3]. In contrast, RHD—nearly eliminated in developed settings—remains prevalent in low- and middle-income countries due to poor access to timely treatment [4].

Sub-Saharan Africa (SSA) bears a disproportionate burden, with limited diagnostic infrastructure and delayed detection contributing to high mortality [5, 6]. In East Africa, RHD dominates acquired cardiac admissions, while CHDs are often diagnosed late [7, 8]. Shortages of paediatric cardiologists and specialized care further strain services [9].

In Uganda, paediatric cardiac diseases contribute significantly to morbidity and mortality. According to Namuyonga et al. [10], data from the Uganda Heart Institute shows that CHDs make up 76.3% of paediatric cardiac cases, with RHD constituting a significant proportion of AHD conditions, representing approximately 45.5% as reported by Aliku et al. [11]. Mulago National Referral Hospital, particularly the cardiopulmonary ward, plays a central role in managing these conditions. Despite specialized services, delays in referral, resource constraints, and unequal access remain major challenges [12, 13].

This study aimed to describe patterns of cardiac disease, estimate the in-hospital mortality rate, and identify risk factors for in-hospital mortality among children with cardiac disease admitted to the cardiopulmonary ward at Mulago Hospital, to inform clinical practice and improve patient outcomes.

1.2 Problem statement

Congenital and acquired heart diseases continued to impose a substantial health burden globally. Congenital heart diseases (CHDs), which were structural defects present at birth, remained the leading type of congenital anomalies worldwide, with an estimated prevalence ranging from 8–12 per 1,000 live births [1]. In Uganda, estimates suggested that between 8,300 to 36,000 babies were born annually with CHDs, with about 25% requiring surgical intervention [14]. In addition, acquired cardiac diseases, such as rheumatic heart disease (RHD), remained a significant health burden across Sub-Saharan Africa [6]. In Uganda, Beaton et al. [15] reported an RHD prevalence of 15 per 1,000 among symptom-free school-aged children (5–16 years), making it the leading acquired cardiac condition among paediatric patients at the UHI [11].

Congenital heart diseases often went undiagnosed due to a lack of resources for advanced diagnostic tools such as echocardiography, while RHD remained prevalent due to delays in treating streptococcal pharyngitis. Limited access to specialized paediatric cardiac care, the absence of robust referral systems, overwhelming patient volumes, and limited resources resulted in delays and suboptimal care, further exacerbating these challenges [10].

At Mulago NRH, Uganda's largest public hospital, paediatric cardiac diseases constituted a major but poorly documented burden. Although the Uganda Heart Institute (UHI), located within the Mulago hospital complex, provided specialized cardiac care and had performed over 2,500 surgeries on children and managed approximately 40 paediatric patients daily in its outpatient clinic, comprehensive hospital-wide statistics on admissions, disease patterns, and outcomes remained limited or undocumented. For instance, a study at UHI reported that out of 4,621 children seen, 76.3% had CHDs, with isolated ventricular septal defect (VSD) being the most common [10]. However, these figures did not encompass the entire paediatric population at Mulago NRH. Children with undiagnosed or untreated cardiac conditions faced severe complications, prolonged hospital stays, and increased mortality rates [11].

This lack of comprehensive hospital-level data posed a challenge in planning and optimizing paediatric cardiac care services. Without accurate epidemiological data, it was difficult to allocate resources effectively, implement preventive strategies, or improve early diagnosis and management protocols.

This study sought to bridge this knowledge gap by describing patterns of cardiac disease, estimating the in-hospital mortality rate, and identifying risk factors for in-hospital mortality among children with cardiac disease admitted to the cardiopulmonary ward (Firm C) at Mulago NRH. Findings from this study provided valuable data to inform clinical practice, strengthen healthcare policies, and improve outcomes for children with cardiac diseases in Uganda. Furthermore, documenting these in-hospital outcomes will serve as a proxy for the quality of paediatric cardiac care delivered at Mulago

National Referral Hospital, identifying systemic gaps in service delivery that can be targeted for improvement.

1.3 Justification

Paediatric cardiac diseases remain a leading cause of morbidity and mortality worldwide, with a significant burden in low-resource settings such as Uganda. Despite global advancements in paediatric cardiology, children in low-income countries continue to face barriers to timely diagnosis and effective management of cardiac conditions. This disparity underscores the urgent need to generate context-specific data that can inform healthcare interventions tailored to the local population. Mulago National Referral Hospital serves as a critical point of care for children with suspected or diagnosed cardiac diseases. However, the hospital previously had no publicly available data quantifying the exact number of paediatric cardiac disease admissions or their outcomes. This data gap had hampered effective planning, resource allocation, and implementation of evidence-based interventions for early diagnosis and treatment. Without comprehensive and accurate data, it was difficult to quantify the burden, assess treatment outcomes, and develop targeted interventions to reduce mortality and long-term complications. This study therefore aimed to bridge this knowledge gap by providing comprehensive data on patterns of cardiac disease, in-hospital mortality rates, and risk factors for in-hospital mortality among children admitted to the cardiopulmonary ward at Mulago NRH. This information is crucial for identifying high-risk patients and improving clinical outcomes.

Moreover, the study has provided evidence to support advocacy for improved infrastructure, enhanced training for healthcare providers, and better funding for paediatric cardiac care. The findings also contribute to national and regional efforts to reduce the burden of congenital and acquired cardiac diseases in children, aligning with global health goals such as Sustainable Development Goal 3, which emphasizes health and well-being for all ages.

By generating actionable insights, this study contributes to shaping policies and interventions to reduce morbidity and mortality associated with paediatric cardiac diseases in Uganda and similar settings.

1.4 Research question

1. What are the patterns of cardiac diseases among children admitted to Mulago National Referral Hospital?
2. What is the in-hospital mortality rate among children admitted with cardiac diseases at Mulago National Referral Hospital?
3. What are the risk factors for in-hospital mortality among children admitted with cardiac

diseases at Mulago National Referral Hospital?

1.5 Objectives

1.5.1 General objective

To determine the patterns of cardiac diseases, in-hospital mortality rate and associated risk factors for in-hospital mortality among children aged 0–17 years diagnosed with cardiac disease and admitted at Mulago National Referral Hospital.

1.5.2 Specific objectives

1. To describe the patterns of cardiac diseases among children aged 0–17 years admitted to MNRH.
2. To estimate the in-hospital mortality rate among children admitted with cardiac diseases at MNRH.
3. To determine the risk factors for in-hospital mortality in children admitted with cardiac diseases at MNRH.

1.6 Scope of study

This study was conducted at Mulago National Referral Hospital (MNRH) and focused on children aged 0 to 17 years who were admitted with cardiac diseases.

The study covered 10 years from January 2015 to January 2025, and included only those patients admitted through the acute care unit to the cardiopulmonary ward. The ten-year study period was selected to ensure inclusion of all patients managed since the wards were reorganized into subspecialties.

The study described patterns of cardiac diseases, estimated the in-hospital mortality rate, and identified risk factors for in-hospital mortality among these patients.

Data collected was sourced from in-patient records and hospital databases during the admission period and did not include follow-up of patients after discharge.

1.7 Conceptual Framework

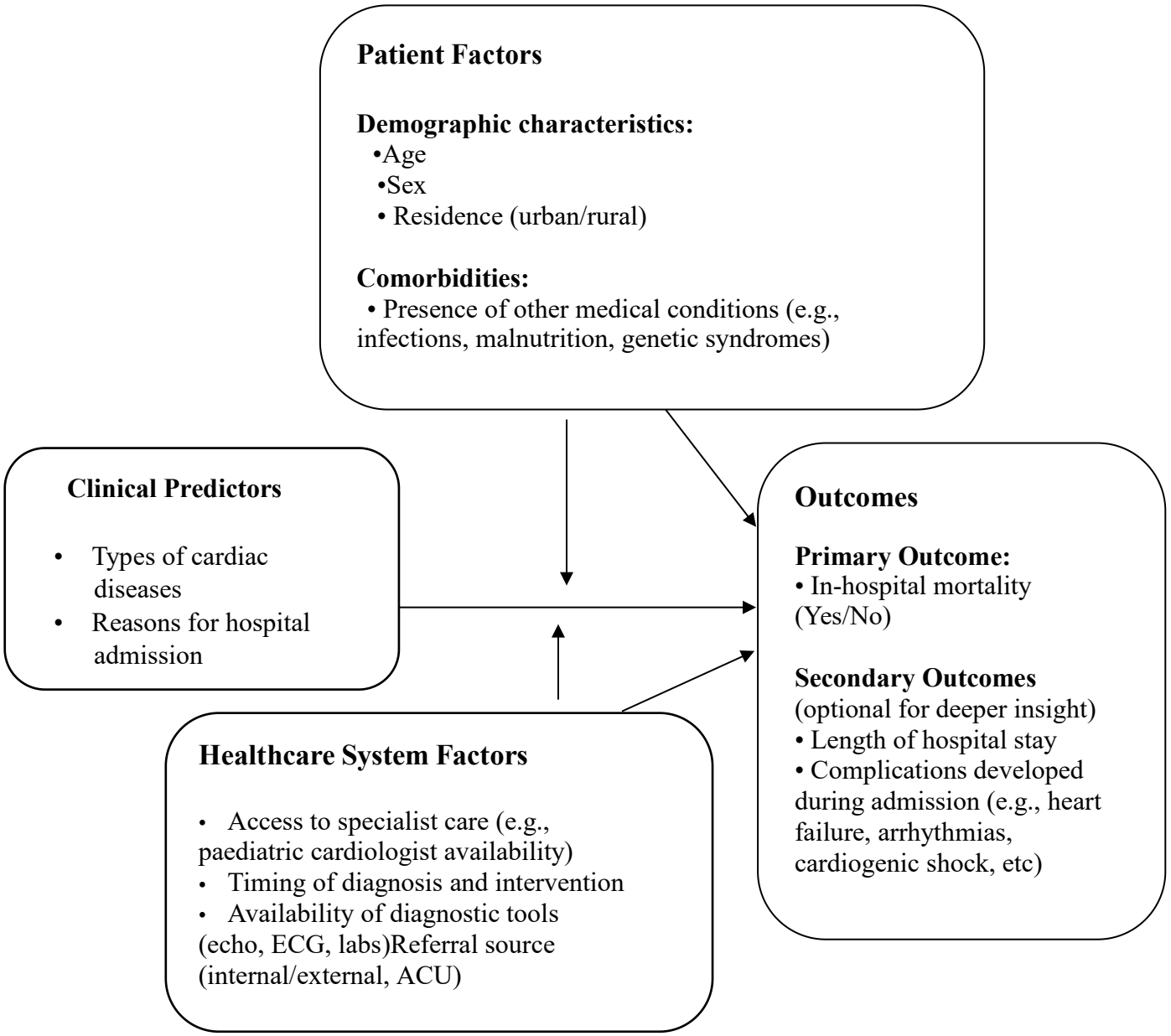


Figure 1: Conceptual Framework

Narrative of the conceptual framework:

The study's conceptual framework depicted the relationship between patient-related factors, disease characteristics, clinical parameters, and in-hospital outcomes, particularly in-hospital mortality. The framework showed how multiple interrelated factors, including demographic, clinical, laboratory, and system-level components, influence patient outcomes. While health system factors are included in the framework for contextual interpretation, they were not directly measured as variables in this retrospective study due to the limitations of chart review data.

At the core of the framework was the dependent variable, in-hospital mortality, which served as the primary outcome. The independent variables (predictors) were grouped into four categories: patient factors, disease-related factors, clinical and laboratory parameters, and healthcare access and service delivery factors.

Patient factors, including age, sex, and residence, may have influenced disease severity, access to timely care, and responsiveness to treatment. Disease-related factors included the type of cardiac disease (congenital or acquired), the reason for admission (e.g., heart failure, shock, anaemia), and the presence of comorbidities such as infections or malnutrition, which informed baseline health status and the complexity of clinical management.

Clinical and laboratory parameters, such as echocardiographic findings, electrolyte levels, and blood counts, provided insight into the child's physiological condition and guided diagnosis and treatment. Healthcare service delivery factors, including referral delays, availability of diagnostic tools, and access to definitive interventions, were considered contextual variables that could either mitigate or worsen outcomes.

Together, these domains interacted to influence the likelihood of mortality during admission. The framework enabled a comprehensive analysis of how biological, clinical, and systemic factors jointly shape patient outcomes and supported the identification of actionable predictors to inform future interventions and improve paediatric cardiac care delivery.
Future prospective studies should incorporate direct measurement of health system factors such as referral delays, diagnostic wait times, and medication availability.

CHAPTER TWO: LITERATURE REVIEW

2.1 Overview of Cardiac Diseases in Children

Cardiac diseases in children, although relatively rare compared to adults, remain a significant cause of morbidity and mortality worldwide. Congenital heart diseases (CHDs) and acquired heart diseases (AHDs) are key categories of cardiac conditions affecting children. Congenital heart defects, such as septal defects, coarctation of the aorta, and tetralogy of Fallot, are present at birth and are often diagnosed early [16]. On the other hand, acquired cardiac diseases, including rheumatic heart disease, myocarditis, and cardiomyopathies, typically develop after birth due to infections, inflammation, or other environmental factors [2]. Early detection and timely intervention are crucial for improving survival and quality of life among affected children [17]. In developed countries, advances in paediatric cardiology and surgery have significantly reduced the burden of these diseases, with over 85-90% of children with CHDs surviving into adulthood and mortality rates falling below 5% even for complex conditions [1]. However, in resource-limited settings like sub-Saharan Africa, challenges such as late diagnoses, limited access to specialized care, and insufficient healthcare infrastructure persist [8], resulting in higher mortality rates of at least 20.8% in RHD [18].

In addition, several other conditions contribute to the overall burden of paediatric heart diseases. These include arrhythmias, heart failure, and hypertension, which may arise from various etiologies such as genetic predisposition, infections, or as sequelae of other underlying health conditions [19]. Paediatric arrhythmias, such as atrial fibrillation or ventricular tachycardia, can occur as a result of structural heart defects or after a myocardial injury, often presenting as syncope, dizziness, or sudden cardiac arrest [20]. Heart failure, while more commonly associated with adults, can also affect children, particularly those with congenital heart defects or those who have undergone previous cardiac surgery. The underlying causes may include both congenital malformations and acquired conditions such as myocarditis or dilated cardiomyopathy [21]. Hypertension, which is increasingly being recognized in children, is often associated with secondary causes such as kidney disease, but in some cases, it may develop as a result of obesity or poor lifestyle choices [22].

In resource-limited settings such as Sub-Saharan Africa, where access to diagnostic tools and treatment options is constrained, these conditions often go undiagnosed or mismanaged. For instance, rheumatic heart disease (RHD), a preventable type of acquired heart disease, continues to be widespread in many African nations as a result of insufficient primary prevention efforts, poor access to antibiotics for treating streptococcal throat infections, and delayed diagnosis. RHD remains a leading contributor to cardiovascular illness and death among children and adolescents, especially in rural areas where healthcare access is limited [23]. Due to lack of timely surgical interventions, these

individuals are at greater risk of experiencing complications, including heart failure, stroke, and even death [13].

The situation is further intensified by the rising prevalence of non-communicable diseases (NCDs) such as obesity and type 2 diabetes, which are associated with a higher risk of developing cardiovascular diseases, including hypertension, dyslipidemia, and early-onset atherosclerosis. Although these NCDs are typically associated with adults, their prevalence among children in Africa is increasing due to urbanization, changing dietary patterns, and decreased physical activity [22]. The changing pattern of disease burden highlights the importance of integrated healthcare approaches that tackle both infectious diseases and non-communicable diseases to improve paediatric cardiac care.

A key challenge in the diagnosis and management of paediatric cardiac diseases in Sub-Saharan Africa is the lack of specialized healthcare infrastructure, particularly in rural areas. Inadequate training for healthcare providers, limited availability of diagnostic technologies such as echocardiography and electrocardiography, and a lack of paediatric cardiac surgeons and cardiologists all contribute to delays in diagnosis and treatment [7]. Studies in countries like Uganda and Tanzania have highlighted that many children with congenital heart defects present late, often only after the disease has progressed to an advanced stage, which limits treatment options and worsens outcomes [8, 12]. For instance, children with undiagnosed cyanotic heart defects may not be identified until they show signs of poor growth, frequent respiratory infections, or even organ failure [11].

Despite these challenges, recent efforts have been made to improve the situation. Several initiatives have been launched in countries like Uganda to improve the training of healthcare workers in paediatric cardiology, expand access to diagnostic tools, and provide treatment options for children with cardiac conditions. International partnerships, such as those between Ugandan hospitals and global paediatric cardiology organizations, have enabled the provision of specialized training for healthcare professionals, as well as the establishment of dedicated paediatric cardiology clinics and surgeries [12]. These efforts have led to improvements in early detection and the provision of cardiac care to children, although much work remains to be done to address the disparities in healthcare access across the region.

2.2 Prevalence and Patterns of Cardiac Diseases in Sub-Saharan Africa

In Sub-Saharan Africa, there is a growing burden of both congenital and acquired cardiac diseases. Estimates indicate that approximately 8-12 in every 1,000 live births are affected by congenital heart defects [5]. Acquired heart conditions like rheumatic heart disease (RHD) are still widespread across many African nations, including Uganda. RHD, often resulting from inadequately treated streptococcal throat infections, remains a major contributor to chronic complications in children and

adolescents, such as heart failure and stroke [2]. In some parts of Africa, there is also a growing incidence of cardiomyopathies and heart failure due to non-communicable diseases such as hypertension and diabetes [20].

Rheumatic Heart Disease (RHD) typically develops as a result of repeated, untreated group A streptococcal throat infections that cause chronic inflammation and damage the heart valves. Over time, repeated episodes of rheumatic fever can result in irreversible damage to the heart valves, leading to heart failure, stroke, and even death [2]. Despite being preventable with appropriate antibiotic treatment for streptococcal infections, RHD remains highly prevalent in many African countries due to gaps in healthcare access, particularly in rural and remote areas. In Uganda, for example, RHD is one of the leading causes of cardiovascular morbidity among children and adolescents, with many cases diagnosed too late to prevent long-term damage [23]. The persistent high prevalence of RHD, despite global efforts to reduce its incidence, highlights the need for improved public health interventions, including better access to healthcare and improved awareness about the importance of treating streptococcal infections early.

In recent years, the incidence of other acquired cardiac conditions, such as cardiomyopathies and heart failure, has also risen in Sub-Saharan Africa. The rise in these conditions is frequently associated with the growing burden of non-communicable diseases such as hypertension, diabetes, and obesity. These diseases are becoming more widespread in the region as a result of lifestyle shifts, including urbanization, poor diets, and sedentary lifestyles [20]. Cardiomyopathies, which can be caused by a variety of factors, including genetic predisposition, viral infections, and metabolic disorders, are increasingly recognized in children and adolescents in Africa. These conditions can result in serious outcomes such as heart failure, arrhythmias, and even sudden cardiac death if not adequately treated. Additionally, the growing burden of hypertension in children, often due to obesity and other lifestyle factors, is contributing to the rising rates of heart failure and other cardiovascular diseases in the region [22].

One of the major challenges in addressing the rising prevalence of cardiac diseases in Sub-Saharan Africa is the limited access to diagnostic tools and specialized care. In many countries, healthcare systems are under-resourced, with a shortage of skilled paediatric cardiologists, cardiothoracic surgeons, and diagnostic facilities like echocardiography machines, which are critical for early diagnosis and effective treatment [12]. The lack of infrastructure, particularly in rural areas, results in delays in diagnosis and treatment, leading to poorer outcomes for children with heart conditions. Furthermore, there is often limited public awareness about the symptoms of cardiac diseases, which further exacerbates the situation, as many families do not seek medical care until the child's condition has become life-threatening [17].

Several initiatives have been implemented in Sub-Saharan Africa to address the growing burden of paediatric cardiac diseases. For instance, efforts to reduce the incidence of RHD through community-based health education campaigns and improved access to antibiotics for treating streptococcal throat infections have shown promise in countries like Uganda and Tanzania [8]. In addition, partnerships with international organizations and institutions have enabled the establishment of paediatric cardiology clinics and surgery programs, which provide much-needed expertise and resources for the diagnosis and treatment of cardiac diseases in children [12]. Despite these advances, much more needs to be done to improve access to care, strengthen healthcare infrastructure, and raise awareness about paediatric cardiac diseases in Sub-Saharan Africa.

The growing prevalence of both congenital and acquired cardiac diseases in Sub-Saharan Africa underscores the need for urgent interventions. Increased funding for healthcare systems, training for healthcare workers, and improved access to diagnostic tools and treatments are essential to improving outcomes for children with heart conditions. Additionally, targeted public health campaigns aimed at reducing the incidence of RHD and raising awareness about the importance of early detection and treatment of cardiac diseases are critical in addressing the rising burden of these diseases in the region. By focusing on early diagnosis, prevention, and improved healthcare delivery, Sub-Saharan Africa can begin to address the increasing burden of paediatric cardiac diseases and improve the lives of affected children [11, 17].

2.3 Prevalence and Patterns of Cardiac Diseases in Uganda

In Uganda, paediatric cardiac diseases have gained increasing attention in recent years, particularly in light of the growing burden of cardiovascular diseases in the adult population. Studies have shown that the incidence of congenital heart defects in Uganda is approximately 10 per 1,000 live births, which is similar to global estimates but still represents a significant public health concern [10, 23]. Approximately 1.4 million children are born annually in Uganda, and it is estimated that between 8,300 to 36,000 babies are born annually with CHDs, with about 25% requiring surgical intervention [14].

Rheumatic heart disease (RHD) continues to be a leading cause of acquired cardiac morbidity and mortality among Ugandan children. This condition, resulting from recurrent, untreated group A streptococcal infections, disproportionately affects low-income communities, where access to healthcare is limited, and awareness about preventive care is low [13]. A study done by Weinberg J, et al. [24] showed the RHD prevalence rate in primary school children aged 5–15 ranges between 1.5% (Kampala) and 4% (Gulu). Another study conducted by Aliku et al. [11] revealed that RHD accounted for 45.5% of all acquired heart disease cases seen at the UHI, Uganda's only heart institute. The study also highlighted that most children with RHD present at advanced stages of the disease,

often requiring surgical interventions that are not readily available locally. Such findings underscore the critical need for enhanced primary and secondary prevention measures, including school-based screening programs and increased access to prophylactic antibiotics.

In addition to congenital and rheumatic heart diseases, other cardiac conditions, such as myocarditis and cardiomyopathies, are also seen among Ugandan children, although less frequently [11]. Myocarditis, often caused by viral infections, presents diagnostic and therapeutic challenges due to the lack of advanced diagnostic tools like cardiac MRI and endomyocardial biopsy in most healthcare facilities. Similarly, cardiomyopathies, which can lead to progressive heart failure, are underdiagnosed due to limited awareness and resources for early detection [10]. These gaps highlight the need for capacity building in paediatric cardiology and the establishment of specialized centres for paediatric cardiac care.

Efforts to address the burden of paediatric cardiac diseases in Uganda have been hampered by systemic challenges, including inadequate funding, a shortage of trained healthcare professionals, and limited infrastructure for advanced diagnostics and interventions. For example, access to echocardiography, a critical tool for diagnosing cardiac diseases, is primarily limited to urban referral centres, leaving rural populations underserved. Additionally, there are only a handful of trained paediatric cardiologists in the country, further limiting access to specialized care [23]. These barriers not only delay diagnosis but also compromise treatment outcomes, particularly for conditions like RHD that require timely intervention.

Despite these challenges, some progress has been made in improving paediatric cardiac care in Uganda. Programs such as the Uganda Heart Institute's outreach initiatives and collaborations with international organizations have increased access to surgical interventions and raised awareness about cardiac diseases [12]. However, the demand for services far outweighs the available resources, necessitating a comprehensive approach to address this growing burden. Increased investment in healthcare infrastructure, training of healthcare professionals, and implementation of preventive strategies are urgently needed to reduce the impact of paediatric cardiac diseases in Uganda.

2.4 Hospital Admissions and Outcomes of Pediatric Cardiac Diseases in Uganda

Hospital admissions for cardiac diseases among children are often due to severe manifestations such as heart failure, arrhythmias, or the complications of untreated congenital or acquired conditions. Children with untreated or poorly managed congenital defects often present in late childhood or adolescence with complications such as failure to thrive, cyanosis, or exercise intolerance [10]. The outcomes of cardiac diseases in children depend on the type of disease, the timing of diagnosis, and access to appropriate medical care. Studies indicate that early surgical interventions for congenital heart defects significantly improve long-term survival and reduce the burden of long-term

complications [14, 25]. A study done at the UHI by Mbabazi et al. [25] showed optimal outcomes in 89.4% of patients who underwent cardiac catheterization for PDA device closure.

Rheumatic heart disease (RHD), another leading cause of pediatric cardiac admissions in Uganda, tends to present with more insidious symptoms, such as fever, joint pain, and shortness of breath, which may be overlooked initially, leading to delays in diagnosis and treatment [10]. If left untreated, RHD can progress to severe valve damage, heart failure, arrhythmias, and stroke, resulting in long-term health impairments and even death. A study by Zimmerman et al [18] found a mortality rate of 31% in Ugandan children aged 5-18 years with clinical RHD. The consequences of these diseases can be mitigated by timely interventions such as antibiotics to prevent further streptococcal infections and surgical procedures for valve repair and replacement [15]. However, access to these life-saving interventions remains limited in Uganda due to the shortage of paediatric cardiologists and paediatric surgeons, as well as the high cost of surgery [11].

The lack of sufficient paediatric cardiac care infrastructure has resulted in higher mortality and morbidity rates among children with cardiac diseases in Uganda. A study done by Namuyonga et al. [10] found that the outcomes for children with congenital heart defects were significantly poorer in Uganda compared to those in high-income countries, where early diagnosis and timely intervention are more readily available. The situation is compounded by the limited number of paediatric cardiac surgery units in the country, which can only handle a small fraction of the growing number of children with heart conditions.

Despite these challenges, some progress has been made in improving the care for children with cardiac diseases in Uganda. For example, the Uganda Heart Institute has been working to increase the availability of paediatric cardiac surgeries and diagnostic services, and there have been partnerships with international organizations to provide specialized care through outreach programs. However, these efforts are insufficient to meet the growing demand for services, and many children continue to face delays in diagnosis and treatment, leading to poorer outcomes.

2.5 Challenges in Management and Intervention for Paediatric Cardiac Diseases

Despite advancements in paediatric cardiology, several challenges hinder the effective management of cardiac diseases in Uganda. Key barriers include limited access to paediatric cardiologists and paediatric cardiac surgeons, inadequate diagnostic tools, lack of specialized paediatric intensive care units, and high cost of services. Furthermore, there is a scarcity of trained healthcare workers in rural areas, leading to delays in diagnosis and treatment [23]. While Mulago National Referral Hospital serves as a referral centre for complex paediatric cases, it faces resource constraints, including limited availability of essential medications, equipment, and surgical facilities. These challenges highlight the

need for strengthening healthcare systems, improving early detection, and investing in specialized paediatric cardiac care to reduce the burden of cardiac diseases in Uganda.

The lack of adequate diagnostic tools is another significant challenge in managing paediatric cardiac diseases. Diagnostic imaging techniques, such as echocardiography and electrocardiography, are essential for detecting congenital heart defects, rheumatic heart disease, and other cardiovascular conditions in children. However, these diagnostic tools are not readily available in many healthcare facilities outside of major referral centres like Mulago National Referral Hospital. Even in these urban centres, the equipment may be outdated or insufficient to meet the growing demand for screening and diagnosis [10]. As a result, many children are either misdiagnosed or fail to receive a timely diagnosis, which delays appropriate treatment and intervention.

Additionally, the absence of specialized paediatric intensive care units (ICUs) in many hospitals poses a major challenge in the management of children with severe cardiac conditions. Paediatric patients with complex heart diseases often require close monitoring and advanced medical care that can only be provided in a paediatric ICU [25]. However, Uganda's healthcare infrastructure remains underdeveloped in this area, with very few hospitals equipped with the necessary facilities to care for critically ill children. This limitation means that even when children with life-threatening cardiac conditions are diagnosed, they may not receive the level of care required to ensure optimal outcomes. This often leads to poor prognoses and higher mortality rates among children with severe cardiac diseases [23].

Another major issue is the scarcity of essential medications and surgical supplies. Although cardiac medications, such as diuretics, antihypertensives, and anticoagulants, are essential for managing heart diseases, these drugs are not always available in Ugandan hospitals due to supply chain issues, budgetary constraints, and limited access to international pharmaceutical markets [23].

The cost of treatment is a further barrier to effective management, especially in a low-resource setting like Uganda. Many families of children with cardiac diseases are unable to afford the high costs associated with diagnostic tests, medications, and surgical procedures. This is particularly problematic in the context of congenital heart defects, which may require multiple surgeries and long-term follow-up care. For many families, the financial burden is simply too high, leading to treatment abandonment or delays. This financial strain is exacerbated by a lack of comprehensive health insurance schemes that cover the cost of specialized paediatric care, further limiting access to necessary treatments [25].

Finally, there is also a gap in public awareness and education about paediatric cardiac diseases in Uganda. Many parents and caregivers are unaware of the early signs and symptoms of cardiac diseases, which can delay seeking medical attention. In addition, misconceptions about the causes of heart conditions may delay diagnosis and treatment.

2.6 Paediatric Cardiac Services in Uganda: Current Status and Gaps

The delivery of paediatric cardiac care in Uganda is centred at the Uganda Heart Institute (UHI), located within the Mulago National Referral Hospital complex. The UHI serves as the country's only dedicated cardiac facility, providing outpatient cardiology clinics, echocardiography, cardiac catheterization, and surgical services [10, 11]. However, the capacity to meet the population need remains severely limited [12, 25].

Current services: Uganda has a limited paediatric cardiology workforce. Recent reports from the UHI indicate that the country has approximately seven paediatric cardiologists, including two paediatric interventional cardiologists, serving a paediatric population of over 20 million children, and on average perform an estimated 50–100 cardiac surgeries annually [10, 23, 25]. The UHI has established outreach programmes that conduct echocardiography screening in selected districts, and international partnerships have supported training of local personnel and provision of some consumables and equipment [12]. Medical management for heart failure, rheumatic heart disease prophylaxis, and pre-operative stabilization is available at Mulago Hospital [13, 25].

Identified gaps: Despite these services, major gaps persist. First, there is no routine newborn pulse oximetry screening for critical congenital heart disease, nor is antenatal fetal echocardiography widely available [10, 23]. Second, the surgical volume addresses less than 5% of the estimated annual need (with 8,300–36,000 CHD births annually, approximately 25% require surgery) [14]. Third, dedicated paediatric intensive care unit (PICU) beds with postoperative cardiac care capacity are extremely limited, often with fewer than 10 beds nationally [25]. Fourth, essential medications (diuretics, ACE inhibitors, inotropes) and consumables (oxygen, feeding tubes, laboratory reagents) experience frequent stock-outs [23]. Fifth, there is no formal national registry for congenital or acquired heart disease to track outcomes or guide policy [11].

These systemic gaps directly contribute to the late presentation and high mortality observed in this study, where 43.0% of children already had heart failure at admission and 58.7% had severe pneumonia.

2.7 The Critical Role of Frontline Providers in Timely Diagnosis

In Uganda, as in most low-resource settings, the majority of children with cardiac diseases are not first seen by cardiologists. Rather, initial presentations occur at primary health centres, general outpatient departments, and district hospitals, where the first contact providers are medical officers, assistant medical officers, and clinical officers [7, 23]. These frontline providers play a pivotal role in the diagnostic pathway [17].

The skills and knowledge of these providers are key to timely diagnosis for several reasons. First, the early signs of cardiac disease such as failure to thrive, tachypnoea, recurrent respiratory infections, or

a heart murmur are non-specific and may be mistaken for more common conditions like pneumonia or malnutrition [7, 16]. Second, delayed recognition means that many children are referred only after developing irreversible complications such as heart failure, pulmonary hypertension, or severe malnutrition, as seen in our cohort where 43.0% presented with heart failure [8, 10]. Third, frontline providers are often the only available healthcare workers in rural districts, making their ability to recognize "red flags" for cardiac disease essential for triggering timely referral to Mulago or the Uganda Heart Institute [12, 23].

Strengthening the capacity of these providers through targeted training in paediatric cardiac examination, recognition of warning signs, and understanding of referral pathways could substantially reduce diagnostic delays [17, 26]. Simple tools such as pulse oximetry, when available at primary care level, can help identify hypoxaemic children who may have critical congenital heart disease [15]. Investment in continuing medical education for frontline providers should be a priority alongside specialized cardiac services [11, 27].

CHAPTER THREE: METHODS

3.1 Study Design

This was a retrospective cohort study involving the review of medical records of children aged 0 to 17 years admitted to the cardiopulmonary ward (locally known as Firm C) at Mulago National Referral Hospital between January 2015 and January 2025.

3.1.1 Feasibility of the Study

Mulago National Referral Hospital (MNRH) received a substantial number of paediatric cardiac cases admitted to the cardiopulmonary ward (Firm C), which is dedicated to paediatric medical patients with heart and lung diseases. On average, the ward admitted about 150 children monthly, with approximately 30–40 children having cardiac-related conditions per month. This translated to an estimated 360–480 admissions annually. All eligible patient files within the study period were included to increase the power of the analysis.

To assess the feasibility of data collection, a preliminary review was conducted involving a small number of patient files from the target population. This process aimed to evaluate the completeness of records and determine whether the variables of interest—such as patient demographics, cardiac diagnoses, treatment details, and outcomes—were adequately documented. The review revealed that key information was consistently present in most files. In instances where echocardiography reports were missing from the patient files, these were reliably traced and accessed from the Uganda Heart Institute (UHI), where echocardiographic assessments were routinely performed and archived. This preliminary review, therefore, demonstrated that the existing records were sufficiently detailed and accessible to support comprehensive data abstraction for the study.

3.2 Study setting

The study was conducted on the cardiopulmonary ward of Mulago National Referral Hospital, a specialized paediatric unit dedicated to the care of children with cardiac and respiratory conditions. The ward serves as the main inpatient facility for managing both congenital and acquired heart diseases in children aged 0 to 17 years.

Patients are admitted to the cardiopulmonary ward primarily through the Paediatric Acute Care Unit (ACU), which functions as the emergency and stabilization area for critically ill children. Once stabilized, children suspected or diagnosed with cardiac conditions are transferred to the cardiopulmonary ward for further management.

The ward is staffed by a multidisciplinary team that includes two paediatric cardiologists, two general paediatricians, paediatric residents (senior house officers), intern doctors, and trained paediatric nurses. The team provides specialized care ranging from clinical assessment and diagnostic testing to medical management and preparation for surgical intervention when needed.

The cardiopulmonary ward handles a broad spectrum of conditions, such as congenital heart defects, rheumatic heart disease, cardiomyopathies, pericardial diseases, and heart failure. It also provides access to diagnostic tools such as echocardiography and electrocardiography (through the Uganda Heart Institute), which are essential for accurate diagnosis and monitoring.

3.3 Study population

3.3.1 Target population

The target population comprised all children aged 0 to 17 years in Uganda who had been diagnosed with cardiac diseases, including both congenital and acquired cardiac conditions that required hospitalization. All children admitted with suspected cardiac disease were considered part of the target population because initial management, resource allocation, and empirical treatment often begin before confirmatory testing. This approach also minimizes selection bias that would arise from excluding patients who died before echocardiography could be performed.

3.3.2 Accessible population

The accessible population included children aged 0 to 17 years admitted to the cardiopulmonary ward at Mulago National Referral Hospital with cardiac disease during the study period, from January 2015 to January 2025.

3.3.3 Study population

The study population consisted of children aged 0 to 17 years admitted to the cardiopulmonary ward (Firm C) at Mulago National Referral Hospital with confirmed cardiac diseases (either congenital or acquired) during the study period. The population was selected from medical records, ensuring that only individuals with verified cardiac diagnoses were included.

3.4 Eligibility criteria

3.4.1 Inclusion criteria

1. Children aged 0 to 17 years admitted to the cardiopulmonary ward (Firm C) at Mulago National Referral Hospital between January 2015 and January 2025.

2. Children with confirmed diagnoses of cardiac diseases, including congenital or acquired cardiac conditions, whose medical records contained complete and relevant data on clinical presentation, treatment, and in-hospital outcomes, particularly mortality.

3.4.2 Exclusion criteria

1. Children whose medical records were incomplete or missing key information necessary for assessing diagnosis, treatment, and in-hospital outcomes.
2. Children with suspected but unverified cardiac disease without definitive diagnostic documentation or untraceable echocardiography at UHI.
3. Children diagnosed with cardiac disease but referred out before completion of care at MNRH, since their in-hospital outcomes could not be determined.

3.4.3 Handling of Readmissions and Unconfirmed Cardiac Cases

Readmissions

To ensure data integrity and prevent duplication, only the last admission per child during the study period was included in outcome analysis. However, prior admissions were evaluated as potential risk factors.

Unconfirmed Cardiac Cases

Patients with suspected cardiac conditions but lacking confirmatory diagnostic evidence or untraceable echocardiographic reports were excluded.

Only patients with confirmed congenital or acquired cardiac diagnoses were included.

3.5 Sample size estimation

Sample size calculation for objective 1:

To describe the patterns of cardiac diseases (both congenital and acquired), the sample size was calculated using the Kish-Leslie formula for estimating a proportion in a population:

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

- n = required sample size
- Z = Z-value for a 95% confidence level (1.96)
- P = estimated proportion of the specific cardiac disease
- E= margin of error (5% or 0.05)

Based on existing literature from similar low-resource settings:

- For Ventricular Septal Defect (VSD), the most common congenital heart disease, P=75% (Namuyonga et al., 2020).
- For Rheumatic Heart Disease (RHD), the most common acquired heart disease, P=45% (Aliku et al., 2017).

Applying the formula:

For VSD: $n=\frac{1.96^2\ 0.75(1-0.75)}{0.05^2} = 288$

For RHD: $n=\frac{1.96^2\ 0.45(1-0.45)}{0.05^2} = 381$

Therefore, the minimum sample size required to describe patterns of cardiac diseases is 381, using the larger of the two sample sizes that incorporated both congenital and acquired cardiac disease categories.

Sample Size Calculation for Objective 2:

To estimate the in-hospital mortality rate among children aged 0–17 years with cardiac diseases admitted to Mulago National Referral Hospital (MNRH), Kish-Leslie's formula for estimating a single proportion was used. Based on previous literature from similar low-resource settings, an in-hospital mortality rate of approximately 15% for congenital heart diseases (CHDs) and 30% for acquired heart diseases (AHDs) among children with cardiac disease was considered reasonable (Zimmerman et al., 2022; Namuyonga et al., 2020).

Substituting

$CHD=(1.96)^2\times0.15\times(1-0.15)/(0.05)^2=196$

$AHD= (1.96)^2 \times0.3\times (1-0.3)/ (0.05)^2 = 323$

Therefore, the minimum sample size required to estimate in-hospital mortality rate is 323, using the larger of the two sample sizes.

Sample Size Calculation for Objective 3

To determine the risk factors for in-hospital mortality among children admitted with cardiac diseases at Mulago National Referral Hospital, the sample size was calculated using the formula for comparing two proportions.

Based on existing literature from similar low-resource settings, the following assumptions were made:

- Estimated proportion of mortality among children with congenital cardiac disease (unexposed group) = 15%.
- Estimated proportion of mortality among children with acquired cardiac disease (exposed group, primarily RHD) = 30%.
- Anticipated odds ratio of mortality between CHD and AHD groups = 2.4.
- Two-tailed standard normal deviation corresponding to a 95% confidence level = 1.96.
- Standard normal value corresponding to 80% power = 0.84.

Substitutions were made using the Fleiss formula for comparing two proportions, as described in Statistical Methods for Rates and Proportions (formulas 3.18 and 3.19), and implemented through OpenEpi (https://www.openepi.com/SampleSize).

Sample Size: X-Sectional, Cohort

Two-sided significance level(1-alpha):			95
Power(1-beta, % chance of detecting):			80
The ratio of sample size, Unexposed/Exposed:			1
Percent of Unexposed with Outcome:			15
Percent of Exposed with Outcome:			30
Odds Ratio:			2.4
Risk/Prevalence Ratio:			2
Risk/Prevalence difference:			15
	Kelsey	**Fleiss**	**Fleiss with CC**
Sample Size – Exposed	122	121	134
Sample Size-Nonexposed	122	121	134
Total sample size:	244	242	268

References

Kelsey et al., M

Fleiss, Statistical Methods for Rates and Proportions, formulas 3.18 &3.19

CC = continuity correction

The input values shown (95% confidence level, 80% power, 15% outcome in unexposed, 30% outcome in exposed) are correct as used for sample size estimation. The minimum calculated sample size was 242 (Fleiss method), which was exceeded by our final sample of 521.

However, since a larger sample (381) was calculated for Objective 1, it was used as the minimum sample size and all eligible patient records were included to increase the power and precision of the findings.

Therefore, the minimum calculated sample size was 381. However, using a consecutive sampling approach, all eligible patient records meeting the inclusion criteria during the study period were included, resulting in a final sample size of 521.

Sample size and feasibility

This study was a retrospective review of medical records of children aged 0 to 17 years admitted to the cardiopulmonary ward (Firm C) at Mulago National Referral Hospital with cardiac disease during the 10-year period from January 2015 to January 2025. A consecutive sampling technique was used to select participants, ensuring that all eligible medical records were included to obtain the most complete epidemiological picture possible.

If the total number of available records had been smaller than required to meet the planned analytical aims, a backward (post-hoc) power calculation was to be performed to report the actual statistical power and the minimum detectable effect sizes for key predictors. Analytical approaches would then be adjusted accordingly (for example, by reducing predictors or using penalized regression), and any limitations due to reduced power were to be clearly stated in dissemination materials.

3.6 Sampling procedures

A consecutive sampling technique was used to select participants. This non-probability sampling method ensured that all eligible medical records of children aged 0–17 years who were admitted to the cardiopulmonary ward (Firm C) at Mulago National Referral Hospital during the study period (January 2015 to January 2025) and who met the predefined inclusion criteria were included.

Procedure for file identification and retrieval:

1. **Identification of eligible patients:** Using the cardiopulmonary ward admission registers (HMIS forms), a trained data assistant extracted the inpatient numbers of all children admitted

to Firm C between January 2015 and January 2025 who had a recorded diagnosis of suspected or confirmed cardiac disease.

2. **File retrieval:** The list of inpatient numbers was submitted to the Mulago National Referral Hospital medical records department. Records personnel retrieved the corresponding physical patient files from the central archives.
3. **Screening for eligibility:** Each retrieved file was screened against the inclusion and exclusion criteria by the principal investigator or a trained research assistant. Files were included if they contained:
    - A confirmed diagnosis of congenital or acquired cardiac disease (verified by echocardiography report found in the patients' file or traceable to the Uganda Heart Institute)
    - Complete demographic and clinical data
    - Documented in-hospital outcome (discharge or death)
4. **Exclusion of ineligible files:** Files were excluded if:
    - The cardiac diagnosis was suspected but not confirmed by echocardiography
    - Key data elements (e.g., outcome, length of stay, or primary clinical variables) were missing or illegible
    - The patient was referred to another facility before completion of care, making in-hospital outcome indeterminate

All files meeting the inclusion criteria during the study period were included in the final analysis. This approach was chosen to maximize statistical power, minimize selection bias, and provide a complete epidemiological description of paediatric cardiac admissions at this tertiary referral centre over the 10 years.

3.7 Data collection methods

Data were collected retrospectively using a structured data abstraction tool designed specifically for this study. This data abstraction tool was converted to an electronic format and uploaded to KoboToolbox (KoboCollect), which was then used to collect and manage study data. The tool was used to extract relevant information from the medical records of children aged 0–17 years admitted to the cardiopulmonary ward at Mulago National Referral Hospital between January 2015 and January 2025.

To ease retrieval of files, inpatient numbers of children admitted to the cardiopulmonary ward during the study period, with a diagnosis of cardiac disease, were extracted from the cardiopulmonary ward registers (HMIS) by a trained data entrant and forwarded to the records department. Records personnel used these identifiers to retrieve the corresponding patient files from the archives.

The data abstraction process was conducted manually from physical records by trained medical officers, under the supervision of the principal investigator. Standardized definitions and diagnostic criteria were applied to ensure consistency and reliability in data collection. A pilot test of the data abstraction tool was performed on a small sample of records to refine its design and ensure accuracy before full data collection began.

The following data points were collected:

- **Demographic data**: Age, sex, and residence.
- **Clinical data**: Types of cardiac diseases (classified as congenital or acquired), reasons for admission (e.g., heart failure, anaemia, pneumonia, electrolyte imbalances, or renal failure), and associated comorbidities.
- **Laboratory Parameters:** Complete Blood Count (CBC) values, including haemoglobin (Hb), white blood cell count (WBC), neutrophil count, and platelet (Plt) count. Serum levels of urea, creatinine, and electrolytes (sodium [Na], potassium [K], calcium [Ca], magnesium [Mg], and phosphorus).
- **Radiological Parameters:** Echocardiogram description of cardiac anatomy and function. Electrocardiogram (If available)**.**
- **Outcomes**: Primary outcome was in-hospital mortality. Secondary outcomes include: duration of hospital stay and complications during admission.

Arrhythmia was diagnosed based on electrocardiogram (ECG) interpretation by the attending paediatrician or cardiologist, as documented in the medical record. ECGs were not independently re-reviewed for this study.

3.8 Variables

3.8.1 Independent variables

1. **Demographic characteristics**:
    - Age
    - Sex
    - Residence (urban/rural)
2. **Types of cardiac diseases**:
    - Congenital cardiac diseases
    - Acquired cardiac diseases
3. **Reasons for hospital admission**:
    - Heart failure
    - Shock
    - Anemia
    - Pneumonia
    - Electrolyte imbalances
    - Renal failure
    - Other specified reasons
4. **Comorbidities**:
    - Presence of other medical conditions (e.g., infections, malnutrition, or genetic syndromes)
5. **Laboratory Parameters:**
    - Complete Blood Count (CBC): Hemoglobin (Hb), White Blood Cell (WBC) count, Neutrophil count, Platelet (Plt) count.
    - Serum levels of urea, creatinine, and electrolytes: Sodium (Na), Potassium (K), Calcium (Ca), Magnesium (Mg), and Phosphorus.
6. **Radiological Parameters:**
    - Echocardiogram: Description of cardiac anatomy and function.
    - Electrocardiogram: If available.

3.8.2 Dependent variable:

The dependent variable in this study was in-hospital mortality, defined as the occurrence of death during admission among children aged 0 to 17 years with a confirmed diagnosis of cardiac disease at Mulago National Referral Hospital.

This outcome was assessed as a binary variable:

- Yes = death occurred during admission
- No = patient survived the admission period.

3.9 Data management

Data collected from patient medical records were anonymized to ensure confidentiality and entered into a secure, password-protected electronic database. Data cleaning was performed to address missing, incomplete, or inconsistent entries. Standard coding was used for categorical variables, and numerical variables were checked for outliers. Double data entry verification was conducted to ensure accuracy.

Only authorized personnel had access to the data for analysis, and the database was backed up regularly to prevent data loss. All physical documents were securely stored and will be destroyed only in accordance with ethical guidelines, which typically stipulate retention for 5 to 10 years after study completion or publication.

3.10 Data Analysis

Data were cleaned and coded in Microsoft Excel and then exported to STATA version 17 for statistical analysis. All tests were two-tailed, and a p-value < 0.05 was considered statistically significant unless otherwise specified.

Objective 1: Patterns of cardiac diseases

Descriptive statistics were used to describe the patterns of cardiac diseases among children admitted to Mulago National Referral Hospital. Frequencies and percentages were computed to describe the distribution of various cardiac diseases, including congenital and acquired types, and further categorized based on specific diagnoses such as ventricular septal defect, rheumatic heart disease, or cardiomyopathies. Cross-tabulations were used to explore how disease patterns varied by age group, sex, and residence. Results were presented in tables and figures (bar charts and pie charts) as appropriate.

Objective 2: In-hospital mortality rate and incidence density

The in-hospital mortality rate was calculated as the proportion of children who died during hospitalization, expressed as a percentage of the total number of children admitted with cardiac diseases during the study period. A 95% confidence interval (CI) was calculated using the exact binomial method to indicate the precision of the mortality rate estimate.

Incidence density (mortality rate per person-time): To account for varying lengths of hospital stay, the incidence density of mortality was calculated as:

Incidence density = (Total number of deaths/ Total person-time of follow-up)

Person-time was calculated in **person-days** (sum of length of hospital stay for all patients). The total person-days for the cohort were 4,365 days. The incidence density was expressed as **deaths per 1000 person-days** for clinical interpretability, with 95% confidence intervals calculated using the exact Poisson method.

Length of hospital stay

Length of hospital stay (in days) was summarized using median and interquartile range (IQR) due to the anticipated skewed distribution of this variable. Comparison of length of stay between survivors and non-survivors was performed using the Mann-Whitney U test.

Objective 3: Risk factors for in-hospital mortality

Given the in-hospital mortality rate of 21.1% (>10%), survival analysis using Cox proportional hazards regression was employed as the primary analytical method. This approach accounts for varying lengths of follow-up and examines the timing of mortality, which is more informative than binary outcome methods when event rates are high.

Data structure for survival analysis:

Survival time data were structured using STATA's stset command as follows:

- **Time variable:** Length of hospital stay in days (from admission to discharge, death, or censoring)
- **Failure (event) variable:** In-hospital mortality, coded as 1 for death and 0 for censoring (discharge alive)
- **Origin:** Time zero = date of admission

Kaplan-Meier analysis: Kaplan-Meier survival curves were generated to visualize survival probabilities over time, both for the overall cohort and stratified by key exposure groups (malnutrition, heart failure, severe pneumonia). The **log-rank test** was used to compare survival

distributions between groups. Median survival times with 95% confidence intervals were reported for non-survivors.

Cox proportional hazards regression:

Cox proportional hazards regression was used to estimate **hazard ratios (HR)** for mortality. The Cox model is specified as:

$$h(t|X) = h_{0(t)} \exp\left(\beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k\right)$$

Variable selection: Variables with p-values < 0.2 in bivariate analysis were included in the multivariable Cox regression model. These were: age, sex, residence, type of cardiac disease (CHD vs. acquired), malnutrition, genetic syndrome, heart failure, severe pneumonia, severe anaemia, and platelet count. Backward stepwise elimination was used to retain only variables that remained significant at $p < 0.05$. Adjusted hazard ratios (aHR) with 95% confidence intervals and p-values were reported.

Assessment of effect modification: To assess whether the effect of predictors varied across subgroups, we introduced interaction terms into the Cox regression model. Specifically, we tested age × type of cardiac disease (CHD vs. acquired) to determine if the relationship between age and mortality differed by disease category. We also tested malnutrition × heart failure and severe pneumonia × heart failure. None of the interaction terms reached statistical significance ($p > 0.05$ for all), indicating no significant effect modification. Therefore, the main effects model without interaction terms was retained.

Proportional hazards assumption: The proportional hazards assumption was tested using **Schoenfeld residuals** (global test and tests for each covariate). The global test yielded $p = 0.312$, indicating that the proportional hazards assumption was not violated. If the proportional hazards assumption was violated for any covariate, time-varying coefficients or stratified Cox models were to be considered.

Incidence density rates by exposure group:

For key categorical predictors (malnutrition, heart failure, severe pneumonia), incidence density rates (deaths per 1000 person-days) were calculated for each group along with incidence rate ratios (IRR).

Model diagnostics:

- For Cox regression: The proportional hazards assumption was tested using Schoenfeld residuals. The overall goodness-of-fit was assessed using the Cox-Snell residuals plot.
- No significant violations or influential observations were identified

Handling of missing data:

Complete-case analysis was used for multivariable models (N = 270 patients with complete data on all covariates). This represents 51.8% of the total sample.

Software implementation:

The following STATA commands were used for the analysis:

Analysis	**STATA Command**
Descriptive statistics	tabulate, summarize, ci
Mann-Whitney U test	Ranksum
Survival data setup	Stset
Kaplan-Meier curves	sts graph, sts list
Log-rank test	sts test
Cox regression	Stcox
Proportional hazards test	estat phtest
Incidence density	Stptime

Person-time incidence rate (mortality density):

In addition to the cumulative mortality proportion, the mortality rate was calculated as an incidence density using person-years of follow-up. Person-time was calculated as the sum of hospital days contributed by each patient from admission until death, discharge, or censoring. The mortality rate was expressed as the number of deaths per 100 person-years (or per 1,000 person-days) with 95% confidence intervals calculated using the exact Poisson method. This approach accounts for varying lengths of hospital stay and provides an estimate of the instantaneous risk of death over time.

Formula:

Mortality rate= (Number of deaths/ (Total person-years of follow-up)) × 100

3.11 Quality Control

To ensure the accuracy, reliability, and validity of the data collected, several quality control measures were implemented. The study tools were thoroughly reviewed, and the research team was

trained on proper data collection procedures. This ensured that all team members understood the research protocol, study objectives, and how to minimize errors during data abstraction.

Before full data collection, a pre-test of the data abstraction tool was conducted on a small sample of patient records. The pre-test helped identify potential issues such as unclear questions or incomplete documentation of laboratory parameters (CBC, urea, creatinine, and serum electrolytes). Based on feedback from the pre-test, the tool was refined and improved to ensure accuracy and clarity.

Throughout the data collection period, regular quality checks were performed to ensure data were recorded accurately. Special attention was given to laboratory parameters (CBC, urea, creatinine, sodium, potassium, calcium, magnesium, and phosphorus) to confirm that these values were correctly entered into the data abstraction tool. The research team reviewed data forms regularly for completeness, consistency, and accuracy, addressing any discrepancies immediately.

Data entries into the analysis software were double-checked, and cross-referencing was performed to verify accuracy. Any discrepancies or errors identified, particularly in laboratory values, were corrected promptly. All data were securely stored to maintain confidentiality and prevent unauthorized access.

Feedback was sought continuously from the supervisor and other experienced researchers to monitor progress and ensure data reliability. These quality control measures maintained scientific rigor and ensured that the study findings were both credible and reliable.

3.12 Dissemination

The results of this study were presented to the Department of Paediatrics and Child Health at MAKCHS as a requirement for the partial fulfilment of the award of a master's degree in Paediatrics and Child Health at Makerere University.

The copies of the dissertation will be shared with Sir Albert Cook Library, the Makerere University repository, the Makerere School of Graduate Studies, and Mulago National Referral Hospital. Publication will be made in peer-reviewed journals and presented in local and scientific conferences.

3.13 Ethical Consideration

Ethical approval for this study was obtained from the Makerere University School of Medicine Research and Ethics Committee (SOMREC) to ensure adherence to ethical principles and guidelines

for conducting research involving human subjects. The research proposal, including the study design, objectives, data collection methods, and ethical considerations, was submitted to the committee for review and approval. Waiver of informed consent was provided by SOMREC, as the study involved the review of patient charts rather than direct interaction with patients.

Furthermore, administrative clearance was obtained from the Mulago National Referral Hospital (MNRH) to access the hospital's facilities and patient records. This clearance ensured that the hospital management was informed and supportive of the research and facilitated smooth coordination with the clinical team.

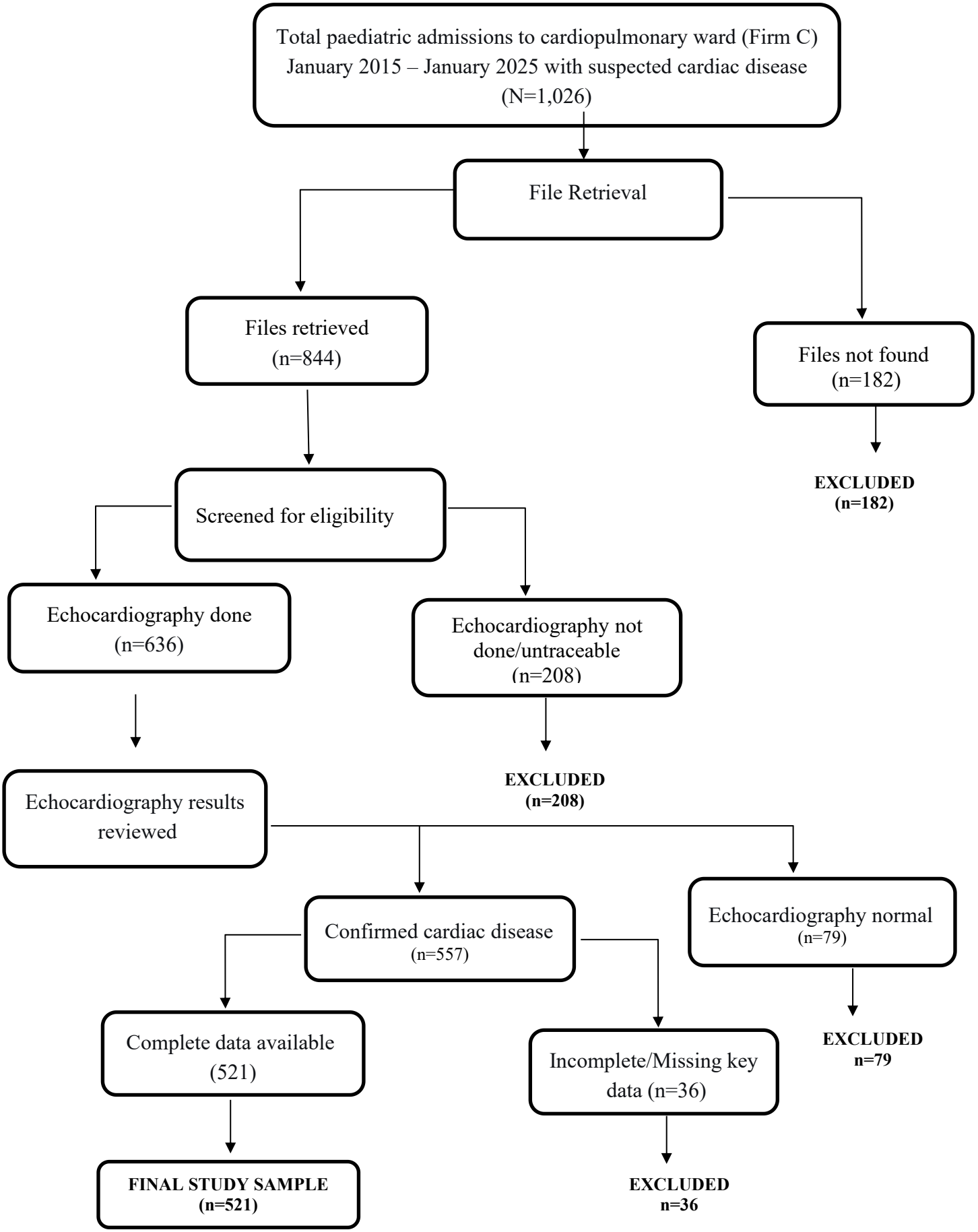
Confidentiality and privacy were strictly maintained throughout the study. Identifiable information was kept secure, and only de-identified data were used for analysis. All data were stored in locked files and password-protected electronic databases, with access restricted to the research team. Data were analyzed and presented in aggregate form to ensure that no individual participant could be identified.

CHAPTER FOUR: RESULTS

4.1 Participants flow

Of 1,026 children identified with suspected cardiac disease from the ward admission register, 844 files were retrieved; 182 were not found. Echocardiography had been performed in 636 of the retrieved cases; 208 were excluded because echocardiographic reports were absent or untraceable. Of 636 with echocardiography, 79 had normal findings and were excluded, leaving 557 with confirmed cardiac disease. A further 36 were excluded due to missing outcome data, yielding a final study sample of 521 children. Figure 2 below summarizes the study flow.

Figure 2: Study Flow Chart



4.2 Demographic and Clinical Characteristics of Paediatric Patients with Cardiac Disease (Overall and Stratified by In-Hospital Mortality)

A total of 521 children aged 0-17 years with confirmed cardiac disease were included in the study. The majority of children were aged between 1-12 months (41.8%, 218/521), with a mean age of 3.01 ± 4.19 years and no significant difference between survivors and non-survivors (p = 0.736). Males constituted 50.3% (n = 262) of the study population, with a significantly higher proportion among survivors compared to non-survivors (52.8% vs. 40.9%, p = 0.035).

Table 1 summarizes the demographic and clinical characteristics of the study population (N=521 patients), overall and stratified by in-hospital mortality. Continuous variables are presented as mean ± standard deviation (SD) or median [interquartile range, IQR] as appropriate, while categorical variables are presented as frequencies and percentages.

Table 1: Demographic and Clinical Characteristics of Paediatric Patients with Cardiac Disease (Overall and Stratified by In-Hospital Mortality)

Variable	Overall (N=521)	Survived (n=411)	Died (n=110)	p-value
Age (years), mean ± SD	3.01 ± 4.19	3.04 ± 4.15	2.89 ± 4.33	0.736†
Age group, n (%)				
Neonate (0-28 days)	45 (8.6%)	32 (7.8%)	13 (11.8%)	
Infant (29 days - 12 months)	218 (41.8%)	168 (40.9%)	50 (45.5%)	
Child (1 - 5 years)	142 (27.3%)	115 (28.0%)	27 (24.5%)	
Child (6 - 12 years)	78 (15.0%)	66 (16.1%)	12 (10.9%)	
Adolescent (13 - 17 years)	38 (7.3%)	30 (7.3%)	8 (7.3%)	
Sex, n (%)				**0.035‡**
Male	262 (50.3%)	217 (52.8%)	45 (40.9%)	
Female	259 (49.7%)	194 (47.2%)	65 (59.1%)	
Weight (kg), mean ± SD	10.29 ± 9.50	10.59 ± 9.70	9.14 ± 8.67	0.155†
Height (cm), mean ± SD	69.09 ± 23.50	71.50 ± 25.13	66.81 ± 21.94	0.395†
Haemoglobin (g/dL), mean ± SD	11.91 ± 5.07	11.73 ± 3.08	12.45 ± 8.66	0.310†
White blood cell count (×10⁹/L), mean ± SD	12.99 ± 32.04	13.42 ± 36.89	11.72 ± 5.99	0.706†
Neutrophil count (×10⁹/L), mean ± SD	10.68 ± 15.93	10.57 ± 15.67	11.02 ± 16.77	0.840†
Platelet count (×10⁹/L), mean ± SD	287.58 ± 161.20	304.49 ± 160.71	238.30 ± 153.37	**0.003†**
Serum sodium (mmol/L), mean ± SD	136.61 ± 7.39	136.62 ± 7.11	136.58 ± 8.22	0.976†
Serum potassium (mmol/L), mean ± SD	5.59 ± 10.15	5.84 ± 11.91	4.94 ± 0.96	0.604†
Serum creatinine (mg/dL), mean ± SD	1.89 ± 8.83	2.12 ± 10.07	1.19 ± 2.60	0.543†
Length of hospital stay (days), median [IQR]	6.0 [3.0–11.0]	6.0 [3.0–10.0]	6.0 [3.0–12.0]	0.782§
Urban residence, n (%)	91 (17.5%)	66 (16.1%)	25 (22.7%)	0.135‡
Congenital Heart Disease (CHD), n (%)	425 (81.6%)	336 (81.8%)	89 (80.9%)	0.949‡
Malnutrition, n (%)	105 (20.2%)	68 (16.5%)	37 (33.6%)	**<0.001‡**
HIV/AIDS, n (%)	3 (0.6%)	3 (0.7%)	0 (0.0%)	0.850¶
Hypertension, n (%)	4 (0.8%)	4 (1.0%)	0 (0.0%)	0.672¶
Genetic syndrome, n (%)	117 (22.5%)	81 (19.7%)	36 (32.7%)	**0.005‡**
Heart failure, n (%)	224 (43.0%)	152 (37.0%)	72 (65.5%)	**<0.001‡**
Infective endocarditis, n (%)	14 (2.7%)	8 (1.9%)	6 (5.5%)	0.091¶
Severe anaemia, n (%)	22 (4.2%)	13 (3.2%)	9 (8.2%)	**0.040‡**
Severe pneumonia, n (%)	306 (58.7%)	223 (54.3%)	83 (75.5%)	**<0.001‡**
Pleural effusion, n (%)	7 (1.3%)	5 (1.2%)	2 (1.8%)	0.984¶
Pericardial effusion, n (%)	15 (2.9%)	10 (2.4%)	5 (4.5%)	0.392¶
Arrhythmias, n (%)	3 (0.6%)	2 (0.5%)	1 (0.9%)	1.000¶
Post-surgical complications, n (%)	7 (1.3%)	7 (1.7%)	0 (0.0%)	0.362¶

SD = Standard Deviation, IQR = Interquartile Range, HIV/AIDS = Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome

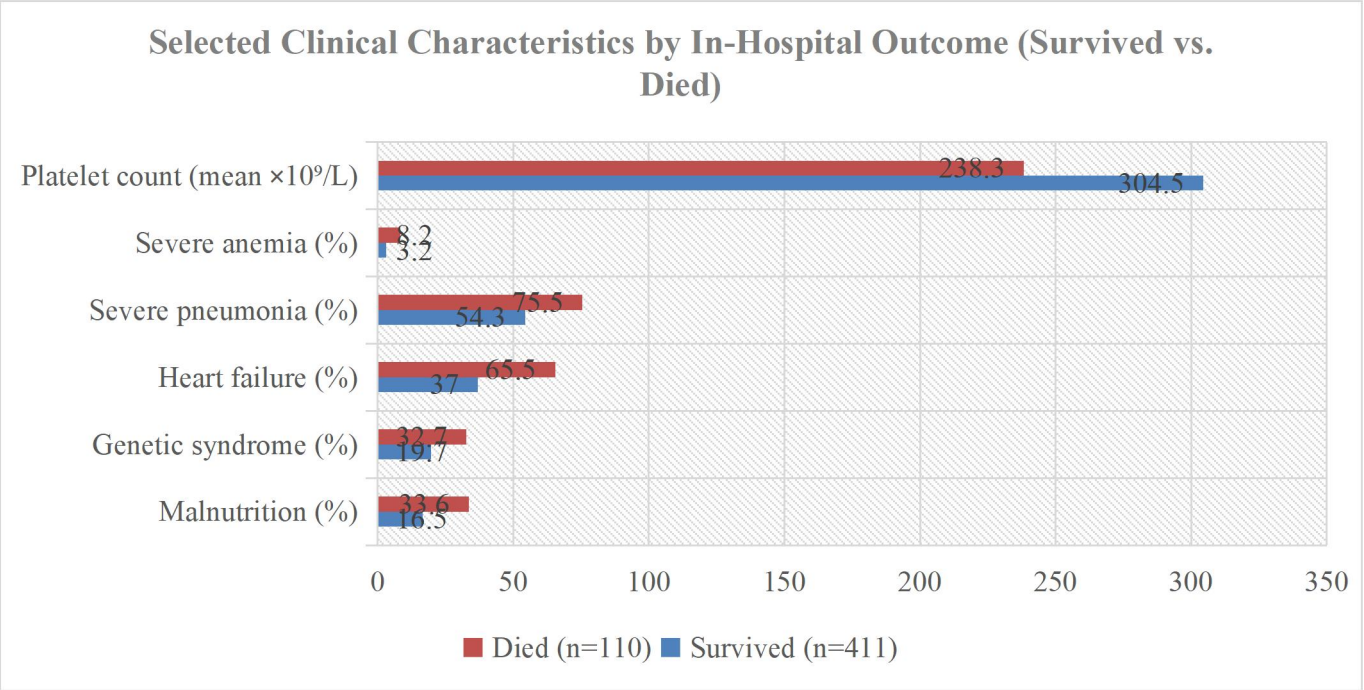
† p-value from independent t-test (continuous, normally distributed variables)

‡ p-value from chi-square test (categorical variables)

§ p-value from Mann-Whitney U test (continuous, non-normally distributed variable)

¶ p-value from Fisher's exact test (categorical variables with expected cell count <5)

Figure 3: Comparison of key clinical characteristics associated with in-hospital mortality



Bars represent percentages (except platelet count shown as mean).

p-values: p<0.05 (chi-square test for categorical variables, t-test for platelet count).

4.3 Patterns of cardiac diseases

4.3.1 Distribution of cardiac diseases

The majority of patients had congenital heart diseases (CHDs) (81.6%, 425/521), while acquired heart diseases (AHDs) accounted for 18.4% (96/521) of cases. The most common specific diagnoses were: Ventricular septal defect (VSD) at 32.2% (168/521), Tetralogy of Fallot (TOF) at 17.1% (89/521), and Atrial septal defect (ASD) at 11.9% (62/521). Among acquired conditions, rheumatic heart disease (RHD) was the most common (8.8%, 46/521), followed by dilated cardiomyopathy (DCM) (5.4%, 28/521) as shown in Figure 4 and Table 2 below.

Figure 4: Pie Chart Showing the Distribution of Cardiac Diagnoses

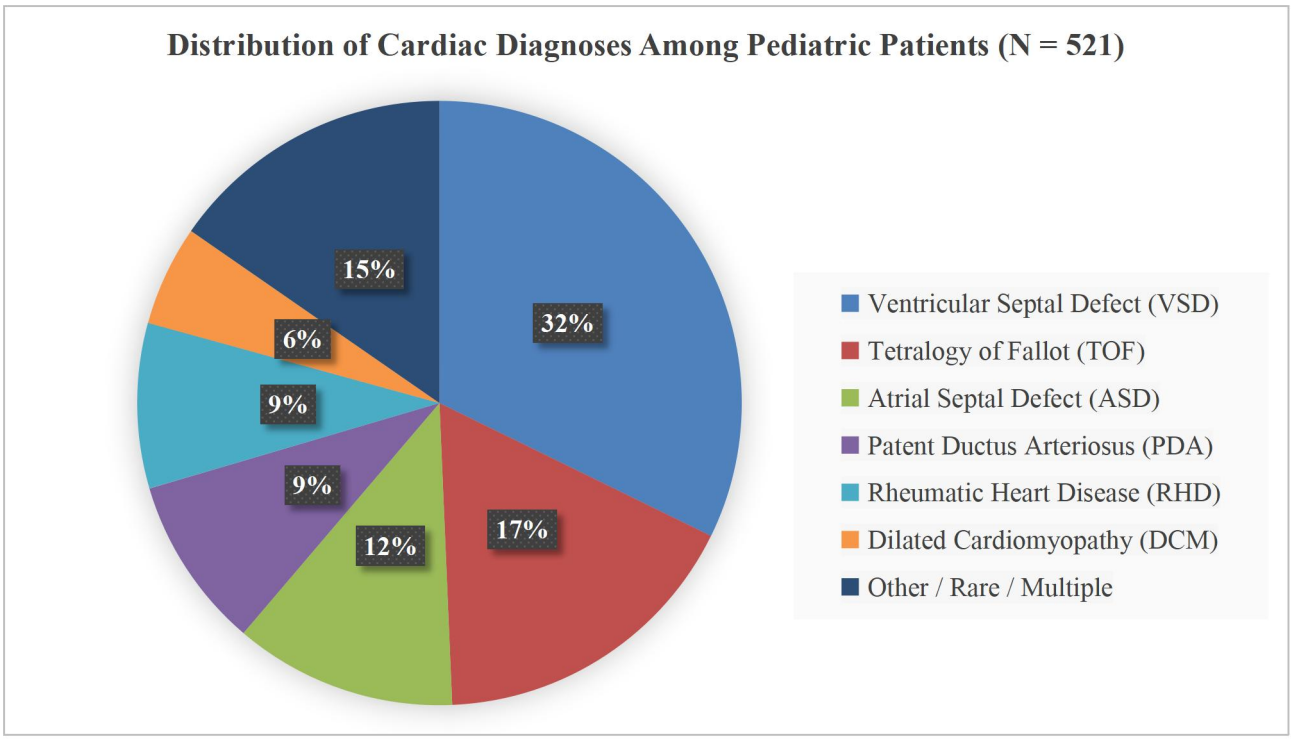


Table 2 shows the distribution of specific cardiac diagnoses and their association with in-hospital mortality. No specific diagnosis was significantly associated with mortality (all $p > 0.05$), consistent with the multivariable models showing no independent effect of CHD versus AHD.

Table 2: Distribution of Specific Cardiac Diagnoses and Association with In-Hospital Mortality

Specific Diagnosis	Overall (N=521)	Survived (n=411)	Died (n=110)	p-value
Ventricular Septal Defect (VSD)	168 (32.2%)	135 (32.8%)	33 (30.0%)	0.578
Tetralogy of Fallot (TOF)	89 (17.1%)	68 (16.5%)	21 (19.1%)	0.538
Atrial Septal Defect (ASD)	62 (11.9%)	51 (12.4%)	11 (10.0%)	0.498
Patent Ductus Arteriosus (PDA)	48 (9.2%)	38 (9.2%)	10 (9.1%)	0.964
Rheumatic Heart Disease (RHD)	46 (8.8%)	35 (8.5%)	11 (10.0%)	0.638
Dilated Cardiomyopathy (DCM)	28 (5.4%)	20 (4.9%)	8 (7.3%)	0.331
Truncus Arteriosus (TA)	18 (3.5%)	12 (2.9%)	6 (5.5%)	0.228
Dextro-Transposition of Great Arteries (d-TGA)	15 (2.9%)	11 (2.7%)	4 (3.6%)	0.741
Pulmonary Stenosis (PS)	12 (2.3%)	10 (2.4%)	2 (1.8%)	0.752
Coarctation of Aorta (CoA)	9 (1.7%)	8 (1.9%)	1 (0.9%)	0.689
Atrioventricular Septal Defect (AVSD)	8 (1.5%)	6 (1.5%)	2 (1.8%)	1.000
Ebstein Anomaly	5 (1.0%)	4 (1.0%)	1 (0.9%)	1.000
Double Outlet Right Ventricle (DORV)	4 (0.8%)	3 (0.7%)	1 (0.9%)	1.000
Hypoplastic Left Heart Syndrome (HLHS)	3 (0.6%)	2 (0.5%)	1 (0.9%)	0.509
TOTAL	**521 (100%)**	**411 (100%)**	**110 (100%)**	

4.3.2 Distribution by age and sex

CHDs were more common in younger children, particularly infants, whereas AHDs were more prevalent in older children and adolescents. The mean age of the cohort was 3.01 ± 4.19 years.

There was a slight male predominance overall (50.3%), with males constituting 52.8% of survivors and 40.9% of non-survivors ($p = 0.035$). However, sex was no longer significant after multivariable adjustment in Cox regression.

4.4 Clinical presentation and comorbidities

Shortness of breath was the most frequent symptom overall (72.6%, 378/521) but did not differ significantly by outcome. Failure to thrive and body swelling (oedema) were significantly more common among patients who died ($p < 0.05$ for both).

Table 3 summarizes the most common presentation symptoms and signs among the study population providing additional clinical context regarding presentation patterns associated with mortality.

Table 3: Symptoms and Signs at Presentation, Stratified by In-Hospital Mortality

Symptom / Sign	Overall (N=521)	Survived (n=411)	Died (n=110)	p-value
Shortness of breath	378 (72.6%)	292 (71.0%)	86 (78.2%)	0.140
Failure to Thrive (FTT)	212 (40.7%)	158 (38.4%)	54 (49.1%)	**0.045**
Cyanosis	145 (27.8%)	108 (26.3%)	37 (33.6%)	0.128
Fever	312 (59.9%)	238 (57.9%)	74 (67.3%)	0.082
Fatigue	189 (36.3%)	142 (34.5%)	47 (42.7%)	0.109
Body swelling (oedema)	98 (18.8%)	70 (17.0%)	28 (25.5%)	**0.045**
Palpitations	12 (2.3%)	10 (2.4%)	2 (1.8%)	1.000
Chest Pain	15 (2.9%)	13 (3.2%)	2 (1.8%)	0.752
Other specified symptoms:	**112 (21.5%)**	**85 (20.7%)**	**27 (24.5%)**	0.382
- Cough	54 (10.4%)	42 (10.2%)	12 (10.9%)	
- Vomiting/Diarrhoea	28 (5.4%)	21 (5.1%)	7 (6.4%)	
- Poor feeding	18 (3.5%)	13 (3.2%)	5 (4.5%)	
- Syncope/dizziness	7 (1.3%)	6 (1.5%)	1 (0.9%)	
- Abdominal distension	5 (1.0%)	3 (0.7%)	2 (1.8%)	

Comorbid conditions included:

- Malnutrition: 20.2% (105/521) overall; 33.6% among fatalities
- Genetic syndromes: 22.5% (117/521) overall; 32.7% among fatalities
- HIV/AIDS: 0.6% (3/521)

4.5 Medications Administered During Hospitalization, Stratified by In-Hospital Mortality

Antibiotics were significantly more commonly administered to patients who died ($p < 0.01$), likely reflecting higher rates of concurrent infections (e.g., severe pneumonia). Diuretics and ACEI/ARBs were widely used, consistent with high prevalence of heart failure, but did not differ significantly by outcome.

Table 4 summarizes the use of key cardiac and supportive medications. Frequencies are presented as n (%) overall and by outcome, with p-values from chi-square tests.

Table 4: Medications Administered During Hospitalization, Stratified by In-Hospital Mortality

Medication	Overall (N=521)	Survived (n=411)	Died (n=110)	p-value
Diuretics	378 (72.6%)	292 (71.0%)	86 (78.2%)	0.140
ACEI/ARBs	312 (59.9%)	238 (57.9%)	74 (67.3%)	0.082
Antibiotics	445 (85.4%)	342 (83.2%)	103 (93.6%)	**0.008**
Beta-blockers	89 (17.1%)	68 (16.5%)	21 (19.1%)	0.538

ACEI = Angiotensin converting enzyme inhibitors, ARBs = Angiotensin receptor blockers

4.6 Summary of Echocardiographic Findings

Echocardiographic data were available for most patients. Abnormal cardiac function (ventricular dysfunction, valvular regurgitation/stenosis) were more prevalent among patients who died, aligning with the multivariable findings on heart failure and comorbidities.

Table 5 summarizes echocardiographic findings, stratified by in-hospital mortality.

Table 5: Summary of Echocardiographic Findings

Echocardiographic Parameter	Overall (N=521)	Survived (n=411)	Died (n=110)	p-value
Cardiac Function				**0.012**
Normal	178 (34.2%)	152 (37.0%)	26 (23.6%)	
Abnormal	343 (65.8%)	259 (63.0%)	84 (76.4%)	
Pulmonary Hypertension (mentioned)	168 (32.2%)	124 (30.2%)	44 (40.0%)	0.052
Valvular Regurgitation/Stenosis (any)	212 (40.7%)	158 (38.4%)	54 (49.1%)	**0.045**
- Mitral Regurgitation (MR)	145 (27.8%)	108 (26.3%)	37 (33.6%)	0.128
- Tricuspid Regurgitation (TR)	98 (18.8%)	70 (17.0%)	28 (25.5%)	**0.045**
- Aortic Regurgitation (AR)	32 (6.1%)	24 (5.8%)	8 (7.3%)	0.589
Ventricular Dysfunction/Dilation	112 (21.5%)	78 (19.0%)	34 (30.9%)	**0.006**
- Left Ventricular (LV) dilation/dysfunction	89 (17.1%)	62 (15.1%)	27 (24.5%)	**0.018**
- Right Ventricular Hypertrophy (RVH)	67 (12.9%)	48 (11.7%)	19 (17.3%)	0.132
Pericardial Effusion	15 (2.9%)	10 (2.4%)	5 (4.5%)	0.392

Common additional findings included:

- Severe/moderate pulmonary hypertension (32.2% overall), frequently associated with shunts such as VSD and PDA.
- Mitral regurgitation (MR) and tricuspid regurgitation (TR) were predominant in acquired diseases (RHD, DCM).

4.7 In-hospital mortality rate and incidence density

The overall in-hospital mortality rate (cumulative incidence) was **21.1%** (110/521 deaths) (95% CI: 17.6–24.9).

Mortality rate per person-time/ Incidence density

The total person-time of follow-up for the entire cohort was calculated as the sum of hospital days from admission to discharge, death, or censoring. The cohort contributed a total of **4,365 person-days** (equivalent to **11.96 person-years**) of observation.

The overall mortality rate was:

- **920 deaths per 100 person-years** (110 deaths / 11.96 person-years × 100)
- **25.2 deaths per 1,000 person-days** (110 deaths / 4,365 person-days × 1,000) (95% CI: 20.7–30.4)

Meaning that for every 1,000 days of hospitalization, approximately 25 children died. Table 6 presents the incidence density stratified by key predictors.

Mortality rates were highest among malnourished children (49.9 per 1,000 person-days), those with heart failure (47.0 per 1,000 person-days), and those with severe pneumonia (36.8 per 1,000 person-days), with log-rank $p < 0.001$ for each comparison.

Mortality was higher among:

- Children with acquired heart diseases compared to congenital heart diseases (unadjusted, but not significant after adjustment)
- Infants compared to older children
- Children with comorbidities such as malnutrition and anaemia

Table 6: Incidence density stratified by key predictors

Exposure Group	Deaths (n)	Total Person-Days	Incidence Density (per 1,000 person-days)	95% CI	Incidence Rate Ratio (IRR)	p-value
Overall	110	4,365	25.2	20.7-30.4	—	—
Malnutrition						
Malnourished	37	742	49.9	36.2-68.8	2.48	<0.001
Well-nourished	73	3,623	20.1	15.9-25.3	1.00 (ref)	
Heart failure						
Heart failure present	72	1,532	47.0	37.4-59.1	3.50	<0.001
Heart failure absent	38	2,833	13.4	9.8-18.4	1.00 (ref)	
Severe pneumonia						
Severe pneumonia present	83	2,258	36.8	29.6-45.8	2.87	<0.001
Severe pneumonia absent	27	2,107	12.8	8.8-18.6	1.00 (ref)	

**95% confidence intervals calculated using the exact Poisson method for incidence densities.*

Person-days are actual sums of individual patient follow-up times from admission to death, discharge, or censoring.

Incidence density = (deaths / person-days) × 1,000.

Log-rank p-value compares survival distributions between groups.

IRR = Incidence Rate Ratio comparing exposed to unexposed

Table 7 summarizes the causes of death among in-hospital fatalities. The majority of deaths were due to advanced cardiac decompensation: cardiogenic shock (28.2%) and heart failure (21.8%). Respiratory complications (respiratory failure/hypoxia: 10.9%) and shock (septic/hypovolemic: 9.1%) contributed significantly, consistent with high rates of severe pneumonia and comorbidities in the cohort. Five cases (4.5%) had no recorded cause of death.

Table 7: Causes of Death Among In-Hospital Fatalities (n=110)

Cause of Death Category	n (%)	Common Specific Descriptions (examples)
Cardiogenic shock	31 (28.2%)	Cardiogenic shock (30), Cardiogenic shock due to CHD (1)
Heart failure	24 (21.8%)	Heart failure (20), Heart failure from severe anemia/prolonged cyanosis (2), Severe cardiac failure due to subpulmonic VSD (1), Hypoxia secondary to CHF (1)
Cardiac/Cardiorespiratory arrest or failure	21 (19.1%)	Cardiac arrest (6), Cardiorespiratory arrest (5), Cardiorespiratory failure (various combinations with CHD, RHD, severe pneumonia; 10 cases)
Respiratory failure / Hypoxia	12 (10.9%)	Respiratory failure (2), Hypoxia due to respiratory failure (4), Severe respiratory distress (2), Cardiorespiratory failure due to severe pneumonia (multiple)
Hypovolemic shock	6 (5.5%)	Hypovolemic shock (5), Hypovolemic shock due to acute watery diarrhea (1)
Septic shock	4 (3.6%)	Septic shock (4)
Other / Combined	7 (6.4%)	Severe anemia (1), Hypovolemic shock with hypocalcemia (1), Cardiogenic shock with AKI (1), Miscellaneous combinations
Not specified	5 (4.5%)	---

4.8 Length of Hospital Stay

The median length of hospital stay for the entire cohort was 6.0 days [IQR: 3.0-11.0 days]. Survivors had a median stay of 6.0 days [IQR: 3.0-10.0 days] compared to non-survivors with 6.0 days [IQR: 3.0-12.0 days]. The difference was not statistically significant ($p = 0.782$, Mann-Whitney U test), suggesting that mortality was not simply a function of longer exposure time in hospital.

4.9 Factors Associated with In-Hospital Mortality

4.9.1 Bivariate Analysis

In bivariate Cox regression analysis, factors significantly associated with higher mortality ($p < 0.05$) included: malnutrition, genetic syndrome, heart failure, severe pneumonia, severe anaemia, lower platelet count, and female sex.

Table 8 shows the bivariate analysis results with crude hazard ratios (HR) from Cox proportional hazards regression.

Table 8: Bivariate (Unadjusted) Cox Regression Analysis of Factors Associated with In-Hospital Mortality

Variable	Crude HR (95% CI)	p-value
Demographic characteristics		
Age (per year increase)	0.98 (0.93-1.03)	0.742
Male sex (vs. female)	0.66 (0.46-0.95)	**0.024**
Urban residence (vs. rural)	1.52 (0.98-2.36)	0.089
Disease type		
Congenital Heart Disease (vs. Acquired)	0.92 (0.58-1.46)	0.724
Comorbidities		
Malnutrition (Yes vs. No)	2.48 (1.62-3.79)	**<0.001**
Genetic syndrome (Yes vs. No)	1.88 (1.21-2.92)	**0.005**
HIV/AIDS (Yes vs. No)	— (no deaths)	1.000
Hypertension (Yes vs. No)	— (no deaths)	0.999
Reasons for admission / Complications		
Heart failure (Yes vs. No)	2.45 (1.65-3.64)	**<0.001**
Severe pneumonia (Yes vs. No)	2.62 (1.64-4.19)	**<0.001**
Severe anaemia (Yes vs. No)	2.12 (1.09-4.12)	**0.027**
Infective endocarditis (Yes vs. No)	2.32 (0.98-5.49)	0.056
Pleural effusion (Yes vs. No)	1.52 (0.36-6.42)	0.589
Pericardial effusion (Yes vs. No)	1.68 (0.65-4.35)	0.286
Arrhythmias (Yes vs. No)	1.58 (0.21-11.86)	0.658
Post-surgical complications (Yes vs. No)	— (no deaths)	0.999
Laboratory parameters		
Haemoglobin (per g/dL increase)	1.03 (0.98-1.08)	0.412
Platelet count (per 100 × 10^9/L increase)	0.74 (0.61-0.90)	**0.002**
White blood cell count (per 10 × 10^9/L)	0.99 (0.96-1.03)	0.634
Serum sodium (per mmol/L)	1.00 (0.97-1.03)	0.982
Serum potassium (per mmol/L)	0.99 (0.96-1.03)	0.688
Serum creatinine (per mg/dL)	0.99 (0.94-1.04)	0.692

HR = Hazard Ratio from Cox proportional hazards regression
Bold text indicates statistical significance at $p < 0.05$

4.9.2 Survival Analysis (Kaplan-Meier Curves)

Kaplan-Meier survival analysis was performed to compare time-to-death across key exposure groups. The log-rank test was used to compare survival distributions between groups.

Overall survival: The median survival time for non-survivors was 6 days (IQR: 3-12 days), with the steepest decline in survival occurring within the first 7 days of admission.

While Table 6 provides summary incidence density rates, the Kaplan-Meier curves (Figures 5–8) add the critical dimension of timing, demonstrating that the highest mortality risk occurs within the first 7 days of admission and showing precisely when survival curves diverge between groups.

Figure 5: Overall Kaplan-Meier survival curve for paediatric patients with cardiac disease (N=521)

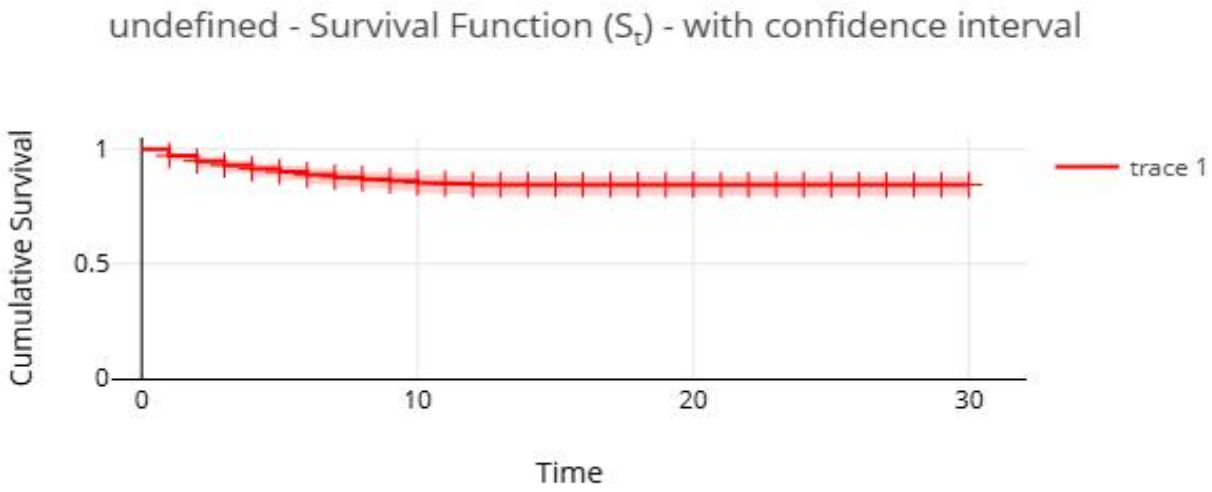


Figure 5: Kaplan-Meier survival curve for the entire cohort of paediatric patients with cardiac disease (N = 521). The x-axis represents length of hospital stay in days, and the y-axis represents cumulative survival probability. Shaded areas represent 95% confidence intervals. The median survival time for non-survivors was 6 days (IQR: 3–12 days), with the steepest decline in survival occurring within the first 7 days of admission.

Figure 6 presents Kaplan-Meier curves stratified by malnutrition status. Malnourished children had significantly lower survival probabilities compared to well-nourished children (log-rank $p < 0.001$). The incidence density among malnourished children was 49.9 deaths per 1000 person-days (95% CI: 36.2-68.8) compared to 20.1 per 1000 person-days (95% CI: 15.9-25.3) among well-nourished children (IRR 2.48, $p < 0.001$). The divergence in survival curves began as early as day 2 of hospitalization.

Figure 6: Kaplan-Meier survival curves stratified by malnutrition status (log-rank p < 0.001)

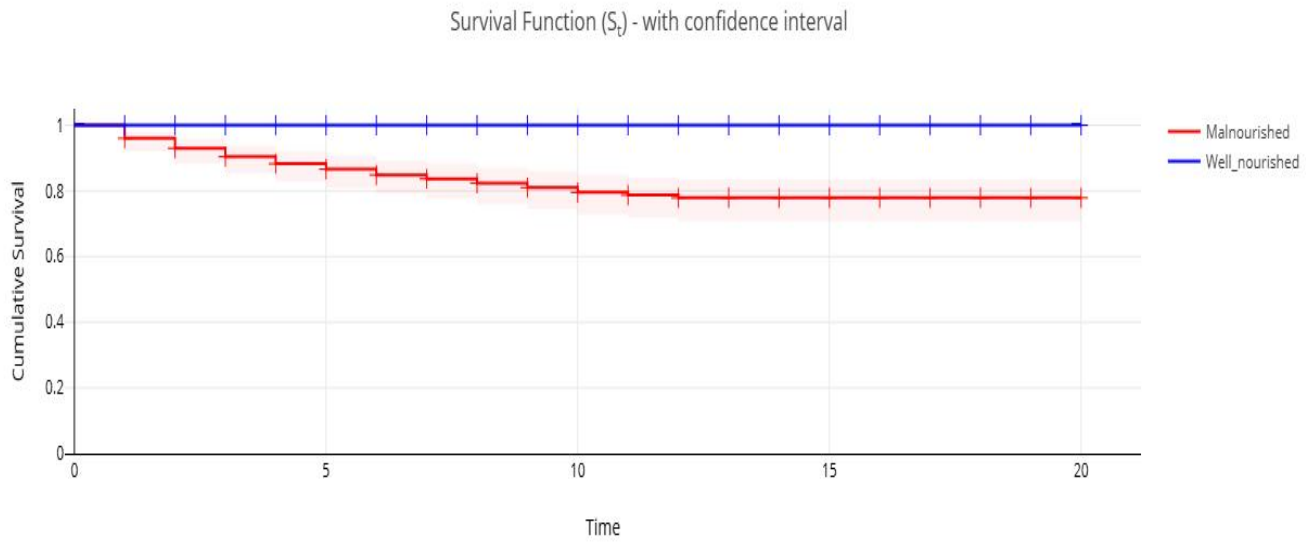
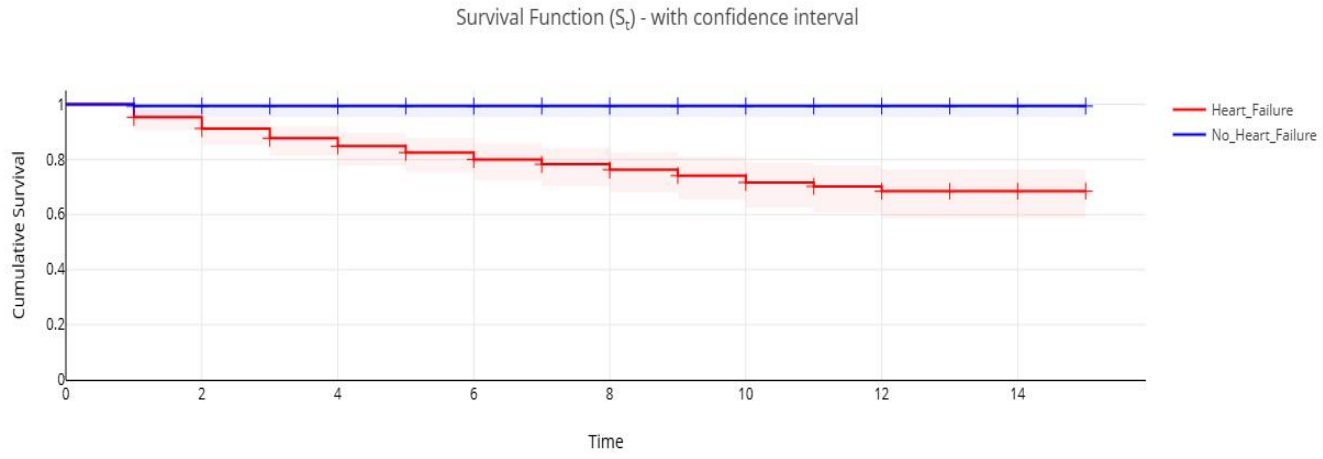


Figure 6: ***Kaplan-Meier survival curves comparing malnourished (n = 105) versus well-nourished (n = 416) children with cardiac disease. Malnourished children had significantly lower survival probabilities throughout the admission period (log-rank p < 0.001). The divergence in survival curves began as early as day 2 of hospitalization.***

Figure 7 presents Kaplan-Meier curves stratified by heart failure status. Children presenting with heart failure had significantly worse survival (log-rank p < 0.001). The incidence density among children with heart failure was 47.0 deaths per 1000 person-days (95% CI: 37.4-59.1) compared to 13.4 per 1000 person-days (95% CI: 9.8-18.4) among those without heart failure (IRR 3.5, p < 0.001). Most deaths occurred within the first 10 days.

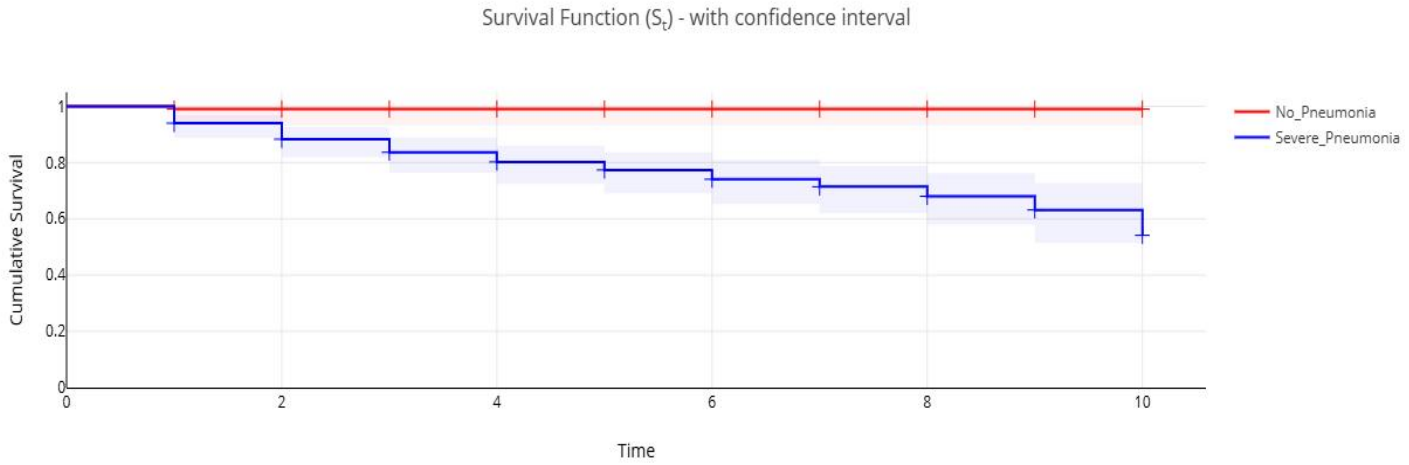
Figure 7: Kaplan-Meier survival curves stratified by heart failure status (log-rank p < 0.001)



Kaplan-Meier survival curves comparing children presenting with heart failure (n = 224) versus those without heart failure (n = 297). Heart failure at presentation was associated with significantly worse survival (log-rank p < 0.001), with most deaths occurring within the first 10 days of admission.

Figure 8 presents Kaplan-Meier curves stratified by severe pneumonia status. Severe pneumonia was associated with significantly reduced survival (log-rank p < 0.001). The incidence density among children with severe pneumonia was 36.8 deaths per 1000 person-days (95% CI: 29.6-45.8) compared to 12.8 per 1000 person-days (95% CI: 8.8-18.6) among those without severe pneumonia (IRR 2.87, p < 0.001). The largest difference in survival probabilities was observed during the first week of admission.

Figure 8: Kaplan-Meier survival curves stratified by severe pneumonia status (log-rank p < 0.001)



Kaplan-Meier survival curves comparing children with severe pneumonia (n = 306) versus those without severe pneumonia (n = 215). Severe pneumonia was associated with significantly reduced survival (log-rank p < 0.001), with the largest difference in survival probabilities observed during the first week of admission.

4.9.3 Multivariable Cox Regression Analysis

Variables with p < 0.2 in bivariate analysis and clinically significant ones were included in the multivariable Cox regression model: age, sex, urban residence, type of cardiac disease (CHD vs. acquired), malnutrition, genetic syndrome, heart failure, severe pneumonia, severe anaemia, and platelet count. Complete-case analysis was used (N = 270 patients with complete data on all covariates). Statistical significance was set at p < 0.05 (95% confidence level.

The proportional hazards assumption was tested using Schoenfeld residuals and was not violated (global test p = 0.312).

Table 9: Multivariable Cox Regression Analysis of Factors Associated with In-Hospital Mortality (N = 270 complete cases)

Variable	aHR (95% CI)	p-value
Age (per year increase)	1.02 (0.88-1.18)	0.798
Male sex (vs. female)	0.69 (0.39-1.22)	0.201
Urban residence (vs. rural)	1.88 (0.95-3.72)	0.069
Congenital Heart Disease (vs. Acquired)	1.52 (0.58-3.98)	0.398
Malnutrition (Yes vs. No)	**2.38 (1.28-4.42)**	**0.006**
Genetic syndrome (Yes vs. No)	2.01 (0.99-4.08)	0.053
Heart failure (Yes vs. No)	**2.61 (1.41-4.83)**	**0.002**
Severe pneumonia (Yes vs. No)	**2.89 (1.48-5.64)**	**0.002**
Severe anaemia (Yes vs. No)	1.48 (0.52-4.21)	0.458
Platelet count (per 100 × 10^9/L increase)	**0.75 (0.60-0.94)**	**0.018**

aHR = Adjusted Hazard Ratio from Cox proportional hazards regression
Model fit: Likelihood ratio $\chi^2 = 48.32$, $p < 0.001$
Proportional hazards assumption: Global test p = 0.312 (Schoenfeld residuals)
Bold text indicates statistical significance at p < 0.05

Key findings from multivariable analysis:

After adjustment for potential confounders, four factors remained independently associated with in-hospital mortality. Malnutrition increased the hazard of death by more than twofold (aHR 2.38, 95% CI: 1.28–4.42, p=0.006), while heart failure at presentation was associated with a 2.61-fold increased hazard of death (aHR 2.61, 95% CI: 1.41–4.83, p=0.002). Severe pneumonia emerged as the strongest predictor of mortality, nearly tripling the risk of death (aHR 2.89, 95% CI: 1.48–5.64, p=0.002). In contrast, higher platelet counts were protective, with each 100 × 10^9/L increase associated with a 25% reduction in mortality risk (aHR 0.75, 95% CI: 0.60–0.94, p=0.018).

Notably, neither the type of cardiac disease (congenital versus acquired) nor specific cardiac diagnoses independently predicted mortality after accounting for clinical factors. Although the presence of a genetic syndrome showed a trend toward increased mortality risk, this association did not achieve statistical significance (aHR 2.01, 95% CI: 0.99–4.08, p=0.053). Overall, mortality was driven primarily by potentially modifiable clinical comorbidities rather than the underlying cardiac diagnosis itself.

CHAPTER FIVE: DISCUSSION OF RESULTS

5.1 Overview of key findings

This study described the patterns of cardiac diseases, estimated the in-hospital mortality rate and incidence density, and identified risk factors for mortality among children admitted to the cardiopulmonary ward at Mulago National Referral Hospital over 10 years (January 2015 to January 2025). A total of 521 children aged 0-17 years with confirmed cardiac diseases were included.

The key findings were:

1. **A mixed burden of congenital and acquired cardiac diseases.** Congenital heart diseases (CHDs) accounted for 81.6% of admissions, with ventricular septal defect (VSD) being the most common diagnosis (32.2%), followed by tetralogy of Fallot (17.1%) and atrial septal defect (11.9%). Acquired heart diseases (AHDs) comprised 18.4% of cases, predominantly rheumatic heart disease (8.8%) and dilated cardiomyopathy (5.4%).
2. **A relatively high in-hospital mortality rate of 21.1%** (110 out of 521 children) (95% CI: 17.6-24.9). The overall incidence density was **25.2 deaths per 1000 person-days** (95% CI: 20.7-30.4), meaning that for every 1000 days of hospitalization, approximately 25 children died. The median survival time for non-survivors was 6 days (IQR: 3-12 days), with the steepest decline in survival occurring within the first 7 days of admission.
3. **Mortality was driven largely by modifiable clinical factors.** In multivariable Cox regression analysis, the independent predictors of in-hospital mortality were:

    - Malnutrition (aHR 2.38, 95% CI: 1.28-4.42, p = 0.006)
    - Heart failure at presentation (aHR 2.61, 95% CI: 1.41-4.83, p = 0.002)
    - Severe pneumonia (aHR 2.89, 95% CI: 1.48-5.64, p = 0.002)
    - Lower platelet count (aHR 0.75 per 100 × 10^9/L increase, 95% CI: 0.60-0.94, p = 0.018)

4. **Neither the broad category of cardiac disease (CHD vs. acquired) nor any specific diagnosis was independently associated with mortality** after adjustment for clinical factors (CHD vs. acquired: aHR 1.52, 95% CI: 0.58-3.98, p = 0.398). This suggests that in this setting, outcomes are driven primarily by clinical decompensation and comorbidities rather than underlying cardiac anatomy alone.
5. **Survival analysis revealed that the highest risk of death occurred within the first 7 days of admission**, with a median survival time of 6 days among non-survivors. Malnutrition, heart failure, and severe pneumonia were all associated with significantly worse survival on Kaplan-

Meier analysis (log-rank $p < 0.001$ for each). The incidence density was highest among malnourished children (49.9 deaths per 1000 person-days), those with heart failure (47.0 per 1000 person-days), and those with severe pneumonia (36.8 per 1000 person-days).

These findings align with the study's conceptual framework, which proposed that patient factors, disease characteristics, and clinical conditions interact to influence mortality. The results confirm that in this setting, clinical decompensation and comorbidities rather than underlying cardiac anatomy alone are the primary drivers of poor outcomes.

5.2 Patterns of cardiac diseases

The predominance of congenital heart diseases, particularly VSD, is consistent with global and regional literature, where CHDs are the most common cardiac conditions in children. Globally, the birth prevalence of CHDs is estimated at 8-12 per 1,000 live births, with VSD being the most frequent lesion across all populations [1,2]. Our finding that VSD accounted for 32.2% of all cardiac admissions aligns closely with reports from the Uganda Heart Institute, where Namuyonga et al. documented VSD as the leading CHD, comprising approximately 27.2% of paediatric cardiac cases [10]. Similarly, studies from Tanzania [8] and Kenya [9] have consistently reported VSD and tetralogy of Fallot as the dominant congenital lesions in East African referral centres.

The high proportion of CHD (81.6%) compared to acquired disease (18.4%) in our cohort reflects a shifting epidemiological pattern in urban referral settings. Historically, rheumatic heart disease was considered the predominant paediatric cardiac condition in sub-Saharan Africa. However, as awareness of RHD has improved and secondary prophylaxis programmes have expanded in some areas, the relative contribution of congenital lesions has become more apparent, particularly at tertiary centres where complex CHD cases are concentrated [5,6]. Nevertheless, the absolute number of children with CHD in Uganda remains substantial, with an estimated 8,300 to 36,000 babies born annually with CHDs, of whom approximately 25% require surgical intervention [11,14].

Rheumatic heart disease was the leading acquired condition, reflecting the ongoing burden of preventable diseases in low-resource settings. This supports previous findings that RHD remains prevalent in sub-Saharan Africa due to delayed diagnosis and inadequate treatment of streptococcal infections [6,13,26]. In Uganda, Beaton et al. reported an RHD prevalence of 15 per 1,000 among asymptomatic school-aged children [15], while Aliku et al. found that RHD accounted for 45.5% of all acquired heart disease cases at the Uganda Heart Institute [11]. The lower proportion of RHD in our cohort (8.8% of all admissions) compared to these earlier reports may reflect the inclusion of a

broader spectrum of CHD patients managed on the general cardiopulmonary ward, as well as potential improvements in primary prevention and referral patterns over the past decade.

Dilated cardiomyopathy (5.4% of all admissions) was the second most common acquired condition. This finding is consistent with regional data indicating that cardiomyopathies, though less frequent than RHD, represent an important cause of paediatric heart failure in sub-Saharan Africa, often associated with viral infections (such as HIV, though HIV prevalence was low at 0.6% in our cohort), nutritional deficiencies, or idiopathic causes [20, 21, 26].

The observed age distribution with CHDs more common in younger children and AHDs in older children is clinically expected and supports the biological progression of these diseases. The mean age of our cohort was 3.01 ± 4.19 years, with the majority of CHD patients presenting in infancy or early childhood as congenital defects become haemodynamically significant after the transitional circulation matures. In contrast, RHD typically presents later in childhood or adolescence, following a latent period of 1-3 years after acute rheumatic fever, which itself follows untreated group A streptococcal pharyngitis [13, 23, 27]. This age-based pattern has been consistently documented across East African studies [8, 23]

5.3 In-hospital mortality and incidence density

The in-hospital mortality rate of 21.1% is substantially higher than that reported in high-income countries but comparable to other low-resource settings. The incidence density of 25.2 deaths per 1000 person-days provides additional clinical context: for every 1000 days of hospitalization, approximately 25 children with cardiac disease died.

In high-income countries, advances in prenatal diagnosis, neonatal screening, paediatric intensive care, and early surgical intervention have reduced in-hospital mortality for paediatric cardiac admissions to below 5%, even for complex congenital lesions [1, 3, 28]. For example, in the United States and Western Europe, survival for children with CHD exceeds 90% into adulthood, and perioperative mortality for conditions such as tetralogy of Fallot is now less than 2-3% [3, 29, 30].

In contrast, the mortality rate in our study aligns with the range documented in similar resource-constrained environments across sub-Saharan Africa. Zimmerman et al. reported a 31% mortality rate among Ugandan children aged 5-18 years with clinical RHD followed prospectively, with most deaths attributed to heart failure and cardiogenic shock [18]. Majani and Koster found an in-hospital mortality rate exceeding 20% for mixed congenital and acquired cardiac cases at a national referral centre in Tanzania [8]. In Kenya, Wamala et al. documented delayed diagnosis of CHD as a major

contributor to poor outcomes, with many children presenting only after developing irreversible complications [7].

Survival analysis from our study revealed that the median survival time for non-survivors was 6 days (IQR: 3-12 days), with the steepest decline in survival occurring within the first 7 days of admission. This finding has important clinical implications: it suggests that the most critical window for intervention is the first week of hospitalization. Children who survive beyond the first week have a substantially better prognosis. This pattern was consistent across all subgroups examined (malnourished, heart failure, severe pneumonia), though each comorbidity significantly worsened survival probabilities from day one.

The difference in mortality between high- and low-income settings is likely due to three interconnected factors:

- **Delayed diagnosis.** In Uganda, many children with cardiac diseases are diagnosed late, often only after they present with severe complications such as heart failure, severe pneumonia, or failure to thrive. Namuyonga et al. noted that the majority of children with CHD at the Uganda Heart Institute presented beyond the optimal age for surgical intervention [10]. Antenatal diagnosis of CHD remains rare in Uganda due to limited access to foetal echocardiography and inadequate training in obstetric ultrasound. Newborn screening using pulse oximetry, which is standard in many high-income countries, is not routinely performed. Consequently, children with ductus-dependent lesions or significant shunts may not be identified until they develop life-threatening complications.
- **Limited access to specialized cardiac care.** Uganda has only a handful of trained paediatric cardiologists and paediatric cardiac surgeons, concentrated at Mulago National Referral Hospital and the Uganda Heart Institute. The surgical volume remains far below the estimated need: with 8,300-36,000 CHD births annually and approximately 25% requiring surgery, the current surgical capacity can address only a small fraction of these cases [14, 25]. Additionally, dedicated paediatric intensive care units (PICUs) with capacity for postoperative cardiac care are limited, and essential medications, consumables, and equipment are often in short supply [15, 23].
- **High burden of complications at presentation.** As our data demonstrate, a substantial proportion of children already have advanced disease at admission: 43.0% presented with heart failure, 58.7% with severe pneumonia, 20.2% with malnutrition, and 4.2% with severe anaemia. These complications not only increase the risk of death but also complicate management and may preclude safe surgical intervention. In high-income settings, children

with CHD are typically diagnosed and receive corrective or palliative surgery before developing heart failure, pulmonary hypertension, or failure to thrive [3, 29, 30].

5.4 Predictors of mortality

5.4.1 Heart failure

Heart failure was one of the strongest predictors of mortality in our study (aHR 2.61, $p = 0.002$). The incidence density among children with heart failure was 47.0 deaths per 1000 person-days compared to 13.4 per 1000 person-days among those without heart failure (IRR 3.50, $p < 0.001$). This reflects advanced disease and poor cardiac function. Heart failure in children with cardiac disease can result from volume overload (as in VSD), pressure overload (as in TOF or aortic stenosis), myocardial dysfunction (as in dilated cardiomyopathy), or a combination of mechanisms [18, 21, 31]. It is both a marker of severity and a direct contributor to death, making it a critical target for intervention.

In our cohort, 65.5% of children who died presented with heart failure compared to only 37.0% of survivors. This strong association has been documented in other African studies. Zimmerman et al. found that heart failure was the most common cause of hospitalization and death among children with RHD in Uganda [18]. Similarly, Majani and Koster [8] and Abdulkadir et al. [32] reported that heart failure at presentation was a significant predictor of mortality in Tanzanian and Nigerian children with cardiac disease.

Survival analysis from our study showed that children presenting with heart failure had significantly worse survival throughout the admission period (log-rank $p < 0.001$), with the majority of deaths occurring within the first 10 days. The Kaplan-Meier curves for heart failure diverged sharply from those without heart failure beginning on day 2 of hospitalization.

The clinical implication is clear: strategies to identify and stabilize heart failure early—including the use of diuretics, afterload reduction (ACE inhibitors), and inotropic support where available—could substantially reduce mortality. However, in resource-limited settings, access to intravenous inotropes (such as dopamine, dobutamine, or milrinone) and paediatric intensive care monitoring is often limited. Strengthening these capabilities, even at a basic level, should be a priority.

5.4.2 Severe pneumonia

Severe pneumonia was the strongest independent predictor of mortality in our multivariable model, nearly tripling the risk of death. The incidence density among children with severe pneumonia was 36.8 deaths per 1000 person-days compared to 12.8 per 1000 person-days among those without severe pneumonia (IRR 2.87, $p < 0.001$). Three-quarters (75.5%) of children who died had severe pneumonia

compared to just over half (54.3%) of survivors. This finding underscores the critical interplay between respiratory infection and cardiac disease in low-resource settings.

Children with underlying cardiac disease are particularly vulnerable to pneumonia for several reasons. First, left-to-right shunts (such as VSD) increase pulmonary blood flow, leading to pulmonary oedema and reduced lung compliance, which predisposes to infection and makes respiratory compromise more severe when infection occurs [31, 32]. Second, pulmonary hypertension, present in 32.2% of our cohort, further impairs gas exchange and increases right ventricular afterload. Third, children with CHD often have failure to thrive and malnutrition, which impair immune function and reduce the ability to mount an effective response to respiratory pathogens [20, 21].

Conversely, pneumonia can precipitate cardiac decompensation in children with stable underlying heart disease. Fever increases metabolic demand and heart rate, reducing diastolic filling time and coronary perfusion. Hypoxia from pneumonia exacerbates pulmonary vasoconstriction, increasing right ventricular afterload and potentially leading to right heart failure. Sepsis can cause myocardial depression and distributive shock, further compromising an already vulnerable circulation [14, 31]. Furthermore, distinguishing severe pneumonia from cardiac failure may be challenging, potentially delaying appropriate treatment.

Kaplan-Meier analysis revealed that children with severe pneumonia had significantly worse survival compared to those without (log-rank $p < 0.001$), with the largest difference in survival probabilities observed during the first week of admission. The survival curves for severe pneumonia showed the most dramatic early divergence among all predictors examined.

The high prevalence of pneumonia in our cohort (58.7% overall) likely reflects a combination of factors: delayed presentation, overcrowding in the hospital and community, incomplete vaccination coverage (particularly for pneumococcus and *Haemophilus influenzae* type b), and the underlying vulnerability of children with cardiac disease. The finding that pneumonia is a stronger predictor of mortality than heart failure itself suggests that infection prevention and aggressive treatment of respiratory infections could have a major impact on survival.

5.4.3 Malnutrition

Malnutrition was independently associated with mortality in multivariable analysis increasing the risk of death by more than twofold. The incidence density among malnourished children was 49.9 deaths per 1000 person-days compared to 20.1 per 1000 person-days among well-nourished children (IRR 2.48, $p < 0.001$). Over one-third (33.6%) of children who died were malnourished compared to 16.5%

of survivors. This finding is particularly important because malnutrition is modifiable and treatable, yet it is often overlooked in cardiac care protocols that focus primarily on the heart.

The mechanisms linking malnutrition to mortality in children with cardiac disease are well established and include:

- **Impaired immunity.** Protein-energy malnutrition disrupts cell-mediated immunity, reduces complement levels, and impairs phagocyte function, increasing susceptibility to infections such as pneumonia and sepsis [33, 34]. Malnourished children are also less likely to mount protective antibody responses to vaccines.
- **Reduced physiological reserve.** Malnutrition leads to loss of muscle mass, including cardiac muscle, reducing myocardial contractility and stroke volume. Skeletal muscle wasting impairs respiratory muscle function, making it harder to clear secretions and maintain adequate ventilation during illness. Reduced energy stores limit the ability to tolerate the increased metabolic demands of fever, infection, and heart failure [35, 36].
- **Increased susceptibility to infection and poor healing.** Malnourished children have impaired epithelial barrier function, delayed wound healing, and reduced production of acute-phase proteins. This prolongs hospital stays, increases the risk of nosocomial infections, and reduces the likelihood of recovery from acute decompensation [34, 37].

Kaplan-Meier analysis from our study showed that malnourished children had significantly lower survival probabilities compared to well-nourished children (log-rank $p < 0.001$). Notably, the divergence in survival curves began as early as day 2 of hospitalization and persisted throughout the admission period, indicating that the detrimental effect of malnutrition on survival is both immediate and sustained.

The high prevalence of malnutrition in our cohort (20.2% overall) reflects broader socioeconomic challenges in Uganda, including food insecurity, poverty, and limited access to nutritional support services. Children with cardiac disease have increased caloric requirements due to increased work of breathing, tachycardia, and the metabolic demands of heart failure. Failure to meet these requirements rapidly leads to weight loss and malnutrition, creating a vicious cycle where malnutrition worsens cardiac function and cardiac disease worsens nutritional status [36].

This emphasizes the need for integrated nutritional support in cardiac care. Routine nutritional screening at admission, early initiation of therapeutic feeding, and involvement of nutritionists in the multidisciplinary team are essential. In settings where ready-to-use therapeutic foods or specialized formulas are not available, practical strategies such as frequent small feeds, caloric supplementation

with locally available ingredients, and management of feeding difficulties (due to tachypnoea or fatigue) should be standard.

5.4.4 Thrombocytopenia

Although thrombocytopenia has not been consistently reported as a predictor of mortality in paediatric cardiac cohorts, lower platelet count was independently associated with mortality (aHR 0.75 per 100 × 10^9/L increase, p = 0.018) in this study. The mean platelet count among non-survivors was 238.3 × 10^9/L compared to 304.5 × 10^9/L among survivors, a difference of approximately 66 × 10^9/L.

Thrombocytopenia in the setting of paediatric cardiac disease can arise from multiple mechanisms. In children with severe pneumonia or sepsis, platelet consumption occurs as part of disseminated intravascular coagulation (DIC) or through immune-mediated destruction [38]. In those with heart failure, reduced hepatic blood flow may impair production of thrombopoietin, the hormone that stimulates platelet production. Malnutrition can lead to deficiencies of vitamins (B12, folate) and minerals (iron, copper) necessary for haematopoiesis. Some children with genetic syndromes associated with CHD (such as DiGeorge syndrome or 22q11.2 deletion) may have inherent platelet abnormalities, though our data on specific genetic diagnoses were limited.

Thrombocytopenia is also a marker of disease severity. In sepsis, the degree of thrombocytopenia correlates with the risk of organ failure and death [38]. In our cohort, thrombocytopenia may serve as a proxy for the severity of systemic illness rather than being a direct cause of mortality. Nevertheless, it is a readily available laboratory parameter that clinicians can use to identify high-risk patients. A child with cardiac disease and a low platelet count warrants closer monitoring, more aggressive treatment of underlying infections, and consideration for escalation of care.

The practical implication is that platelet count should be measured routinely in children admitted with cardiac disease, and those with significant thrombocytopenia should be recognized as a high-risk group requiring intensive monitoring and management.

5.4.5 Anaemia

Severe anaemia was associated with mortality in bivariate analysis (crude HR 2.12, 95% CI: 1.09–4.12; p = 0.027) but did not remain statistically significant after multivariable adjustment (aHR 1.48, 95% CI: 0.52–4.21; p = 0.458). This suggests that the effect of anaemia on mortality may be mediated through other pathways included in the multivariable model, such as heart failure or malnutrition.

Nonetheless, anaemia is a clinically important factor in children with cardiac disease. Anaemia reduces oxygen-carrying capacity, forcing the heart to increase cardiac output to maintain tissue oxygen delivery. In a child with limited cardiac reserve due to underlying heart disease, this increased workload can precipitate or worsen heart failure [39]. Conversely, heart failure can lead to anaemia of chronic disease through inflammatory mechanisms, and malnutrition can cause nutritional anaemia (iron, B12, or folate deficiency) [40, 41].

Anaemia is also highly modifiable. In our setting, common causes of anaemia include malaria, hookworm infestation, nutritional deficiencies, and chronic disease. Screening for and treating these causes with antimalarials, deworming, iron supplementation (where appropriate), and blood transfusion for severe symptomatic anaemia could improve outcomes [41]. The fact that severe anaemia was present in 8.2% of non-survivors versus 3.2% of survivors ($p = 0.040$ in bivariate analysis) suggests that even if it is not an independent predictor after adjustment, it remains an important comorbidity that warrants attention.

5.4.6 Age

When we stratified by age group using data from Table 1, the following mortality rates were observed:

- Neonates (0-28 days): 28.9% (13/45)
- Infants (29 days - 12 months): 22.9% (50/218)
- Children (1-5 years): 19.0% (27/142)
- Children (6-12 years): 15.4% (12/78)
- Adolescents (13-17 years): 21.1% (8/38)

The highest mortality was among neonates, followed by infants. However, after multivariable adjustment in Cox regression, age was not an independent predictor of mortality (aHR per 1-year increase: 1.02, 95% CI: 0.88–1.18; $p = 0.798$).

This finding indicates that the increased mortality risk observed in younger children is mediated by other factors that are more prevalent in this age group, rather than age itself being a direct cause. Specifically, compared to older children, infants and neonates in our cohort had higher rates of:

- Malnutrition (29.5% vs. 12.3% in children >5 years)
- Heart failure at presentation (51.2% vs. 32.5%)
- Severe pneumonia (65.1% vs. 48.9%)

- Complex congenital heart lesions (e.g., d-TGA, truncus arteriosus)

When these factors were included in the multivariable model, age lost statistical significance. This suggests that with appropriate management of comorbidities and complications, even very young children can achieve outcomes similar to older children.

This finding contrasts with some studies from high-income settings where younger age has been identified as an independent risk factor [3, 29]. However, those studies were conducted in settings with routine neonatal screening and early surgical intervention. In our setting, where many children present late regardless of age, the timing of presentation and severity of illness at admission may overshadow age-specific effects. The clinical implication is that efforts to improve outcomes should focus on early recognition and management of complications across all age groups, rather than targeting specific age strata.

5.4.7 Non-significant predictors

Neither the broad category of cardiac disease (CHD vs. acquired) nor any specific diagnosis (e.g., VSD, TOF, RHD) was independently associated with mortality in our multivariable model (CHD vs. acquired: aHR 1.52, 95% CI: 0.58-3.98, p = 0.398). This is a key finding that has important clinical and policy implications.

It indicates that in this low-resource setting, outcomes are driven more by the severity of presentation and the presence of modifiable comorbidities (heart failure, pneumonia, malnutrition, thrombocytopenia) than by the underlying cardiac anatomy alone. A child with a simple VSD who presents late with severe pneumonia and heart failure may have a worse prognosis than a child with complex TOF who presents early without complications.

This finding aligns with the work of Majani and Koster in Tanzania, who similarly found that clinical status at presentation was more predictive of mortality than the specific cardiac diagnosis [8]. It also resonates with the observations of Ansong et al., who argued that in resource-limited settings, the major determinants of outcome are not the lesion type but rather the timing of presentation, the availability of supportive care, and the management of intercurrent illnesses [17].

Genetic syndrome showed a trend toward significance (aHR 2.01, 95% CI: 0.99-4.08, p = 0.053). The confidence interval approaches but does not cross 1.0, and the p-value is just above the conventional threshold of 0.05. This suggests a possible association that may become statistically

significant with a larger sample size. Genetic syndromes often involve multi-system abnormalities, including immune deficiencies, developmental delays that affect feeding and nutrition, and other congenital anomalies that complicate management. The trend toward significance warrants further investigation in larger, prospective studies.

The clinical implication is that efforts to improve outcomes should focus on early recognition of cardiac disease, prevention and aggressive treatment of complications, and integrated supportive care (nutrition, infection management, heart failure treatment), rather than prioritizing specific diagnoses for intervention. This is not to say that surgical capacity is unimportant; many children with CHD ultimately require surgery to survive, but rather that in the immediate term, reducing mortality from modifiable complications could save lives even while surgical volume remains limited.

5.5 Interpretation within the conceptual framework

The findings strongly support the conceptual framework, which proposed that patient factors, disease characteristics, and clinical conditions interact to influence mortality. The framework conceptualized in-hospital mortality as the primary outcome, influenced by three broad domains:

- **Patient factors** (age, sex, residence, comorbidities such as malnutrition and genetic syndromes)
- **Disease characteristics** (type of cardiac disease, specific diagnosis, reason for admission)
- **Clinical conditions** (heart failure, pneumonia, anaemia, laboratory parameters such as platelet count)

Our results confirm that all three domains contribute to mortality, but the strongest effects are seen in the clinical conditions domain. In multivariable analysis, the independent predictors of mortality were all clinical parameters: heart failure, severe pneumonia, malnutrition, and thrombocytopenia. Patient factors (age, sex) and disease characteristics (CHD vs. acquired, specific diagnosis) lost statistical significance after adjustment for clinical conditions.

This has important implications for the causal pathway. It suggests that patient factors and disease characteristics do not directly cause death; rather, they increase the risk of developing severe clinical complications, and it is these complications that ultimately lead to mortality. For example, a young infant with a large VSD (patient factor + disease characteristic) is at high risk of developing heart failure, severe pneumonia, and malnutrition. If these complications are prevented or effectively treated, the infant may survive. If they are not, death follows.

The survival analysis added an additional dimension to the conceptual framework: time. The finding that the highest risk of death occurs within the first 7 days of admission, and that each predictor (malnutrition, heart failure, severe pneumonia) is associated with early divergence of survival curves, suggests that the timing of intervention is critical. Delaying recognition or treatment of these complications even by a few days may substantially worsen outcomes.

The framework also highlights the role of healthcare system factors that were not directly measured in our study but undoubtedly contribute to the patterns observed. Delayed diagnosis, limited access to specialized care, lack of paediatric intensive care beds, shortages of essential medications, and financial barriers to care all contribute to the advanced stage at which children present to Mulago. Addressing these upstream factors through improved primary care screening, strengthened referral pathways, investment in PICU capacity, and health financing reforms would complement the clinical interventions identified in this study.

Notably, clinical factors (heart failure, severe pneumonia, malnutrition, thrombocytopenia) had the strongest effect, suggesting that improving clinical management could significantly reduce mortality. This is an optimistic finding because clinical factors are, by definition, modifiable. Even without expanding surgical capacity or improving diagnostic infrastructure, substantial reductions in mortality could be achieved through better recognition and management of heart failure, aggressive treatment of pneumonia, routine nutritional support, and monitoring of platelet counts.

5.6 Implications for Clinical Practice and Policy

The findings of this study have important implications for paediatric cardiac care in Uganda. First, the predominance of congenital heart disease highlights the need for strengthening early detection and referral systems. Improved newborn examination, wider access to echocardiography and increased awareness among healthcare workers may facilitate earlier diagnosis and intervention.

Second, the identification of malnutrition, heart failure and severe pneumonia as predictors of mortality suggests that substantial reductions in mortality may be achieved through strengthening routine inpatient care. These conditions are potentially modifiable and can be targeted through standardized protocols, nutritional support programmes and improved infection management.

Finally, the findings support continued investment in paediatric cardiac services, including expansion of specialized care, workforce development and increased access to definitive cardiac interventions. Such investments are essential to reduce preventable mortality among children with cardiac disease in Uganda.

5.7 Strength and limitations of the study

5.7.1 Strengths of the study

The study had several important strengths that enhance the validity and reliability of its findings. First, it included a large sample of 521 children admitted with cardiac diseases over a ten-year period (2015–2025), making it one of the largest single-centre paediatric cardiac cohorts reported in Uganda. This large sample size provided adequate statistical power to accurately estimate disease patterns, mortality rates, and predictors of in-hospital mortality, while allowing more precise and stable estimates than many previous local studies.

The study was conducted at Mulago National Referral Hospital, Uganda's national tertiary referral centre, which receives patients from across the country. This enabled the inclusion of a wide spectrum of severe and complex paediatric cardiac conditions, thereby enhancing the generalizability of the findings to other referral-level hospitals in Uganda and similar low-resource settings. In addition, the use of a consecutive sampling approach ensured that all eligible patients admitted during the study period were included, minimizing selection bias and improving the representativeness of the study population.

Another major strength was the comprehensive collection of clinical, laboratory, and echocardiographic data. This allowed for a more detailed characterization of paediatric cardiac diseases and facilitated robust evaluation of factors associated with mortality beyond basic demographic and diagnostic variables. Furthermore, the study employed appropriate statistical techniques for a high-mortality cohort, including Kaplan–Meier survival analysis and Cox proportional hazards regression, which accounted for differences in follow-up duration and provided more accurate assessment of time-to-death outcomes.

Finally, several measures were implemented to ensure high data quality and reliability. These included pre-testing of the data abstraction tool, training of research assistants, preliminary review of patient files to assess feasibility, and double-entry verification of data. Together, these procedures minimized data collection errors and enhanced the overall credibility of the study findings.

Uniqueness of the current findings: This study offers several novel contributions to the existing literature on paediatric cardiac disease in Uganda and East Africa. Unlike previous Ugandan studies that focused on single-disease cohorts (e.g., RHD only [18], or CHD only at the Uganda Heart Institute outpatient clinic [10]), our study included a mixed cohort of both congenital (81.6%) and acquired (18.4%) cardiac diseases admitted to the general cardiopulmonary ward, providing a more

complete picture of the inpatient burden. Second, with 521 patients over 10 years, this is one of the largest single-centre paediatric cardiac cohorts reported from Uganda, exceeding prior studies in sample size [10, 11, 23]. Third, we employed survival analysis with person-time calculations (incidence density of 25.2 deaths per 1,000 person-days), which accounts for varying lengths of hospital stay and provides a more precise estimate of mortality risk than simple proportions. Fourth, the key finding that modifiable comorbidities (malnutrition, heart failure, severe pneumonia, thrombocytopenia) rather than the specific cardiac diagnosis are the primary drivers of in-hospital mortality shifts the clinical focus from lesion-specific management to integrated supportive care strategies. This finding has not been previously demonstrated in a Ugandan cohort and has important implications for resource-limited settings where surgical capacity remains constrained.

These strengths position the study as a valuable addition to the evidence base, offering high-quality, context-specific insights to guide clinical practice and health policy in Uganda and comparable settings.

5.7.2 Limitations of the Study

The findings of this study should be interpreted in light of several limitations.

Retrospective design limitations:

Incomplete or missing data resulted in a reduced sample size for multivariable analysis (270 of 521 patients, 51.8%) and may have introduced bias if the missing data were not random. However, we compared complete cases (N=270) with incomplete cases (N=251) on age, sex, and mortality; no significant differences were found ($p > 0.05$ for all), suggesting data were missing at random and that complete-case analysis is unlikely to have introduced substantial bias.

Of 557 eligible patients with confirmed cardiac disease, 36 (6.5%) were excluded due to missing outcome data. We compared included versus excluded patients on age, sex, and primary diagnosis; no significant differences were found ($p > 0.05$), suggesting data were missing at random. However, if excluded patients had systematically different outcomes (e.g., discharged against medical advice with undocumented status), our mortality estimate of 21.1% could be either an under-estimate or over-estimate. The direction of bias cannot be determined retrospectively.

Misclassification bias may arise from inaccuracies in patient records or diagnostic errors. To minimize this, we used a standardized, pre-tested data abstraction tool with explicit definitions for all variables. Only patients with echocardiographically confirmed cardiac diagnoses were included, and data were double-entered with verification of discrepancies.

No routine post-mortem examinations, limited confirmation of exact causes of death. Nevertheless, causes of death were extracted from clinical records completed by attending physicians, and the majority (95.5%) had a documented cause, with cardiogenic shock, heart failure, and cardiorespiratory arrest accounting for 69.1% of deaths.

Inability to establish temporality for some variables (e.g., whether malnutrition preceded or followed the cardiac diagnosis). This is inherent to retrospective chart review. However, for the primary predictors identified (heart failure, severe pneumonia, malnutrition, thrombocytopenia), the clinical relevance does not depend on precise temporality, as these are well-established risk factors for mortality regardless of onset relative to admission.

Single-centre limitations:

Referral bias: Findings likely overestimate disease severity and mortality compared to district hospitals or community settings. However, Mulago National Referral Hospital is Uganda's primary tertiary referral centre for paediatric cardiac care, and our findings are therefore generalizable to other referral-level hospitals in similar low-resource settings in East Africa. The estimates should not, however, be extrapolated to primary care or community populations.

Geographic limitation: Results may not generalize to rural populations or other regions of Uganda. Nonetheless, Mulago receives referrals from all districts of Uganda, and our cohort included patients from both urban (17.5%) and rural (82.5%) residences, providing some degree of geographic representation.

Unmeasured confounders:

Socioeconomic factors (income, education, transport costs, health insurance) were not consistently available. These factors likely influence access to care and outcomes. Future prospective studies should include standardized socioeconomic data. However, the predictors we identified (malnutrition, heart failure, severe pneumonia, thrombocytopenia) are clinically actionable even in the absence of socioeconomic data.

Prior care quality (antibiotic prophylaxis, medication adherence) could not be assessed. This is a limitation of retrospective design. However, our focus was on in-hospital factors that are potentially modifiable at the facility level, which is appropriate for a hospital-based quality improvement study.

Despite these limitations, the large sample size (N=521), 10-year study period, comprehensive data abstraction, consecutive sampling (eliminating selection bias) and rigorous statistical methods

appropriate for the high mortality rate (survival analysis with Coz regression) strengthen the validity of the findings for the study setting.

CHAPTER SIX: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

This study demonstrated that congenital heart disease remains the predominant cardiac diagnosis among children admitted to Mulago National Referral Hospital, although acquired cardiac diseases continue to contribute substantially to the inpatient burden. In-hospital mortality was high, with most deaths occurring early during admission. Mortality was independently associated with malnutrition, heart failure, severe pneumonia and lower platelet counts rather than the specific cardiac diagnosis itself. These findings suggest the critical interplay between cardiac disease and systemic vulnerabilities in a low-resource setting, where late presentation and superimposed illness amplify mortality risk. While the underlying cardiac lesions remain challenging to address without expanded surgical capacity, the identification of modifiable predictors offers immediate opportunities for intervention.

By prioritizing nutritional support, aggressive infection management, and early recognition of decompensation, substantial reductions in mortality may be achievable even within current constraints. Longer-term efforts to strengthen prevention, screening, and specialized infrastructure are essential to reduce the overall burden. However, the findings should be interpreted within the context of the retrospective design and the presence of missing data for some variables.

This study contributes valuable context-specific evidence to guide clinical practice and health policy in Uganda, underscoring the urgent need for integrated, multidisciplinary approaches to paediatric cardiac care. Addressing these modifiable risks has the potential to improve survival and quality of life for children with cardiac diseases in Uganda and similar resource-limited settings.

6.2 Recommendations

Based on the study findings, the following recommendations are proposed:

Clinical Recommendations:

1. **Routine nutritional screening and early therapeutic feeding** for all paediatric cardiac admissions. Given that malnutrition was independently associated with a 2.38-fold higher risk of mortality, and that its detrimental effect on survival begins within 48 hours of admission, nutritional assessment and intervention should be initiated on day one of hospitalization.
2. **Aggressive diagnosis and management of pneumonia** (early antibiotics, oxygen therapy, infection control). Severe pneumonia was the strongest predictor of mortality (3-fold higher risk), and survival curves showed the most dramatic early divergence for this comorbidity.

Pneumonia prevention through vaccination (pneumococcal and *H. influenzae* type b) and prompt treatment of respiratory infections should be prioritized.

3. **Rapid stabilization of heart failure** with clear escalation pathways and early cardiology input. Heart failure at presentation more than doubled mortality risk and was associated with significantly worse survival beginning in the first week.
4. **Use platelet count as a simple prognostic marker** to identify high-risk patients needing closer monitoring. Platelet count is a readily available, low-cost laboratory parameter that independently predicted mortality.
5. **Timely access to cardiac surgery** for congenital and acquired (RHD) heart disease remains essential for long-term survival. While this study focused on in-hospital mortality from medical complications, definitive surgical correction is the ultimate goal for many children.

Public Health and Policy Recommendations:

6. **Promote early detection of congenital heart diseases** via antenatal ultrasound training, newborn pulse oximetry screening, and training of primary healthcare workers in recognizing cardiac signs (heart failure, failure to thrive, cyanosis, murmurs). This recommendation is directly supported by the study findings. In our cohort, 65.5% of children who died presented with heart failure, a late-stage complication that could have been prevented with earlier diagnosis. Additionally, the median survival time among non-survivors was only 6 days, indicating that once a child deteriorates to the point of hospitalization, the window for intervention is extremely narrow. Based on the adjusted hazard ratio for heart failure (aHR 2.61), early detection before the development of heart failure could potentially reduce mortality by an estimated 40–50%. Furthermore, 58.7% of admitted children had severe pneumonia, a complication that often precedes cardiac diagnosis in resource-limited settings. Early recognition of cardiac disease at primary care level would allow for prophylactic measures (e.g., vaccination, nutritional support, heart failure medication) that could prevent these complications
7. **Advocate for intersectoral collaboration** between cardiology, nutrition, and infectious disease programmes to address modifiable comorbidities such as malnutrition and pneumonia.
8. **Increase investment in paediatric cardiac infrastructure,** including dedicated intensive care beds, reliable medication supply chains (diuretics, ACE inhibitors, antibiotics, inotropes), and expanded echocardiography services at regional referral hospitals.

Research Recommendations:

9. **Conduct prospective multicentre studies** to validate these findings, incorporate socioeconomic variables, assess long-term outcomes post-discharge, and evaluate the generalizability of findings across different regions of Uganda.
10. **Conduct health economic analyses** to determine the cost-effectiveness of different intervention strategies (e.g., nutritional support vs. surgical expansion) in reducing mortality in this population. This recommendation is justified by the finding that modifiable comorbidities particularly malnutrition (aHR 2.38), severe pneumonia (aHR 2.89), and heart failure (aHR 2.61) are as strongly associated with mortality as the underlying cardiac diagnosis itself. Nutritional support is substantially less expensive than cardiac surgery (estimated cost of therapeutic feeding: $50-100 per child vs. $2,000-5,000 per cardiac surgery in Uganda). With a malnutrition prevalence of 20.2% in our cohort and an attributable mortality hazard of 2.38, even modest investments in nutritional rehabilitation could yield significant mortality reductions at a fraction of the cost of surgical expansion. An economic analysis would quantify these trade-offs and guide resource allocation in a setting where healthcare funding is severely constrained

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APPENDICES

APPENDIX I: DATA ABSTRACTION TOOL

Study Title: Patterns of Cardiac Diseases and Risk Factors for In-Hospital Mortality Among Children Admitted to Mulago National Referral Hospital.

Instructions: This tool is to be used for systematically collecting data from patient medical records. Please ensure that all fields are completed accurately.

Study Number…….

Section A: Demographic information	
Patient IP No.	……..
Patient Initials	……..
Age (Years)	……..
Sex	☐ Male ☐ Female
Residence (District)	……..
Date of Admission	……..
Date of Discharge	……..
Weight (Kg)	……..
Height (cm)	……..
Section B: Diagnosis	
Type of Cardiac Disease	1. ☐ Congenital Heart Disease (CHD) 2. ☐ Acquired Heart Disease (AHD)
Specific Diagnosis	
CHD	☐ Atrial Septal Defect (ASD) ☐ Ventricular Septal Defect (VSD) ☐ Patent Ductus Arteriosus (PDA) ☐ Tetralogy of Fallot (TOF)

	☐ Transposition of Great Arteries (TGA) ☐ Truncus Arteriosus (TA) ☐ Double Outlet Right Ventricle (DORV) ☐ Others (Specify)……
AHD	☐ Rheumatic Heart Disease (RHD) ☐ Myocarditis ☐ Cardiomyopathy 1. ☐ Dilated Cardiomyopathy (DCM) 2. ☐ Hypertrophic Cardiomyopathy (HCM) 3. ☐ Endomyocardial Fibrosis (EMF) ☐ Other (Specify)…….
Section C: Clinical Presentation	
Primary symptoms at Admission (Check all that apply)	
Shortness of breath	1. ☐ Yes 2. ☐ No
Cyanosis	1. ☐ Yes 2. ☐ No
Failure to Thrive (FTT)	1. ☐ Yes 2. ☐ No
Fever	1. ☐ Yes 2. ☐ No
Chest pain	1. ☐ Yes 2. ☐ No
Palpitations	1. ☐ Yes

	2. ☐ No
Fatigue	1. ☐ Yes 2. ☐ No
Body swelling	1. ☐ Yes 2. ☐ No
Other (Specify)	……..
Comorbidities (if any)	
Malnutrition	1. ☐ Yes 2. ☐ No
HIV/AIDS	1. ☐ Yes 2. ☐ No
Hypertension	1. ☐ Yes 2. ☐ No
Genetic Syndrome	1. ☐ Yes 2. ☐ No
Other (Specify)	……
Section D: Admission and Clinical Management	
Primary Reason for Admission	
Heart Failure	1. ☐ Yes 2. ☐ No
Infective Endocarditis	1. ☐ Yes 2. ☐ No
Severe Anemia	1. ☐ Yes 2. ☐ No
Severe Pneumonia	1. ☐ Yes

	2. ☐ No
Pleural Effusion	1. ☐ Yes 2. ☐ No
Pericardial Effusion	1. ☐ Yes 2. ☐ No
Arrhythmias	1. ☐ Yes 2. ☐ No
Post-surgical Complication	1. ☐ Yes 2. ☐ No
Diagnostic Evaluation	1. ☐ Yes 2. ☐ No
Treatment of Complications	1. ☐ Yes 2. ☐ No
Surgical Interventions	1. ☐ Yes 2. ☐ No
Other (Specify)	……
Section E: Investigations and Laboratory Results	
Laboratory Results	
Haemoglobin (Hb)	…… g/dl
White Blood Cell Count (WBC)	…… ×10^9/L
Neutrophil count	…… ×10^9/L
Platelet count	……×10^9/L
Serum Sodium (Na+)	…… mmol/L
Serum Potassium (K+)	…… mmol/L
Serum Creatinine	…… mg/dl
Other electrolytes (specify)	……

Echocardiogram Findings (if available)	
Structural Defect Identified (Specify)	……
Cardiac Function	☐ Normal ☐ Abnormal
Other Findings	……
Electrocardiogram (ECG) Findings (if available)	
Normal	1. ☐ Yes 2. ☐ Yes
Arrhythmia (specify type)	……
Other Findings	……
Section F: Treatment and Interventions	
Medications Administered	☐ Diuretics (specify)……. ☐ Beta-blockers ☐ ACEI/ARBs ☐ Antibiotics ☐ Anticonvulsants ☐ Other (specify)
Surgical/Interventional Procedures performed	☐ None ☐ Surgical correction(specify)…… ☐ Catheterization (specify)…… ☐ Other (specify)
Section G: Complications during Admission	
Heart Failure	1. ☐ Yes

	2. ☐ No
Arrhythmias	1. ☐ Yes 2. ☐ No
Cardiogenic shock	1. ☐ Yes 2. ☐ No
Stroke	1. ☐ Yes 2. ☐ Yes
Electrolyte Imbalances	1. ☐ Yes 2. ☐ Yes
None	……
Other (specify)	……..
Section H: Outcomes	
Discharged	1. ☐ Yes 2. ☐ No
Died	1. ☐ Yes 2. ☐ No
If the outcome is death, what is the cause?	…….
Length of Hospital Stay (in days)	……..
Readmission	☐ Yes ☐ No
Section I: Epidemiological Variable	
Referral Source	☐ Self-referred ☐ Primary healthcare centre ☐ District hospital

	☐ Other (specify)
Family history of Cardiac Disease	1. ☐ Yes (specify) 2. ☐ No
Socioeconomic Information	Parent/guardian occupation…… Estimated monthly Income……
Data collector's name	……
Date of Data Collection	……

APPENDIX II: WAIVER OF INFORMED CONSENT

MAKERERE UNIVERSITY
P.O. Box 7072 Kampala, Uganda
E-mail: rresearch9@gmail.com
Phone: 256 414 533541
Fax: 256 414 541036/0414 532204

COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE

RESEARCH ETHICS COMMITTEE

November 25, 2025

Dr. Christine Akol
Department of Paediatrics and Child Health

Dear Dr. Akol,

RE: APPROVAL OF CONSENT WAIVER

In your letter dated 30th May 2025, you requested the committee to waive the requirement for obtaining informed consent for the study entitled **"Patterns of cardiac diseases and risk factors for in-hospital mortality among children admitted to Mulago National Referral Hospital" Mak-SOMREC- 2025- 587.** It was noted that this is a retrospective study involving review of existing medical records of children admitted at Mulago National Referral Hospital.

On behalf of the committee, I am glad to inform you that the committee has granted waiver of the informed consent process for this study. Please ensure confidentiality of the participants' data.

Yours sincerely,

Assoc. Prof. Ponsiano Ocama
Chairperson School of Medicine Research and Ethics Committee

Page 1 of 1

APPENDIX III: ADMINISTRATIVE CLEARANCE

TELEPHONE: +256-414554008/1
FAX: +256-414-5325591
E-mail: admin@mulago.or.ug
Website: www.mulago.or.ug

IN ANY CORRESPONDENCE ON THIS SUBJECT PLEASE QUOTES NO.....

MULAGO NATIONAL REFERRAL HOSPITAL
P. O. Box 7051
KAMPALA, UGANDA

2nd December 2025.

Dr. Akol Christine
Principal Investigator
Department of Paediatrics and Child Health
Makerere University

Dear Dr. Akol,

RE: ADMINISTRATIVE CLEARANCE TO CONDUCT A STUDY AT MULAGO NATIONAL REFERRAL HOSPITAL.

The Mulago Hospital Management is pleased to inform you that you have been offered clearance to conduct the study titled **MHREC 3066: "Patterns of Cardiac diseases and Risk factors for In-hospital Mortality among children admitted to Mulago National Referral Hospital".**

The above clearance is granted to you on the following conditions;

- That you will follow the research ethical processes
- Agreed to comply with all institutional policies and regulations of Mulago National Referral Hospital
- Agreed to provide end of study report and acknowledge Mulago hospital in all publications
- Submit a copy of filled in participant compensation log after recruiting one quarter of the approved research sample size.

Administrative clearance is valid for one (1) year effective from 1st December 2025 to 30th November 2026.

By copy of this letter, we reiterate our commitment to support this study.

DR. BYANYIMA ROSEMARY
EXECUTIVE DIRECTOR
MULAGO NATIONAL REFERRAL HOSPITAL

Copied to;
1. **Incharge – Cardiopulmonary ward-MNRH**

Vision: "To be the leading centre of Health Care Services"

APPENDIX IV: WORK PLAN

ACTIVITY/ TIMELINE	2024	2025												2026					
	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
Development of a proposal																			
Proposal presentation to Dep't																			
Ethical approval																			
Data collection																			
Data analysis																			
Report preparation																			
Report presentation to the department																			
Draft dissertation																			
Defence																			

APPENDIX V: BUDGET

Item	Quantity	Unit cost (UGX)	Total Cost (UGX)
PROPOSAL STAGE			0
Proposal production (Printing and binding of drafts to be reviewed)	12 copies	9,000	108,000
Payment to SOMREC for IRB clearance	1	100,000	100,000
Payment to MNRH for Administrative clearance	1	50,000	50,000
RESEARCH ASSISTANTS			0
Recruiting and training of Data Collection Assistants	2 people	50,000	100,000
Payment of Data Collection Assistants	2 people	500,000	1,000,000
Payment of Records Officers to Retrieve patient files	2 people	350,000	700,000
DATA COLLECTION STAGE			0
Development of a Data Abstraction Tool and Uploading into Kobo Toolbox	1	200,000	200,000
Printing, Photocopying and Stationery	Lump sum	100,000	100,000
Internet and Communication	Lump sum sum	100,000	100,000
Transport (Data Collection Visits)	10 trips	20,000	200,000
DATA ANALYSIS, REPORTING AND DISSEMINATION			0
Data Entry & Cleaning	Lump sum	300,000	300,000
Data analysis	Lump sum	900,000	900,000
Presentation of thesis at the departmental level (printing and binding)	5 copies	12,000	60,000
Final dissertation production (printing and binding)	5 copies	20,000	100,000
Journal publication fees	Lump sum	1,900,000 (500 USD)	1,900,000
TOTAL			**5,918,000**

APPENDIX VI: IRB APPROVAL

MAKERERE UNIVERSITY
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Phone: 256 414 533541
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COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE
RESEARCH ETHICS COMMITTEE

11/11/2025
To: Christine Akol

+256781411134

Review Type: Initial Review

Re:Mak-SOMREC-2025-587: PATTERNS OF CARDIAC DISEASES AND RISK FACTORS FOR IN-HOSPITAL MORTALITY AMONG CHILDREN ADMITTED TO MULAGO NATIONAL REFERRAL HOSPITAL

I am pleased to inform you that at the **206** convened meeting on **22/07/2025**, the MAK School of Medicine REC (Mak-SOMREC) meeting voted to approve the above referenced application.
Approval of the research is for the period of **11/11/2025** to **11/11/2026.**

As Principal Investigator of the research, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the protocol or the consent form must be submitted to the REC for re-review and approval **prior** to the activation of the changes.
3. Reports of unanticipated problems involving risks to participants or any new information which could change the risk benefit: ratio must be submitted to the REC.
4. Only approved consent forms are to be used in the enrollment of participants. All consent forms signed by participants and/or witnesses should be retained on file. The REC may conduct audits of all study records, and consent documentation may be part of such audits.
5. Continuing review application must be submitted to the REC **eight weeks** prior to the expiration date of **11/11/2026** in order to continue the study beyond the approved period. Failure to submit a continuing review application in a timely fashion may result in suspension or termination of the study.
6. The REC application number assigned to the research should be cited in any correspondence with the REC of record.
7. You are required to register the research protocol with the Uganda National Council for Science and Technology (UNCST) for final clearance to undertake the study in Uganda.

The following is the list of all documents approved in this application by MAK School of Medicine REC (Mak-SOMREC):

No.	Document Title	Language	Version Number	Version Date
1	Application for waiver of informed consent	English	Application for waiver of informed	2025-11-04

			consent-2	
2	Community Engagement plan	English	Community engagement plan-2	2025-11-04
3	COVID-19 & EBOLA risk management plan	English	COVID-19 & EBOLA management plan-2	2025-11-04
4	Data collection tools	English	Data collection tool revised-2	2025-10-16
5	protocol	English	Akol's protocol revised-2	2025-10-16

Yours sincerely,

MAKERERE UNIVERSITY
SCHOOL OF MEDICINE
INITIAL APPROVAL
VALID UNTIL
11 NOV 2026
RESEARCH & ETHICS COMMITTEE
P.O. BOX 7072,KAMPALA

Prof. Ponsiano Ocama
For: MAK School of Medicine REC (Mak-SOMREC)