ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY, DEPARTMENT OF NURSING

SURVIVAL STATUS AND IT'S ASSOCIATED FACTORS AMONG UNDER-FIVE CHILDREN MANAGED WITH CONGENITAL HEART DISEASES IN TIKUR ANBESSA SPECIALIZED HOSPITAL AND CARDIAC CENTER, ADDIS ABABA, ETHIOPIA, 2023: A RETROSPECTIVE COHORT STUDY

BY: DABA SUYUM JALETA, (BSCN)

ADVISORS: Dr. GIRUM SEBSIBIE (PHD, Asst Proff.)

Sr. YESHIWORK BIRHAN (MSc)

A RESEARCH THESIS SUBMITTED TO NURSING DEPARTMENT, SCHOOL OF NURSING AND MIDWIFERY, COLLEGE OF HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE IN NEONATAL NURSING

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SCHOOL OF NURSING AND MIDWIFERY

DEPARTMENT OF NURSING

MASTER OF SCIENCE RESEARCH PROJECT SUBMISSION FORM

Name of investigator	Daba Suyum Jaleta Phone: +251923014132; Email: dabaseyoum@gmail.com
Name of Advisor(s)	Dr. Girum Sebsibie (BScN, MSc, PHD; Primary advisor) Phone: +251920856732; Email: girumseb@gmail.com
	Sr. Yeshiwork Berhan (BScN, MSc; Co-advisor) Phone: +251993933411; Email: yeshiworkberhan@gmail.com
Full title of the research project	Survival Status And It's Associated Factors Among Under Five Children Managed With Congenital Heart Diseases In Tikur Anbessa Specialized Hospital and Cardiac Center, Addis Ababa, Ethiopia, 2022/2023: A Retrospective Cohort Study
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Address of investigator	Email: dabaseyoum@gmail.com Phone: +251923014132

ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY, DEPARTMENT OF NURSING

APPROVAL SHEET

I, the undersigned MSc student, declare that I have submitted my original work on a title : **Survival Status And It's Associated Factors Among Under Five Children Managed With Congenital Heart Diseases In Tikur Anbessa Specialized Hospital and Cardiac Center, Addis Ababa, Ethiopia, 2022/2023: A Retrospective Cohort Study** for the examination.

Submitted by:

Daba Suyum (BSc) Sign. _____ 20/6/2023

Name of student **Signature** **Date**

This thesis work has been submitted for examination with my approval as an advisor.

Approved by:

1. Dr. Girum Sebsibie (Asst Proff ,PHD, MSc, BSc): Sign. _____20/6/2023
   Name of Advisor Signature Date

Mrs. Yeshiwork Berhan (MSc , BScN): Sign._____20/6/2023Name of Co-Advisor Signature Date

DECLARATION

This is to certify that the thesis prepared by **Daba Suyum** Jaleta entitled: **Survival Status And It's Associated Factors Among Under Five Children Managed With Congenital Heart Diseases In Tikur Anbessa Specialized Hospital and Cardiac Center, Addis Ababa, Ethiopia, 2022/2023: A Retrospective Cohort Study** and submitted in partial fulfillment of the requirements for degree of Masters of science in Neonatal Nursing complies with the regulation of the University and meets the accepted standards with respect to originality and quality. This thesis has not been presented for degree at any other University, and that all sources of materials used for the thesis have been fully acknowledged.

Role **Name** **Sign** **Date**

Principal Investigator: Daba Suyum (BSc) Sign. _____ Date: 20/6/2023

Advisor: Dr. Girum Sebsibie (Asst Proff ,PHD, MSc, BSc): Sign. _____Date: 20/6/2023

Co-Advisor: Mrs. Yeshiwork Berhan (MSc , BScN): Sign._____ Date: 20/6/2023

APPROVAL BY THE BOARD OF EXAMINATION

This thesis on tittle **Survival Status And It's Associated Factors Among Under Five Children Managed With Congenital Heart Diseases In Tikur Anbessa Specialized Hospital and Cardiac Center, Addis Ababa, Ethiopia, 2022/2023: A Retrospective Cohort Study** by **Daba Suyum** is accepted in its present form by the board of examiners as satisfying thesis requirement for the degree of Masters of science in Neonatal Nursing.

EXAMINER:

Mr. Debela Gala (Ast proff. MSc, BSc): _____ 20/6/2023

NAME RANK SIGNITURE DATE

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ACRONYMS AND ABBREVIATIONS

AHR	Adjusted Hazard risk
AS	Aortic stenosis
ASMR	Age specific mortality rate
ASD	Atrial septal defect
AV	Atrioventricular
AVSD	Atrio-ventricular septal defect
CCE	Cardiac center Ethiopia
CVD	Cardiovascular disease
CCHD	Critical Congenital heart disease
CHD	Congenital heart disease
COA	Coarctation of the aorta
DORV	Double-outlet right ventricle
EA	Ebstein anomaly
HLHS	Hypoplastic left heart syndrome
HR	Hazard ratio
ICD	International classification of disease
IAA	Interrupted aortic arch
LMIC	Low- and middle-income countries
NCD	Non-communicable diseases
OR	Odd ratio
PA	Pulmonary atresia
PDA	Patent ductus arteriosus
PHT	Pulmonary hypertension
PI	Principal Investigator

PS	Pulmonary artery stenosis
PTA	Persistent truncus arteriosus
SD	Standard deviation
SV	Single ventricle
SDI	Socio-demographic index
SDG	Sustainable Development Goals
SPSS	Statistical Package for Social Sciences
TOF	Tetralogy of Fallot
TGA	Transposition of great arteries
TASH	Tikur Anbessa Specialized Hospital
TAPVR	Total anomalous pulmonary venous return
TA	Trcuspid atresia
UK	United Kingdom
UN	United nation
UVH	Univentricular heart
VLBW	Very low birth weights
VSD	Ventricular septal defect

ABSTRACT

Background: Congenital heart disease CHD is the most prevalent significant congenital abnormality, affecting around 9 out of every 1000 live infants. The aggregated 1-year and 5-year survival rates for patients with congenital heart disease from 6 and 8 studies for all CHD were 87.0% and 85.4%, respectively.

Objective: The purpose of this study is to assess survival status and related factors among under-five infants with congenital heart disorders treated at TASH, Addis Ababa, Ethiopia, and Cardiac Centre from January 2018 to December 2022.

Methods: An Institution based retrospective follow-up study design was used among under-five children managed with congenital heart disease that were admitted at TASH and Cardiac Center, Ethiopia; registered from Jan 2018 to Dec 2022. Data was collected by pretested checklist from 224 randomly selected charts. The Kaplan-Meier survival analysis, the log-rank test, and the effect of each covariate on mortality using cox proportional hazard are used to measure survival status in various groups. For data analysis, SPSS version 26 was employed.

Result : Total of 224 charts with 95.32% response rate were analyzed to determine survival status and associated factors of under-five children managed with CHD and 34 of them died whereas 190 of them were censored during the study period. The survival status of all infants born with CHD in this study was 84.8% to five years. Cox regression analysis identified covariates significantly associated with mortality as weight at admission (AHR 19.023,95% CI [2.542,142.925]; P = 0.004), types of interventions (AHR73.016,95% CI [3.226,1652.2]; P = 0.007), pre-operative condition (AHR 65.097,95% CI [11.322,374.25]; P =0.0001), family history of heart disease (AHR 10.81,95% CI [2.218,52.673]; P = 0.003), maternal history of substance use (AHR 46.67,95% CI [4.405,494.31]; P = 0.001) and maternal history of viral infection (AHR 52.034,95% CI [7.320,369.83]; P< 0.0001).

Conclusion and recommendation: The survival status of all infants born with CHD in this study was 84.8% to five years. Weight at type of interventions, preoperative condition, other maternal condition are associated with survival. The early cardiac intervention and priority for critical CHD are among recommendation to improve survival.

Keywords: Congenital heart disease, Survival status, associated factors, Cox regression, log rank, Kaplan Meier.

1. INTRODUCTION

1.1 Background

Congenital heart disease CHD is the most prevalent significant congenital abnormality, affecting around 9 out of every 1000 live infants[1]. The prevalence of congenital heart disease (CHD), which dramatically increases childhood morbidity and mortality, is a global public health concern. This is especially true in developing nations, particularly in sub-Saharan Africa, where facilities for early diagnosis and management of non-communicable diseases in the pediatric age group are frequently lacking, despite the fact that these diseases are emerging as a major health and socioeconomic issues[2]. Even though the majority of CHD cases have moderate lesions that do not require treatment, approximately 20-25% of CHD cases are serious and require early intervention or surgery during the first year of life[3].

The global prevalence of congenital heart disease (CHD) at birth has been estimated to be 5-9 per 1,000 live births, but among newborns with very low birth weights (VLBW) of less than 1,500g, it was as high as 20-40 per 1,000[4]. The projected worldwide annual deaths from congenital heart disease was 261, 247 in 2017. In the first year of life, the rate of decline in the prevalence of congenital cardiac disease significantly varies by SDI quintile. The long-term survival rate of a patient with congenital cardiac disease was reported to be 87.0% and 85.4%, respectively (P0.001)[5].

The one-year survival rate for neonates with critical congenital heart abnormalities has risen over time to 75.2% (P0.001), compared to 97.1% for those with isolated noncritical CHDs. Patients diagnosed after one day of age had the best survival rates (82.5%; HR = 0.54; P0.001), whereas those diagnosed before one day of age had a lower 1-year survival rate (71.7%), and screening using pulse oximetry may increase these rates even further. Gender, sex, age upon diagnosis, and birth weight are all related to survival status (P0.001)[6].

Critical congenital heart disease (CCHD) encompassed abnormalities that were more likely to require medical intervention within the first year of life and could manifest as hypoxemia. These defects include aortic coarctation (COA), double-outlet right ventricle (DORV), Ebstein anomaly (EA), hypoplastic left heart syndrome (HLHS), interrupted aortic arch (IAA), pulmonary atresia (PA), single ventricle (SV), tricuspid atresia (TA), total anomalous

pulmonary venous return (TAPVR), dextro transposition of the great arteries (TGA)[7]. The prognosis for children born with severe CHD in developed countries has improved as medical and surgical therapy has advanced, but in some underdeveloped regions, access to therapy for the more serious diseases is still not available[8].

In 2016, the United Nations (UN) ratified the Sustainable Development Goals (SDGs), which established a target of fewer than 12 neonatal deaths per 1000 live births and fewer than 25 child deaths per 1000 live births. Congenital heart disease, which makes up approximately one-third of all congenital birth abnormalities, must be prioritized if avoidable infant mortality and non-communicable diseases (NCDs) are to be eliminated in the SDG era[5]. According to research, the rate of premature deaths from cardiovascular diseases (CVDs) ranges from 42% in low-income countries to 4% in high-income countries[9].

The majority of African and Asian impoverished countries had the highest national CHD incidence rates, including the Burundi (30.6/1000), Somalia (31.9/1000), and Central African Republic (33.8/1000)[10]. Although Africa is believed to have one of the greatest prevalence of cardiac illnesses in children and young people, including CHD, the key findings include evidence that the CHD burden is underestimated, owing mostly to the poor outcomes of African children with CHD[11]. Although the prevalence of Congenital Heart Defects (CHD) in Ethiopia is unknown, an estimated 1% of all CHDs are critical, with an annual birth prevalence of 36/1000 in the general population [12].

1.2 Statement of problem

Congenital heart disease (CHD) is the leading cause of birth abnormalities and, after infectious diseases, the second leading cause of death in children under the age of five[13]. Despite significant advances in diagnosis and medical therapy, congenital heart disease continues to be a major cause of newborn mortality and morbidity, resulting in significant personal and communal hardship[14]. In affluent countries, survival rates for CHD patients have improved, reaching 90% in some cases, contributing to an increase in the number of adult CHD patients. However, CHD is still associated with substantial mortality in developing nations, with an average of 4.9 deaths per 100,000 cases compared to 1.2 deaths per 100,000 cases in industrialized regions[15]. The presence of a coexisting medical condition (HR, 2.10; P = 0.001), poor preoperative condition (HR 2.22; P = 0.002), and clinical presentation of heart failure at diagnosis (HR = 1.57, P = 0.004) were all independent risk factors for poor survival outcome [3].

Congenital heart disease was the leading cause of an estimated 261, 247 deaths globally in 2017, according to the Lancet's 2017 Global Burden of Disease study, a 34•5% drop from 398, 580 fatalities in 1990. In 2017, 180,624 infants under the age of one died as a result of congenital cardiac disease. Deaths and mortality from congenital cardiac disease were higher in the poor and low-middle Socio-demographic index (SDI) quintiles. In that order, Oceania, North Africa, the Middle East, the Caribbean, central Sub-Saharan Africa, and Southeast Asia had the highest child mortality rates due to congenital heart disease[10]. Approximately one-third of CHD patients have a severe condition that necessitates intervention within the first year of life [16].

Ethiopia, as one of the Sub-Saharan African countries, is making great success in combating key communicable illnesses as well as maternal, neonatal, and child health concerns. Considering the absence of available data on the prevalence of CHDs in Ethiopia, the burden of CVDs in Ethiopia may be significantly larger than anticipated.[17]. According to studies, the prevalence of CHD among children with congenital anomalies is 35.8%, which is somewhat higher than the global average (33.3%) among all significant congenital defects[18].

Because of the high birth rate and high newborn death rate in Sub-Saharan Africa, the incidence of CHD is substantially understated[19]. Early diagnosis is critical because it is It is anticipated that one-third to more than half of all children born in underdeveloped nations with severe CHD will die during the first month of life if they are not recognized, diagnosed, and treated, and the other half will die before their first birthday.[20].

The limitation in the numbers of literature makes it difficult to determine the exact survival of under-five children with CHD and its associated factor in Ethiopia. However, some studies estimated that child mortality due to congenital cardiac disease associated with Down syndrome was 19% among the 116 children enrolled in the study at Tikur Anbessa Specialized Hospital (TASH)[21]. According to the CHD estimate in 1% of the whole population, we should predict 900-1000 cases of serious CHD patients each year requiring surgery or catheter treatment [12]. To the extent principal investigator identified, there is no study conducted that aims to determine survival status and associated factors among children managed with congenital heart disease in Ethiopia. Therefore, this study was needed to fill a literature gap and to identify any modifiable factors related to survival status of under-five children in the study area.

1.3 Significance of study

A scarcity of research on survival status and associated factors among under-five children managed with CHD in the study area raises the burden of the problem and casts a shade on a high rate of newborn mortality due to CHD. It is difficult to say something about the survival status of children managed with CHD at Tikur Anbesa Specialized Hospital (TASH) and Cardiac center Ethiopia, due to the lack of published data indicating the findings. This study used was used as a baseline data for those who wish to conduct on the same topic and may help fill the gap in scientific literature.

Understanding the survival status and risk factors of CHDs at Tikur Anbessa specialised hospital and Cardiac Centre Ethiopia was critical in order to develop strategies for better patient care. In addition to this, it was used improve the survival of children suffering from congenital heart disease by raising the standard of care and drawing attention to the management of congenital heart disease. The finding of this research helps patients, clinicians, policymakers, and other service providers in identifying areas where the emphasis has to be given to the development of strategies that will improve the survival rate of infants with congenital heart disease.

2. LITERATURE REVIEW

2.1 Embryonic development of the human heart

The mechanism by which the human heart develops in the embryo is intricate. The seemingly simple function of the heart of pumping blood rich in oxygen and nutrients necessitates many critical and time-sensitive developmental steps, all of which must occur in the correct order to prevent structural and functional abnormalities known as congenital heart disease. The formation of the heart is comprised of nine basic processes: formation of the three germ layers (gastrulation), establishment of the first and second heart fields, formation of the heart tube, cardiac looping, convergence, and wedging, development of septa (common atrium, atrioventricular canal), construction of the outflow tract, development of heart valves, formation of the conduction system, and development of the vasculature (coronary arterial)[22].

The epicardium forms early in the septation process as a layer of squamous epithelial cells and related connective tissue that extends from tissue dorsal to the heart at the level of the atrioventricular (AV) junction. The septum primum, which develops perforations to create the foramen secundum, splits the atrial chamber into two chambers. Following the primary atrial septum, a second atrial septum develops to the right of it, creating a one-way valve (right-to-left blood flow) between the two atria in the developing baby[23].

2.2 Congenital heart disease

A structural heart defect apparent at birth is referred to as congenital heart disease, and it makes up around one-third of all significant congenital malformations[23]. Although genetic abnormalities, teratogen exposure, or maternal diabetes account for around 20% of CHD incidence, there is significant uncertainty regarding risk factors for the remaining 80% of patients[8].

Around 10% of births globally are affected by CHD. Furthermore, approximately 20-25% of CHDs are deemed critical, requiring medical and surgical care to survive. Due to the prevalence of this illness, which necessitates a combination of catheter-based, pharmaceutical, and surgical treatment, early intervention for CHDs in young children is regarded to be crucial[15]. When caring for children with heart disease, the decision between tertiary and primary healthcare is irrelevant. Pediatric cardiac success in low-resource nations is attainable when it is integrated into wider health-system development programs, particularly surgical scale-up efforts, as advocated by the Lancet Commission on Global Surgery[24].

The 12 anomalies identified as critical congenital heart disorders (CCHDs) are likely to necessitate treatment during the initial year of life. There were 5 lesions in all that cause hypoxemia on occasion but infrequently, such as coarctation of the aorta (CoA), double outlet right ventricle (DORV), Ebstein anomaly (EA), interrupted aortic arch (IAA), and single ventricle, as well as 7 severe lesions that typically present with hypoxemia: tetralogy of Fallot (TOF), pulmonary atresia (PA), tricuspid atresi (SV) hypoplastic left heart syndrome, total anomalous pulmonary venous return, transposition of the great arteries, and truncus arteriosus[25].

Non-CCHDs are birth defects that do not require early treatment or oxygen monitoring. This study comprised aortic stenosis (AS), atrial septal defect (ASD), patent ductus arteriosus (PDA), pulmonary artery stenosis (PS), and ventricular septal defect (VSD)[26].
Acyanotic CHD accounted for around 80.7% of all instances, with the most common kind being ventricular septal defect (VSD), which was detected in 19.7% of cases, followed by atrioventricular septal defect (AVSD), which was seen in 17.3%, and patent ductus arteriosus (PDA), which was seen in 15.9%. The most common cause of cyanotic cardiac disease was

tetralogy of Fallot (TOF), which accounted for 5.1% of all cases, followed by double outlet right ventricle (DORV) at 4.1% and truncus arteriosus (TA) at 3.4[20]. Patients frequently reported with dyspnea (6.4%), cyanosis (17.8%), coughing (10.2%), fever (8.3%), murmur (3.8%), pallor (3.82%), and tachypnea (5.7%) as a result of the observed congenital heart anomalies[27].

Since its inception, the discipline of juvenile cardiovascular medicine has been led by novel ways of therapy, patient care, and clinical research. Advances in surgical technique, the development of techniques for managing intensive care and myocardial preservation, the introduction of interventional cardiology, high-resolution imaging, transplantation medicine, extracorporeal support, and interventional electrophysiology are a few examples of life-saving technologies in CHD[28].

2.3 Survival status of under-five children with CHD

Congenital heart disease is expected to affect 11, 998, 283 people worldwide as of 2017, an increase of 18.7% from the 10, 105, 235 common cases in 1990. The projected worldwide annual deaths from congenital heart disease was 261, 247 in 2017[5]. In spite of the fact that 80% of CHD patients lack clear risk factors, genetic disorders, teratogen exposure, and maternal diabetes account for about 20% of CHD incidence[8].

The survival rate to one-year for newborns having critical congenital heart abnormalities has improved over time, standing at 75.2% ($P<0.001$) compared to 97.1% for those diagnosed with isolated noncritical CHDs, according to a study conducted in Metropolitan Atlanta on 6965 infants with CHDs (1830 with CCHDs). Patients detected after one day of age have had the highest rates of survival (82.5%; HR = 0.54; $P<0.001$) whereas those diagnosed before the age of one day, the 1-year survival rate was lower (71.7%), and screening with pulse oximetry may further boost these rates. Gender, sex, age at diagnosis and birth weight are significantly associated with survival status ($P<0.001$). Infants with an early diagnosis, low birth weight, and mothers older than 30 years old had a considerably increased risk of 1-year mortality[6]

The global age-specific mortality rate (ASMR) of cardiovascular disease (CHD) fell by approximately 38.1% from 6.3 per 100,000 people in 1990 to 3.9 per 100,000 people in 2017. Males exhibited slightly higher ASMR than females. Notably, despite the fact that ASMR declined by 1.92% per year from 1990 to 2017, children under the age of five accounted for the majority of CHD-related deaths worldwide[10].

A prospective study in Sweden with an average (SD) follow-up of 8.86 years identified 21 982 children with CHD. Individuals with CHD had a 16.51 times higher risk of overall death when compared to matched controls. The first group of CHD patients (Lesion 1) with the most severe complicated anomalies (such as tetralogy of Fallot, atrioventricular septal defect, transposition of the great vessels, double inlet ventricle, hypoplastic left heart syndrome, and common arterial trunk) had a 64.07 (95% CI; P.001) higher mortality risk than controls. The mortality risk for the second group (septal defects, patent ductus arteriosus, coarctation of the aorta, and Ebstein abnormality) was 10.90 times higher than the risk in controls (95% CI; P.001). Patients with CHD who received cardiac intervention had a lower mortality rate. Male

and female cumulative survival rates were 87% and 90%, respectively, compared to 98% and 99% in controls [29].

A systematic review and meta-analysis of a patient's long-term survival with congenital heart disease discovered that the pooled 1-year and 5-year survival rates for all CHD were 87.0% and 85.4%, respectively (P0.001). At 1 year (P=0.047) and 5 years (P=0.013), a more recent study period was associated with improved survival. Individuals with ventricular sepal defect had the highest 5-year survival rate (96.3%, 95% CI; P0.001), whereas those with hypo plastic left heart had the lowest (12.5%, 95% CI; P0.001)[30]. Despite substantial advances in CHD hemodynamic therapy, many CHD patients continue to suffer from serious extra cardiac and cardiac comorbidities that have a poor influence on their quality of life. [16].

A population-based retrospective cohort study in China indicated that among 312 children with isolated CHDs, those with prenatal diagnoses had a significantly poorer 1-year survival rate than those with postnatal diagnoses (77.1% vs. 96.1%; P.001). When it comes to isolated Critical congenital heart disorders (CCHD), the prenatal diagnosis had a considerably worse 1-year survival rate than the postnatal diagnosis (73.4% vs. 90.0%; P.001)[26].

According to the Global Burden of Disease Study, low- and middle-income countries (LMICs) account for 80% of non-communicable disease mortality, including cardiovascular disease (CHD). Furthermore, According to the World Health Organization (WHO), 1.5 million live births, or 1% of all live births, have CHD each year. According to WHO estimates, 90% of these children have insufficient or no access to care, with the majority residing in low- and middle-income countries (LMICs), particularly Sub-Saharan Africa[32]. About 26.58% of Ghanaian children with CHD diagnoses were under one year old, with ventricular septal defects (VSD) and patent ductus arteriosus (PDA) being the most commonly found. The most common comorbidities seen in CHD patients were Down syndrome 7 (13.7%), upper respiratory tract infection (9.89%), and bronchopneumonia (16.48%)[27].

According to data on congenital heart disease in East Africa published in 2019, by the year 2017 the mortality rate per 1000 for CHD was 33.6 in Kenya, 35.4 in Uganda, and 38.3 in Tanzania. This result was considerably high compared to industrialized nations, where the infant mortality rate per 1000 people was 3.7 in the United Kingdom(UK), 5.7 in the USA, 2.3

in Sweden, and 5.7 in Japan 1.9 [31]. According to the 2017 Global Burden of Disease study, Ethiopia's CHD-related infant mortality rate ranged from 68.5 to 113.6 per 100,000[5]. In children aged between two months and 24 months in Hawassa, Ethiopia, CHD (commonest Ventricular septal defect 25(39%)) was documented in 41(64%) of Heart Failure cases[33].

The death rate among 116 children with CHD and Down syndrome in TASH, Addis Ababa was 50.86%; the total survival of cases is under observation as most deaths occurred during infancy. PDA was a common CHD found in 57 (36.5%), VSD in 31, ASD in 30, atrioventricular septal defect (AVSD) in 29, Tetralogy of Fallot was found in 4, and other CHDs were found in 5 (3.2%) cases[17]. Infants with CHD had a survival rate of 43.3%, according to a second retrospective cohort study conducted in Addis Ababa to assess the prevalence of congenital abnormalities[34].

2.4 Risk factors associated with survival status of under-five children with CHD

A 2017 global study on the incidence and death trend of CHD found a substantial positive link between CHD incidence and mortality in both 1990 (P = 0.018) and 2017 (P 0.001). Despite the identical CHD occurrences, high-SDI countries had lower CHD mortality than high-middle SDI nations[10]. Several studies have found that CHD is connected with risk factors such as advanced maternal age above 30 years (P0.001), previous maternal history of abortion (P-value 0.001), and a positive history of CHD among siblings (P0.001)[14].

Mothers with type 1 diabetes (adjusted odds ratio [OR] 2.32) diabetes mellitus type 2 (OR 2.85), hypertension (OR 1.87), congenital heart defects (OR 3.05), anaemia (OR 1.31), connective tissue disorders (OR 1.39), epilepsy (OR 1.37) and mood disorders (OR 1.25) were associated with a significantly higher frequency of congenital cardiac disease in their children [35].

A retrospective comparative analytical study in 2018 in Alhassa, Saudi Arabia; revealed among 88 patients diagnosed with HLHS prenatal and postnatal a 63% overall survival rate after one year. There was a difference in survival (65% vs. 60%) for postnatal vs. prenatal diagnosis, as well as according to intervention (80% vs. 0%) for individuals with HLHS who received surgery against those who declined treatment (P0.0001)[36].

Infants with complex lesions such as LVOT blockage, truncus arteriosus, and interrupted coronary arteries aortic arch all had 1-year survival rates below 50%. Weight at diagnosis of 2000g (HR, 2.61; P = 0.01), the presence of a coexisting medical condition (HR, 2.10; P = 0.001), poor preoperative condition (HR 2.22; P = 0.002), and clinical presentation at diagnosis of heart failure (HR = 1.57, P = 0.004) were all independent risk factors for poor survival outcome[3].

The first-trimester screening has a considerable impact on the range of CHDs and the outcomes of second-trimester pregnancies with CHDs. Early diagnosis of severe CHDs (P 0.0001) and major comorbidities resulted in a higher pregnancy termination rate in the first trimester (P 0.001)[39].

Finnish researchers identified CHD-related causes of death to be ASD (13.2%), PDA (21%), COA (13.46%), VSD(15.5%), TOF(7%), TGA(5.4%), HLHS(1.4%),UVH (2.9%) and other (11%). The freedom from sudden death due to simple CHD underwent surgery was 99% and 91% for severe CHD after surgery with a Hazard ratio of 9.9 at 95%CI ($P < 0.0001$). The risk and incidence of sudden mortality were reduced to zero in individuals with ASD, VSD, TOF, and TGA who had surgery. The non-cardiac cause of death for children with CHD was respiratory disease specifically Pneumonia(RR: 11; $p < 0.0001$), Infectious disease(RR = 6.7; P<0.0001) accidents(RR:1.6; P = 0.002) and neoplasm (RR: 5.9; P = 0.019)[40]. There was a statistically significant difference between individuals who had surgery and those who did not (81% vs. 19%; P0.0001)[36].

According to a study conducted in a developing country, Ghana about 37% of children diagnosed with CHD have respiratory system comorbidities that Bronchopneumonia (16.5%) is the most common.. The common CHD detected at the facility were 31.4 percent ventricular septal abnormalities and 5.88 percent PDA which is consistent with reported incidences in other low-resource countries. The most prevalent clinical symptoms associated with congenital cardiac anomalies were dyspnea (6.4%), cyanosis (17.8%), coughing (10.2%), fever (8.3%), murmur (3.8%), pallor (3.82%), and tachypnea (5.7%)[27].

Very low birth weight (VLBW) <1500g of children at birth was significantly associated ($P < 0.001$) with some types of CHD such as ASD, VSD, PFO, PDA, TOF, and AVSD. Parental factors such as; Maternal folic acid supplements (P = 0.001), gestational age (P = 0.001), mother drinking (P = 0.001), smoking (P = 0.001), viral infections (P=0.015), and Apgar ratings at 1 minute (P = 0.002) and 5 minutes (P = 0.001) were all linked to an elevated risk of CHD in the offspring[4].

Prenatal detection of several complex CHDs resulted in a decreased 1-year survival rate compared to postnatal diagnosed infants (77.1% vs 96.1%; P.001). With increasing age at diagnosis, the 1-year survival rate increased[36]. These all factors are considered as factor affecting survival status of under-five children that are factor of interest in this study.

2.5 Conceptual framework on survival status and associated factors of under-five children managed with CHD

The following conceptual framework, drawn from several sources, depicts the link between dependent and independent variables. Socio-demographic, risk factors, interventions, and disease features are the independent variables that influence the outcome variables. For example survival of children with CHD was associated with socio-demographic factors, and neonatal factors (sex, birth weight, age at diagnosis), and severity of the CHD types are all factors that determine the survival status of the baby([7][36]). Maternal factors such as age, maternal substance use, folic acid supplementation during pregnancy, viral infection, chronic illnesses and place of residence were also a factor affecting the survival of children([4] [35]). Presence of comorbidities with severe and non-critical congenital heart disease and first-trimester diagnosis also affect the survival status of children managed with CHD[39].

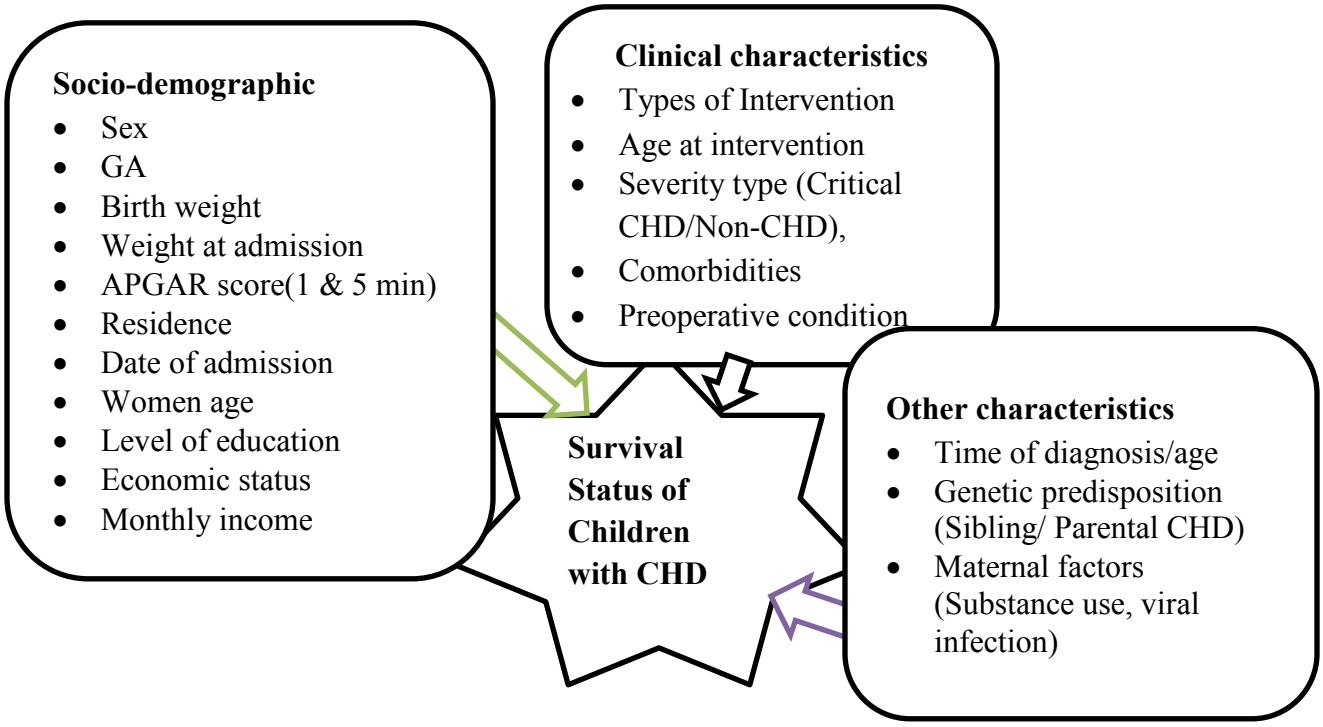


Figure 1: Conceptual framework for assessing Survival status and associated factors among under-five children managed with congenital heart diseases in TASH and Ethiopia Cardiac Center, Addis Ababa, Ethiopia from Jan 2018 to Dec 2022

3. OBJECTIVES

3.1 General objective

To evaluate the survival status and associated factors among under-five children with congenital cardiac disorders treated at TASH and Ethiopia Cardiac Centre in Addis Abeba, Ethiopia, between January 2018 and December 2022.

3.2 Specific objectives

- To assess the survival status of under-five children managed with congenital heart disease in TASH and Cardiac Center, Addis Ababa, Ethiopia from Jan 2018 to Dec 2022
- To identify factors associated to survival status of under-five children managed with congenital heart disease in TASH and Cardiac Center Ethiopia, Addis Ababa, Ethiopia from Jan 2018 to Dec 2022

4 METHODS

4.1 Study area and period

The study was conducted at Tikur Anbesa Specialized Hospital (TASH) and Cardiac Centre Ethiopia (Children's Heart Fund of Ethiopia), both in Addis Ababa, Ethiopia's capital city. TASH is the largest specialized public hospital in Addis Ababa and the largest tertiary-level referral hospital in Ethiopia. It also offers the public specialized clinical services, such as pediatric CHD therapy, and is open 24 hours a day, seven days a week. TASH diagnoses and treats approximately 370,000 to 400,000 patients each year.

The Cardiac Centre, Ethiopia (Children's Heart Fund of Ethiopia) was established in 1992 at the Zewditu Memorial Hospital in Addis Ababa, Ethiopia. It has been in operation since 2009 in Addis Ababa Tikur Anbesa Specialized Hospital (TASH). However, it was a separate independent organization having professionals, administrative and financial management. The cardiac center is independently serving as a specialized referral center for all types of congenital heart defects that was brought in from across the nation. A total of 18,861 individuals have received free cardiac management services since it began operating, 2900 of whom are pediatric patients.

The research was carried out between December 2022 G.C and June 2023 G.C.. by extracting data from the charts of hospitalized infants with congenital cardiac disease.

4.2 Study design

A retrospective cohort study design was conducted among under-five children managed with congenital heart disease were admitted into TASH and Cardiac Center, Ethiopia.

4.3 Source population

The source populations are all children who were diagnosed with CHD and admitted in the TASH and Cardiac Center Ethiopia

4.4 Study population

All under-five children who were diagnosed with congenital heart disease and managed in TASH and Cardiac Center Ethiopia from Jan 2018 to Dec 2022

4.5 Study unit

The study units are randomly selected under-five children diagnosed with congenital heart disease managed at TASH and Cardiac Center Ethiopia January 2018 to December 2022 and who met the eligibility requirements

4.6 Inclusion Criteria

- All under-five children diagnosed with CHD
- Being Managed at TASH & ECC from January 2018 to December 2022
- Take a minimum of one cardiac management at TASH and Cardiac Center Ethiopia

4.7 Exclusion Criteria

- Children with other associated major anomalies or chromosomal syndromes
- Incomplete patient chart

4.8 Sample size determination

A single population proportion formula was used to calculate the sample size with assumptions of 95% confidence interval (CI), 5% margin of error (d), p=0.833 (considering similar distribution of CHD around the world)[28], $z\alpha/_2 = 1.96$ and taking 83.3% under five survival proportion to five year in other developing country)[3]. Because there is no comparable study in the same area we used a proportion from similar study conducted in developing country.

$$n = (z\alpha/_2)^2 \times \frac{p(1-p)}{d^2} \qquad n = (1.96)^2 \times \frac{0.833(1-0.833)}{0.05^2} = \underline{\mathbf{214}}$$

After adding 10% for the possible missing values, the final sample size was **235.**

The sample size for the second goal was estimated using the twofold population proportion formula and the two most significant predictors, surgical intervention and severity type of

CHD. To decrease the role of chance the variable that gives a large sample size was used as an independent predictor. The sample size is obtained using the Epi info statistics program version 7.2.3.1.

$$\frac{[Z\alpha/2\sqrt{\left(1+\frac{1}{r}\right)P1(1-P1)}+Z\beta\sqrt{\left(P1(1-P1)+\frac{P2(1-P2)}{r}\right]}2}{(P1-P2)^2}$$

Table 1: Sample size calculation to assess Survival status and associated factors among under-five children managed with congenital heart diseases in TASH and Ethiopia Cardiac Center, Addis Ababa, Ethiopia from Jan 2018 to Dec 2022

Variable	**Assumption**	**Risk Ratio**	**Total sample size**	**After adding 10% missing data rate**
Surgical intervention,	P1 = 65 P2 = 87	0.74	134	148 [40]
Severity	P1 = 77.2 P2 = 94.1	0.82	156	172 [7]
Underlying anomaly	P1 =68.8 P2 = 95.4	0.7	78	86 [6]

Where P1 is the percentage of those that were exposed to the outcome.

P2 = is the percentage of those who were not exposed to the outcome.

Z/2 = 95% confidence interval, which is 1.96. ZB = 80% power

And r denotes the non-exposed to exposed ratio (1:1).

Since there is no Predictor variable with a larger sample size compared with the previously calculated sample size by single population proportion; the final sample size was **235**.

4.9 Sampling procedure

Study areas are purposively selected for being prominent referral hospitals providing cardiac intervention for all patients despite their diagnosed type of CHD. Systematic random sampling technique was used to select study participants proportionally from both study areas. All children who were diagnosed with CHD admitted at TASH and cardiac Center from Jan 2018 to Dec 2022 were listed and numbered from 1 to N (4870) (where N is population) in the sequence medical record number of the patient chart. There are 1970 children and 2900 children diagnosed with CHD in TASH and Cardiac Center Ethiopia respectively from Jan 2018 to Dec 2023 years. In order to minimize sample size variation within each year and study area, each year's sample was allocated proportionally after identifying a total population of the years.

At the start, the sampling interval (K) was calculated by dividing the total managed CHD throughout the study period by 235, yielding (K = N/n = 21). Finally, one number was chosen at random between 1 and kth to begin sample selection, and that number is included in the sample. The next selection was then repeated every 21st unit.

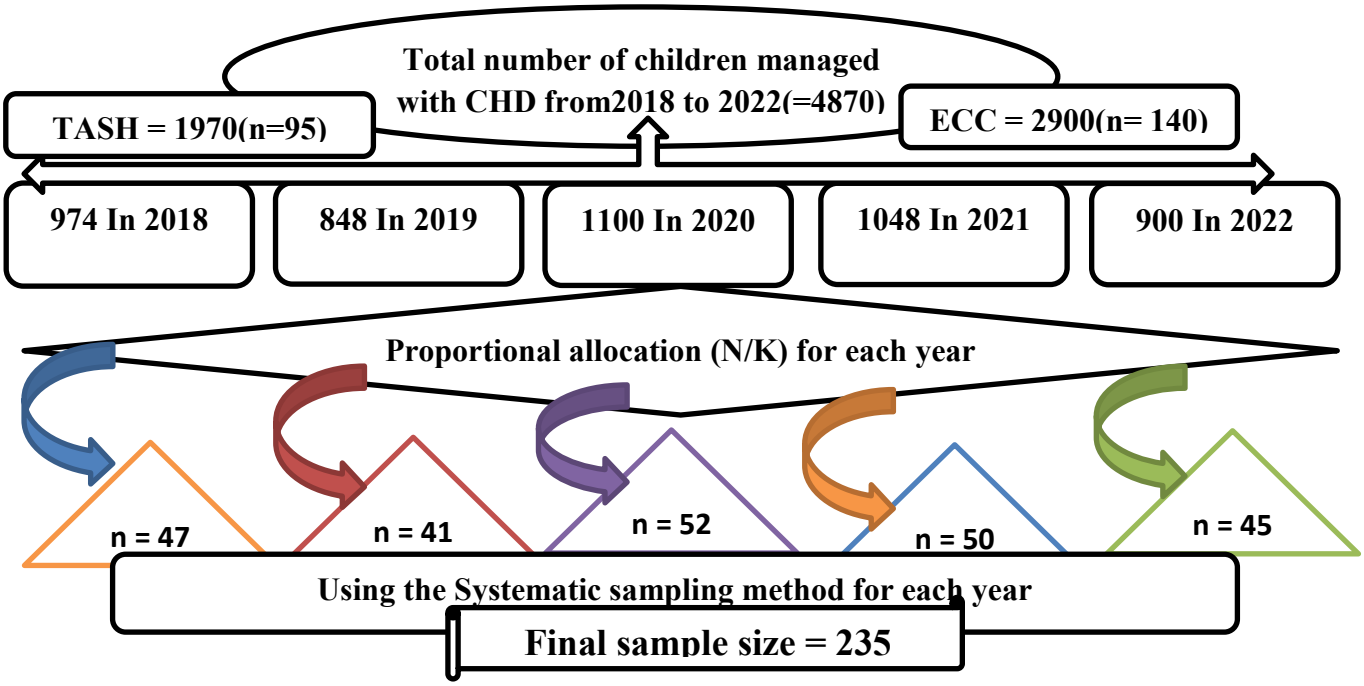


Figure 2 : Sampling technique for survival status and associated factor among under-five children managed with CHD from Jan 2018 to Dec 2022 in TASH & Cardiac Center Ethiopia

4.10 Variables

4.10.1 Dependent variable

- Survival status (Death/Censored)

4.10.2 Independent variables

- **Socio-demographic variables:** (Sex, GA, Birth weight, APGAR score, Residence, Dates, Women age, Place of delivery)
- **Other characteristics:** Time of diagnosis/age, Genetic predisposition (Sibling/ Parental CHD)
- Maternal factors(Substance use, viral infection, drug treatment & chronic illness
- **Clinical characteristics:** Severity type (Critical CHD/ Non CCHD),Comorbidities, Intervention

4.11 Operational definition

Survival status: is an event that measures from time of birth/diagnosis to death in month to five years as a result of congenital heart disease. Since problem of interest was apparent at birth; age of the baby was used as a time scale.

Censoring: occurs when incomplete information is available about the survival time (event not occurs, transferred) of some individuals.

CHD was defined as: Patients with a recognized International classification of illness ICD-8, ICD-9, or ICD-10 diagnosis of CHD who have had at least one hospital amission, outpatient visit, or death certificate[41].

Lesion group 1: are patients with conotruncal defects (such as the common arterial trunk or persistent truncus arteriosus (PTA), transposition of the great vessels, double-outlet right ventricle, double-outlet left ventricle, discordant atrioventricular connection, tetralogy of Fallot, and aortopulmonary septal defect).

Lesion group 2: Defined as patients with non-conotruncal defects (common ventricle/ single ventricle (SV), AVSD, Ebstein's anomaly, total anomalous pulmonary venous return (TAPVR),). and hypoplastic left heart syndrome).

Lesion group 3: are patients with coarctation of the aorta, interrupted aortic arch (IAA), pulmonary atresia (PA), tricuspid atresia (TA).

Lesion group 4: are patients with the ventricular septal defect.

Lesion group 5 was defined as patients with atrial septal defect.

Lesion group 6 included all other heart and circulatory system anomalies(Aortic stenosis (AS) Patent ductus arteriosus (PDA) Pulmonary artery stenosis (PS)) and all other CHD diagnoses not included in lesion groups 1 to 5.[1]

Severity classification

Critical CHD: Severe CHD requiring early intervention. These are the first 12 CHD types in hierarchical classification (Lesion group 1, 2 3)

Non Critical CHD: Simple type of CHD (Lesion group 4, 5, 6)

Children in poor pre-operative condition were characterized as having Cardiovascular compromise necessitating resuscitation or severe metabolic acidosis necessitating breathing assistance [3].

Managed CHD: Those managed with either of Medical, surgical or Catheterization management

4.12 Data collection technique, instrument, and Quality control

The data collection was done by a chart reviews using 5% pretested hospital data extraction tool at Tazma Cardiac Center prepared by reviewing different kinds of literature ([3-6], [14, 17], [35-39]) and through telephone interview of patient's families retrospectively about current survival status of the children. This instrument consists of five sections (Socio-demographic, Risk factor, Disease characteristics, Intervention and outcome) with different variables. The organized checklist was integrated into the electronic data collecting tool (Kobo toolbox), and reviewed data was gathered with a mobile phone. Three BSc nurses and one senior MSc nursing supervisor were recruited from TASH staff for this research throughout data collecting. For three days, data collectors and supervisors were taught on the study's objectives and data collection instruments.

4.13 Data Analysis

Data was collected using a checklist and kept on the Kobo Collect website for humanitarian assistance. After being cleaned up before analysis, Data was downloaded in Microsoft Excel (Xls) format and exported to SPSS version 26. SPSS version 26 was used for all data analyses.[42] For categorical variables, frequencies and percentages were utilized, whereas means or medians were used to explain continuous variables.

To analyze the survival status of children managed with CHD under different conditions and at different time intervals, Kaplan-Meier survival analysis was employed. Log-rank test was employed to compare survival status in groups for univariate analysis. A single-variable Cox proportional hazards regression was used to evaluate the adjusted each covariate's effect on mortality. Variables with p values less than 0.25 were eliminated. added to the Cox proportional hazards regression in the multivariate analysis to find the independent risk factors linked with death. The ratio computes the likelihood of a specific event occurring over a given time period. The hazard ratio was judged significant if the 95% confidence interval (CI) excluded one [43].

4.14 Ethical clearance

This thesis was approved by Addis Ababa University College of Health Science School of Nursing and Midwifery post-graduate program; Departmental Research Ethics Review Committee (DRERC) of nursing school provided ethical clearance. The written ethical clearance was provided to Tikur Anbessa specialized hospital clinical directorate pediatric department research review committee reviewed the proposal and approved for data collection procedures. Similar step was taken in Ethiopian child heart fun hospital, ECC to conduct data collection. Full information was provided for personnel working on record office about the purpose and risk of this study.

4.15 Dissemination of the result

After the research was completed, the findings were presented at the thesis defense, and the finished product was submitted to the Addis Ababa University School of Nursing and Midwifery post-graduate program. The study's findings will also be communicated through publications and presentations at scientific conferences and seminars.

5 3RESULT

5.1 Socio demographic characteristics

Total of 235 children with managed congenital heart disease randomly selected from totally registered 4870 CHD cases chart of under-five year children were included for survival analysis from both institutions. From those, 11 of them were excluded 9 being for incompleteness of charts and 2 for having major chromosomal abnormality with CHD and finally 224 charts (95.32% response rate) were left for analysis. According to descriptive analysis, 109(48.7%) male and 115(51.3%) female, were managed which 123(54.9%) of them from Addis Ababa a capital city of the country and 101(45.1%) of them were from out of Addis Ababa either from rural area or regional cities. According to age classification majority of mothers 190(84.8%) were belonging to 20-35 years with mean age of 29.38 SD 5.25 years; having economic status average 126(56.3%), below average 65(29%), and 12(5.4%) of them above average. Maternal level of education, employment status and monthly income are considered in order to categorize the economic status of the mothers. The majority of children (147(65.6%)) were born at term with a mean gestational age of 38.1 weeks and a standard deviation of 1.58 weeks. Mean birth weight of children was 3112.18g with standard deviation of 430.8g from the mean. z

Out of 109 male children with CHD, 90(82.6%) of them are censored and among 115 female children 100(87.0%) of them are censored during the follow-up. Based on their gestational age out of 147 children born at term 133(90.5%) of children are censored during follow up. Other socio demographic characteristics were included on the following table. (Table 2)

Table 2: Socio demographic characteristics Children Managed With Congenital Heart Diseases In Tikur Anbessa Specialized Hospital and Cardiac Center, Addis Ababa, Ethiopia, from Jan 2018 to Dec 2022 (n = 224)

Covariates	Category	Total Number (%)	Survival Status	
			Censored Number (%)	Death Number (%)
Sex	Male	109(48.7)	90(82.6)	19(17.4)
	Female	115(51.3)	100(87.0)	15(13.0)
Gestational Age	Preterm	40(17.9)	20(50)	20(50)
	Term	147(65.6)	133(90.5)	14(9.5)
Age at Enrollment	≤ 24 Months	201(89.7)	168(83.6)	33(16.4)
	25-36 Months	19(8.5)	18(94.7)	1(5.3)
	>36 Months	4(1.8)	4(100)	0
Place of residency	Addis Ababa	123(54.9)	107(87.0)	16(13.0)
	Out of Addis Ababa	101(45.1)	83(82.2)	18(17.8)
Maternal age	20-35 Years	190(84.8)	167(87.9)	23(12.2)
	>35 Years	34(15.2)	23(67.6)	11(32.4)
Birth weight(g)	2500g to 3999g	194(86.6)	178(91.80	16(10.2)
	<2500g	30(13.4)	12(40)	18(60)
Weight at admission	≤ 5kg	45(20.08)	31(68.8)	14(31.1)
	>5kg	179(79.91)	159(88.8)	20(11.2)
APGAR Score at 1 min	<7	34(19.1)	22(64.7)	12(35.3)
	≥7	144(80.9)	122(84.7)	22(15.3)
APGAR Score at 5min	<7	3(1.6)	1(33.3)	2(66.7)
	≥7	175(98.4)	143(81.7)	32(18.3)
Order of birth	1st Birth	94(42)	86(91.5)	8(23.5)
	2nd Birth	79(35.2)	63(79.7)	16(20.3)
	3rd and above	51(22.8)	41(80.4)	10(19.6)
Maternal level of education	Cannot read and write	92(41.1)	80(87)	12(12)
	Primary level	52(23.2)	42(80.8)	10(19.2)
	Secondary Complete	17(7.6)	12(70.6)	5(29.4)
	College diploma	27(12.1)	25(92.6)	2(7.4)
	Bachelor degree	27(12.1)	22(81.5)	5(18.5)
	Unknown	9(4.0)	9(4)	
Employment status of mother	Government Employee	37(16.5)	31(83.8)	6(16.2)
	Self employed	48(21.4)	39(81.3)	9(18.8)
	House wife	139(62.05)	120(86.3)	19(13.9)
Economic status	Below average	65(29)	53(81.5)	12(18.5)
	Average	126(56.3)	104(82.5)	22(17.5)
	Above average	12(5.4)	12(100)	0
	Unknown	21(9.4)	21(100)	0

5.2 Clinical characteristics

The majority of the 202 (90.2%) children participated in this study were identified with congenital heart disease before the age of 24 months, with a mean diagnosis time of 12.45 months. The most commonly diagnosed type of CHD was PDA 76(33.9%) followed by VSD 40(17.9%), PS 21(9.4%), ASD 18(8%), TOF 18(8%) and PDA with VSD 11(5%). The left less commonly diagnosed CHD were TGA 4(1.8%), IAA 1(0.4), LVOO 2(0.9), AVSD 3(1.3%), Aortopulmonary window 3(1.3%), TA 2(0.9%), CoA 4(1.8%), DORV 2(0.9%), TAPVR 2(0.9%), Ebstein anomaly with PS, ASD,TR & PDA 1(0.4%), ASD with VSD 2(0.9%), PDA with ASD 1(0.4%) and ASD with PS 3(1.3%).

According to CHD lesion group classification most Severe form of CHD, lesion group 1 was diagnosed in 29(12.9%) cases and the majority of cases are mild form of CHD lesion group 6, 106(46.4%). Cardiac surgery is the common cardiac intervention given in this study having frequency of 168(75%) followed by Catheterization 44(19.6%) and Medical/Pharmacological 12(5.4%) intervention. The mean time of surgical intervention was 25.22 month of their age with minimum within first month and maximum at 56month of age. Out of 121(54%) children presented with history of associated comorbidities 96(79.3%) of them censored while the rest of them were died during the study follow-up. Upper respiratory tract infection 45(37.2 %%), pneumonia 65 (53.7%) and Severe PHTN 11(9.1%) are comorbidities identified in children diagnosed with CHD.

The following table summarizes clinical characteristics of participants (Table 3).

Table 3: Clinical characteristics of under-five children managed with congenital heart diseases in TASH & Ethiopia Cardiac Center, Addis Ababa, Ethiopia from Jan 2018 to Dec 2022(n=224)

Covariates	Category	Total Number (%)	Survival Status	
			Censored Number (%)	Death Number (%)
Age at diagnosis	≤ 24 months	202(90.2%)	168(83.1%)	34(16.8%)
	24 -36 months	18(8%)	18(100)	0
	> 36 months	4(1.8%)	4(100%)	0
CHD lesion groups	Lesion group 1	29(12.9%)	21(72.4%)	8(27.6%)
	Lesion group 2	7(33.13%)	6(85.7%)	1(14.3%)
	Lesion group 3	26(11.6%)	14(53.8%)	12(46.2%)
	Lesion group 4	40(17.9%)	37(92.5%)	3(7.5%)
	Lesion group 5	18(8.03%)	17(94.4%)	1(5.6%)
	Lesion group 6	104(46.4%)	95(91.3%)	9(8.7%)
Severity types	Critical	62(27.7%)	41(66.1%)	21(33.9%)
	Non	162(72.3%)	149(92.0%)	13(8.0%)
Associated comorbidities	Yes	121(54%)	96(79.3%)	25(20.7%)
	No	103(46%)	90(90.9%)	9(9.1%)
Types of comorbidities	URTI	45(37.2%%)	38(84.4%)	7(15.6%)
	Pneumonia	65(53.7%)	48(73.8%)	17(26.2%)
	Severe PHTN	11(9.1%)	10(90.9%)	1(9.1%)
Interventions	Medical/Pharmacologic	12(5.3%)	3(25%)	9(75%)
	Surgical	168(75%)	146(86.9%)	22(13.1%)
	Catheterization	44(19.6%)	41(84.8%)	3(6.8%)
Preoperative condition	Poor	20(11.7%)	1(5.0%)	19(95.0%)
	Good	151(88.3%)	145(96.0%)	6(4.0%)
Family History of Heart disease	Yes	19(8.5%)	11(57.9%)	8(42.1%)
	No	205(89.2)	179(87.3%)	26(12.6%)
Maternal viral infection	Yes	12(5.4%)	2(16.7%)	10(83.3%)
	No	212(88.7%)	188(87.4%)	24(12.6%)

NB: CHD lesion groups [Lesion group 1(TGA, DORV, TOF and Aortopulmonary window), Lesion group 2 (AVSD, Ebstein's anomaly with PS, ASD, TR and PDA, TAPVR), Lesion group 3 (CoA, IAA, TA, PA), Lesion group 4 (VSD), Lesion group 5 (ASD), Lesion group 6(AS, PS, PDA)]

5.3 Kaplan-Meier Survival Status of Under-Five Children Managed With Congenital Heart Diseases

The Kaplan-Meier survival analysis was performed to evaluate the survival status of study participants based on hierarchical CHD categorization, and Kaplan-Meier survival curves for the study population were produced based on the Severity type (Critical and non-critical CHD) of diagnosed CHD. The five year survival probability in this study was 84.8% and the log rank (Mantel cox) shows there is no statistically significance difference on survival probability between sex of children managed with CHD(X^2 = 1.474 at 95% CI, P = 0.225). Survival status for those managed with non-critical CHD was 91.95% to first 12 months and 59.7% to five year with median survival time 36 months. The Log rank (Mantel-cox) indicated that there is a difference between overall survival probability of children managed with critical and non-critical CHD that was statistically significant (X^2 =28.62; P < 0.0001).

Based on hierarchical classification of CHD groups, there is statistical significance between the distribution of survival time in different group of CHD lesions and the overall median survival time is 58 months at 95% CI (55, 61) LR = 31.4; P < 0.0001). The following figure shows Kaplan Meier survival curve indicating significant distribution of survival function based on severity group of diagnosed CHD (Fig 5)

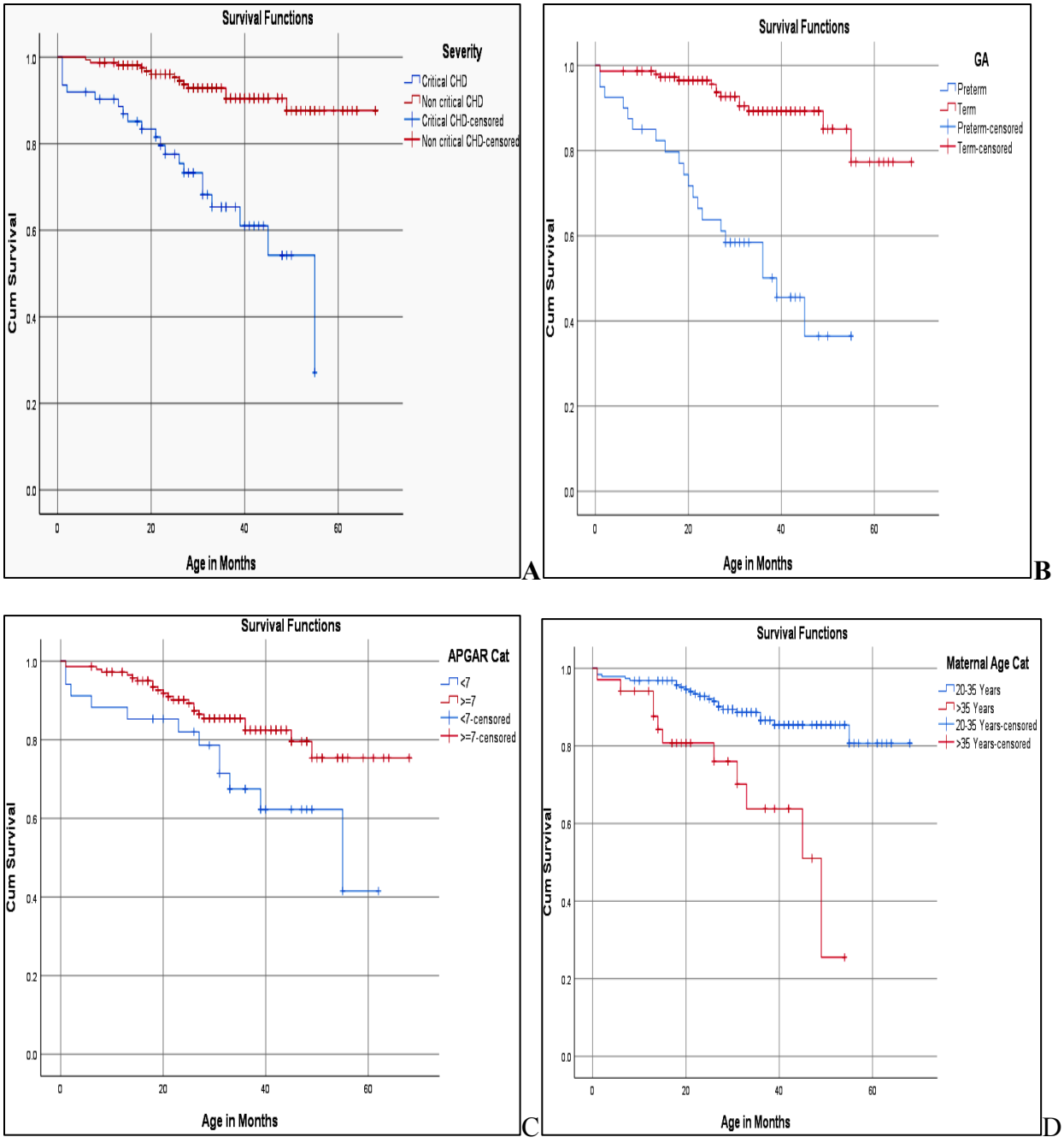


Figure 3: The KM survival curves compare distribution of survival function between groups, severity(A), Gestational age(B), APGAR score at 1 min(C) and maternal age (D) of children managed with CHD at TASH and ECC from Jan 2018 to Dec 2022(n=224)

The survival probability of children with weight at admission ≤ 5kg was 68.5% Vs.88.5% when compared with those admitted with weight > 5kg with median survival time of 55 months (95% CI [42, 68]; LR : 10.96; P = 0.001). The KM curve indicates significant difference in survival time between both groups.

Based on KP Meier analysis for other variables log-rank statistical test indicated statistical significance in survival curve for gestational age, APGAR score at first and fifth minutes, order of birth, weight at admission, maternal age, presence of associated comorbidities, CHD lesion and severity groups, type of intervention, genetic predisposition, maternal substance use and history of maternal viral infection (P Value <0.05) (Table 4).

Table 4: Median survival time and log-rank test survivors of under-five children managed with CHD at TASH and ECC from Jan 2018 to Dec 2022(n=224)

Variable	**Category**	**Median survival time in months (95% CI)**	**Log rank test**	**P- value**
Gestational age	Preterm	39(25, 52.7)	36.3	**0.0001***
	Term	56(52, 59)		
Birth weight	Low BW	22(17.35, 26.64)	79.612	**0.0001***
	Normal BW	61(57.94, 64.39)		
Weight at admission	≤ 5kg	55(42, 68)	10.96	**0.001***
	>5kg	61(58, 63)		
APGAR score at first minutes	<7	55(27.7, 82.28)	5.075	**0.024****
	≥7	58(54.5, 62.06)		
APGAR score at fifth minutes	<7	27(0, 67)	5.66	**0.017****
	≥7	56(52.7, 60)		
Economic status	Below average	41(35.9, 46.09)	6.665	0.083
	Average	32(29.14, 34.85)		
	Above average	32(23.51, 40.9)		
Maternal age	20-35	60(57.9, 63.6)	15.292	**0.0001***
	>35	49(33.1, 64.9)		
Presence of associated comorbidities	Yes	36(33.4, 38.6)	4.1	**0.043****
	No	33(29.55, 36.45)		
CHD severity groups	Critical	55(36.70, 73.26)	28.6	**0.0001***
	Non critical	63(60.8, 65.74)		
Type of intervention	Pharmacologic	31(11.37, 50.6)	47.7	**0.0001***
	Surgical	35(32.63-37.36)		

	Catheterization	34(26.7, 41.32)		
Employment status	Government	28(21.07, 34.93)	1.556	0.459
	Self	31(27.28, 34.7)		
	Housewife	36(32.9, 39.04)		
Family History of CHD	Yes	36(17.5, 54.35)	28.1	**0.0001***
	No	61(58 , 63)		
Maternal substance use	Yes	31(21.14, 40.86)	53.12	**<0.0001***
	No	60(57.398, 63.487)		
Over all		**58 (55.5 , 61.46)**		

NB: **Significant (P-value 0.05), *significant (P-value 0.01), and HR=1

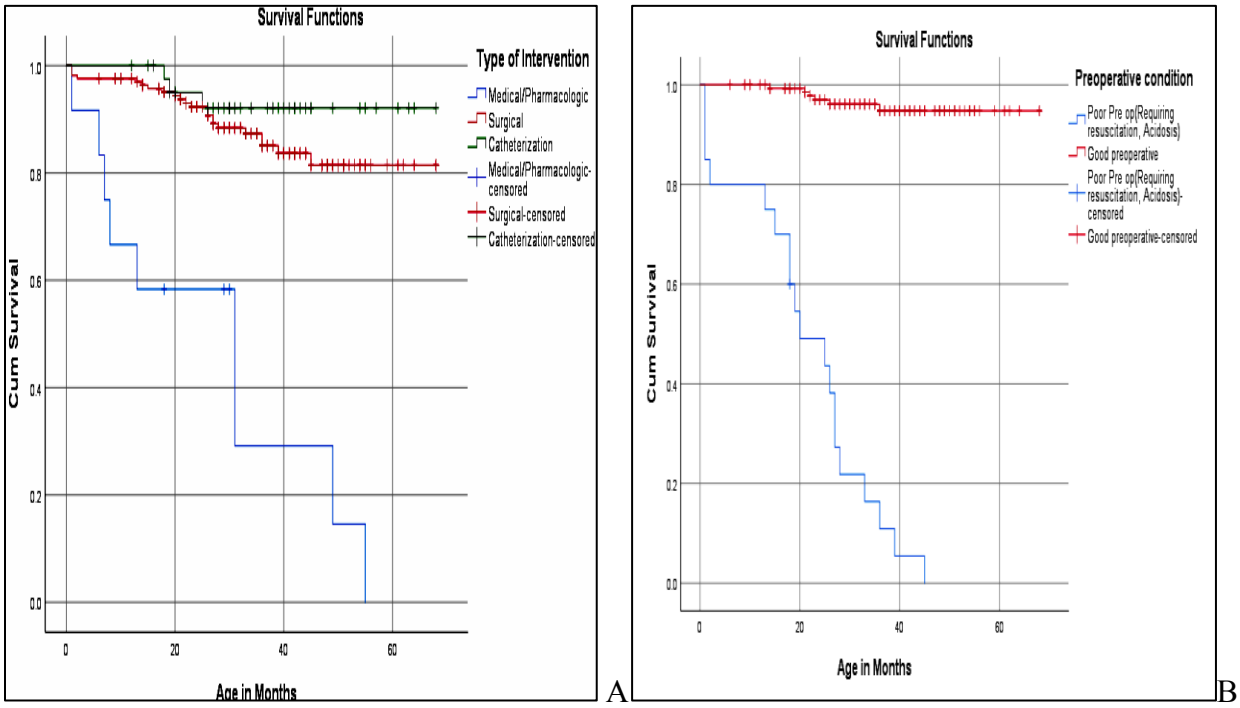


Figure 4 : The KM survival curves compare distribution of survival function between groups, type of intervention(A), preoperative condition(B) of children managed with CHD at TASH and ECC from Jan 2018 to Dec 2022(n=224)

5.4 Factors associated to survival status of Under-five children managed with CHD

To study the relationship between survival probability and covariates, the Cox proportional hazard regression model was utilised. The independent variables were examined separately with the outcome variable, and those with a P-value less than 0.25 were included in the multivariate Cox regression model, as were non-collinear independent variables. Covariates fit multicollinearity check and doesn't varies with time interval (fit proportionality assumption) were included to bivariate and multivariate cox regression and their hazard ratio was analyzed to determine their effect on survival status.

Gestational age, birth weight, weight at admission, maternal age, severity group, hierarchical classification, type of intervention, types of intervention, preoperative condition, family history of heart disease, maternal substance use and history of maternal viral infection are variables associated in bivariate regression ($P< 0.25$).

Multivariate cox regression identified that six covariates; weight at admission, types of intervention, Preoperative condition, family with history of heart disease and maternal history of viral infection were significantly associated with survival status of children managed with CHD and significantly increased proportional hazards of mortality ($P < 0.05$)(Table 5).

Out of 224 study participants, children with a weight ≤ 5kg (20.4%) are 19.02 AHR (95% CI: [2.542, 142.925]; P = 0.004) times more likely to die at every time point in months from 0 to 59 months of age than those admitted with a weight greater than 5kg. Children managed with pharmacologic (medical) type of management are 73.02, 95% CI: [43.226, 165.2]; P = 0.007) times more likely to be at risk of mortality compared to cardiac catheterization intervention. Surgical management has a protective effect on mortality, that morality was reduced by 98.6% in surgical management compared to others, AHR 0.0136 at 95% CI (0.0006, 0.510), P = 0.31.

For surgically managed children in this study, the preoperative clinical condition was the most significant predictor of mortality. At every time point, children with poor pre-operative conditions are 65.09 AHR (95% CI: [11.32, 374.25]; P < 0.0001) times more likely to die than those with good pre-operative clinical conditions. Children with a family history of cardiac

problems are 10.8 (95% CI: [2.218, 52.673]: P = 0.003) times more at risk of mortality compared to those with no history.

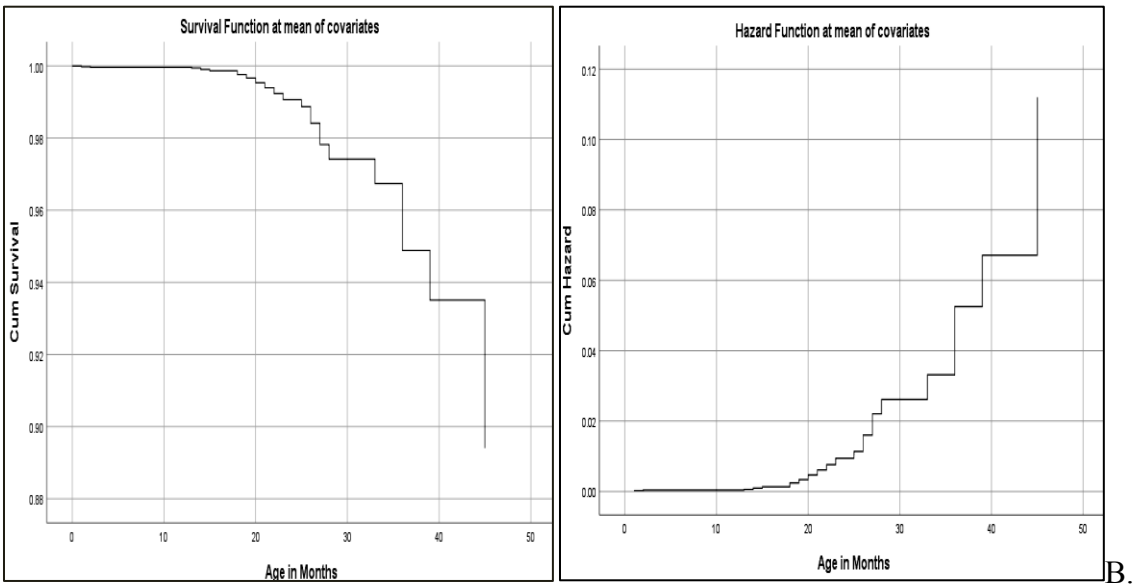
Table 5: Bivariate and Multivariate Cox regression analysis to identify factors associated to survival status of Under-five children managed with CHD managed with CHD at TASH and ECC from Jan 2018 to Dec 2022(n=224)

Covariates	Censored Number (%)	Death Number (%)	**CHR (95% CI)**	**AHR (95% CI)**	**P- value**
GA: children born at preterm gestation					
Term	180(92.4)	14(9.5)	1	1	
Preterm	20(50)	20(50)	6.25(3.15, 12.4)	2.678(0.443, 16.197)	0.283
Birth weight					
2500g to 3999g	178(91.80	16(10.2)	1	1	
<2500g	12(40)	18(60)	13.2(6.4, 27.17)	1.430(0.203, 10.089)	0.719
Weight at admission					
>5kg	31(68.8)	14(31.1)	1	1	
≤ 5kg	159(88.8)	20(11.2)	3(1.51, 5.93) 0.002	19.023(2.542,142.925)	**0.004****
APGAR at 1 min					
≥7	122(84.7)	22(15.3)	1	1	
<7	22(64.7)	12(35.3)	2.29(1.09, 4.44)	2.044(0.424, 9.831)	0.372
Maternal age					
25-35	167(87.9)	23(12.2)	1	1	
≥35	23(67.6)	11(32.4)	3.84(1.85, 7.96)	4.565(0.925, 22.519734)	0.062
Severity group					
Non critical	149(92.0%)	149(92.0%)	1	1	
Critical	41(66.1%)	41(66.1%)	5.452(2.715,10.951)	1.0567(0.089, 12.518)	0.965
Hierarchical classification					
Lesion group 6	95(91.3%)	9(8.7%)	1	1	
Lesion group 1	21(72.4%)	8(27.6%)	0.707(0.088, 5.714)	8.964(0.542, 148.056)	0.1253
Lesion group 2	6(85.7%)	1(14.3%)	1.415(0.577, 3.467)	14.617(0.937, 227.88)	0.056
Lesion group 3	14(53.8%)	12(46.2%)	0.184(0.049, 0.697)	1.11(0.11, 11.19)	0.983
Lesion group 4	37(92.5%)	3(7.5%)	0.121(0.015,	0.633(0.0683,	0.687

			0.980)	5.87)	
Lesion group 5	17(94.4%)	1(5.6%)	0.251(0.097, 0.653)	0.0417(0.001, 2.83)	0.14
Type of intervention					
Catheterization	41(84.8%)	3(6.8%)	1	1	
Surgical	146(86.9)	22(13.1%)	2.001(0.598, 6.69)	0.0136(0.0006, 0.510)	0.90383
Pharmacologic	3(25%)	9(75%)	16.14(4.35, 59.79)	73.016(3.226, 1652.2)	**0.007****
Pre-Operative condition					
Good	145(96.0%)	6(4.0%)	1	1	
Poor	1(5.0%)	19(95.0%)	45.006(17.676, 114.589)	65.097(11.322, 374.25)	**<0.0001***
Family history of heart disease					
No	179(87.3%)	26(13%)	1	1	
Yes	11(57.9%)	8(42.1%)	5.307(2.655, 10.606	10.810(2.218, 52.673)	**0.003****
Maternal substance use					
No			1	1	
Yes			9.107(4.42, 18.75)	46.67(4.405, 494.31)	**0.001***
Maternal viral infection					
No	188(87.4%)	24(12.6%)	1	1	
Yes	2(16.7%)	10(83.3%)	16.17(9.59, 38.32)	52.034(7.320, 369.83)	**< 0.0001***

NB: - **Significant (P-value < 0.05), *significant (p-value<0.01) and HR=1 is reference variable.

Children born to mothers with a history of viral infection (12[5.4%]: including identified 8 HIV and 4 syphilis cases) are 52 (95% CI: [7.320, 369.83]; P < 0.0001) times as likely to die than individuals who do not have no history of maternal viral infection. Children of any type of substance user's 16(7.2%) mothers are 46.7 (95% CI: [4.405, 494.31]; P < 0.0001) times more likely to die from congenital heart disease compared with those without maternal substance use. The following figure presents the survival and proportional hazard at the mean of covariates (Fig 7).

A. 

B.

Figure 5: Cox regression Survival and hazard function at a mean of covariates among under-five children managed with congenital heart diseases in TASH & Ethiopia Cardiac Center, Addis Ababa, Ethiopia from Jan 2018 to Dec 2022(n=224)

5.5 Multicollinearity Test

A predictor variable in a multiple Cox-regression model can predict the others linearly to a large extent. Multicollinearity occurs when predictor covariates in the Cox-regression model are linked. This is problematic since the relationship between each predictor variable and the outcome variable should be independent of one another. To confirm multicollinearity, used the variance inflation factor (VIF) for each predictor variable (based on the binary cox-regression outcome). According to certain recommendations, a collinearity level of less than 10 is acceptable and if VIF > 10 or tolerance < 0.01 there is significant multicollinearity that needs to be corrected. A VIF of more than 4 suggests the need for additional investigation. The maximum VIF value in this sample was 2.07, with a mean VIF of 1.03. The minimal Tolerance value in these study variables was 0.734. As a result, there was no multicollinearity, and the study's conclusions may be understood.

Table 6 : Multicollinearity Test for variables in study of survival status and associated factor among under-five children managed with CHD at t TASH and ECC from Jan 2018 to Dec 2022(n=224)

Variable	**VIF**	**1/VIF(Tolerance)**
Associated comorbidities	1.191932	0.839
CHD Lesion groups	1	1
Genetic predisposition/Family Hx of HD	1.177	0.849
Clinical finding at presentation(presenting symptoms)	1.114	0.897
Maternal Substance use	1.348	0.741
Maternal Viral Infection	1.479	0.675
Sex of baby	1.290	0.775
Birth Weight	2.073	0.482
Weight at admission	0.968	1.033
APGAR at 1mi	1.181	0.847
APGAR at 5mi	1.203	0.831
Order of birth	1.179	0.848
Maternal Residence	1.274	0.784
Economic status of family	1.193	0.774
Maternal level of education	1.283	0.779
Preoperative condition	0.96	1.03
Mean	1.267	0.805

5.6 Test of Proportional Hazard Assumption

It is necessary to assess, use fitted proportional hazard models, and accept multivariate analysis conclusions based on binary and multicollinearity outcomes. In this study, the proportional hazard assumption test and global testing were used to determine if continuous and categorical variables fulfilled the proportionality assumption. The proportionality assumption was found to be violated by covariates with p values less than 0.05

Table 7 : Test of proportionality's assumptions for predictor variables in survival status and associated factors among under-five children managed with CHD at TASH and ECC from Jan 2018 to Dec 2022(n=224)

VARIABLES	CHI2 (X2)	P-VALUE
Gestational age	2.014	0.365
Birth weight	4.078	0.137
APGAR score at 1 min	0.517	0.689
APGAR score at 5min	0.852	0.832
Order of birth	4.026	0.085
Weight at admission	9.463	0.458
Associated Comorbidities	1.518	0.581
CHD lesion groups	3.676	0.064
Types of interventions	2.846	0.161
Preoperative condition	74.02	0.72
Family History of Heart disease	0.566	0.523
Maternal Age	12.05	0.276
Maternal substance use	4.067	0.112
Maternal viral infection	8.766	0.611
Re operation	2.650	0.184
Clinical presentation	4.111	0.192
Comorbidities	5.823	0.241
Age at postnatal diagnosis	7.378	0.087

6 DISCUSSION

The purpose of this retrospective cohort study was to assess the survival status and factor associated with for children under the age of five who were treated for CHD at Tikur Anbessa specialized hospital (TASH) and Ethiopian Child Heart Fund/Cardiac Centre Ethiopia (ECC). The survival status of all infants born with CHD in this study was 84.8% to five years. Our findings for the survival rate for patients with CHD in a poor nation with severe limitations in human resources and knowledge were similar to those reported in a recent systematic meta-analysis of 16 population studies with pooled 5-year survival rates of 85.4%. [3, 30]. The consistency of the findings in the current study could be attributed to the high percentage of mild and moderate CHD cases in our study, such as PDA 76 (33.9%), VSD 40 (17.9%), PS 21 (9.4%), and ASD 18 (8%), which could have resulted in greater survival rates.

Male and female individuals have identical survival rates of 82.6% and 87%, respectively (X2 = 1.474, P = 0.225). Although the survival status of children managed with CHD was high according to a study conducted in Sweden that revealed the survival probability of males and females to be 87% and 90%, respectively, the finding in this study indicates similarity in the difference between the survival statuses of both sexes[29]. As expected, critical CHDs remain a public health priority, with mortality (33.9% vs. 8%) and survival probability (66.1% vs. 92%) varying with CHD severity, and survival was lower in patients with CCHD, with a median survival time of 55 months (95% CI(38.7, 73.25), Log rank (X2 = 28.6, P = 0.0001). This finding was consistent with a research undertaken in another developing nation, Malaysia, where the critical CHD death rate was 34%[3].

The mortality risk was expected to be high in higher hierarchical classification, as indicated by a Swedish study that found the mortality risk in lesion group 1 (such as tetralogy of Fallot, atrioventricular septal defect, transposition of the great vessels, double inlet ventricle, hypoplastic left heart syndrome, and common arterial trunk) to be 64.07 (95% CI; P.001)[29]. However, the hazard of death was increased by 14 times in lesion group 2 and 9 times in CHD lesion group 1 compared to the simplest type of CHD lesion group 6, that Has no significant association with survival status in current study (P = 0.056 and 0.125 respectively). The

difference may be due to lack of adequate facilities in our study setup to manage the most severe form of CHD managed in comparison groups.

In surgically managed patients in current study, the chance of death was reduced by 98.7% without statistical significance (P = 0.90383). Children managed medically while waiting for surgical intervention were 73 times more likely to die compared to those receiving surgical or cardiac catheterizations. This is a significant indicator that attention should be given to cutting waiting times for surgical intervention. Our findings agree with other findings in a study from Saudi Arabia that survival was higher for groups that underwent surgery than those that did not (81% vs. 19%) [36]. Given our findings, we suggest that pharmacologic and medical therapy should not be regarded as a risk factor for poor outcomes, but rather that surgical intervention has significant prognostic significance.

Preoperative circumstances are among the main variables related with the survival of children managed with CHD in this study, which is consistent with findings from other studies done in underdeveloped countries[3]. Children with poor preoperative conditions are 65 times more likely to die at every age from 0 to 59 months compared to those with good preoperative conditions. This implies that preoperative stabilization is important to increase the survival of children with CHD. Weight at the time of diagnosis was also a factor affecting survival status in this study. Those children with a weight at diagnosis of 5 kg were 19 times more likely to die from CHD at every change in time point than those with a weight at admission of >5kg. The finding from this study indicates increased survival probability in children with CHD having adequate weight gain.

Family history of cardiac problems is another significant covariate identified by multivariate Cox regression analysis to be significantly associated with the survival status of children managed with CHD. The hazard risk increases 10.8 times in children with any type of genetic contribution, either from siblings or other relatives, at every time point while controlling for other covariates. Similarly, children of mothers with a history of substance use are 10.8 times more at risk of mortality compared with those with no history.

Another major covariate related with the survival status of children with CHD is maternal viral infection. Children born to moms who had a history of viral infection had a 52-fold higher mortality risk than the rest of the children in this study. This was consistent to the study from Ghana, which found that those factors are significantly associated with the poor outcome of preschool children diagnosed with CHD[4]. The survival curve at mean of covariates (Figure 6) indicates the survival status of children was high in the early plot of the curve, especially before 20 months for all covariates. According to the hazard function plot at the mean of covariates, mortality was significantly expected to occur after two years of age for all covariates.

Although there is no available data to analyze the effect of prenatal diagnosis in this study, previous studies showed that survival status improved for different prenatally diagnosed types of CHD, such as COA. Prenatal echocardiography was recommended as an effective screening method for CHD, and prenatal diagnosis of CHD can increase the survival probability of children [25, 31]. Survival function in this study was high for those diagnosed within 12 months of age. This may be due to the fact that a large number of children in this study are diagnosed within 12 months of age (60.3%) with a survival probability of 86% vs. 83%, but log rank excluded that there was no statistically significant difference between survival in groups (X^2 = 0.04, P = 0.89). These findings may indicate the survival advantage of early diagnosis by increasing the probability of getting cardiac intervention.

Achieving the 2016 United Nations (UN) Sustainable Development Goals (SDGs) endorsement targeted to minimize neonatal mortality of less than 12 deaths per 1000 live births and child mortality of less than 25 deaths per 1000 live births will be ensured when priority is placed on congenital heart disease[5]. In developing countries of Africa, including Ethiopia, where the burden of congenital heart disease is hidden due to limited literature, the findings of our study indicate the essentiality of screening and early cardiac intervention to decrease mortality risk [10]. The scarcity of resources to address cardiac intervention was worsening the burden in developing nations by complicating socioeconomic status.

6.1 Strength and Limitation of the Study

Strength

- High response rate
- The first study in Ethiopia
- The study was considered for any violation of proportional hazard assumptions
- Taking censored observations into account was also a significant strength of this study because it provides a more precise estimate for survival analysis.

Limitations

- Because the study relied on secondary sources, some crucial covariates obtained from the mother were absent.
- Non representativeness of the study since it was analyzed survival status of children managed on only two institutions purposively.
- Possibility of underreporting and missing data
- Limitation of literature in the similar study area
- Difficulty to analyze survival status of most severe form of CHD such as Hypo plastic left heart syndrome due to early mortality unless got cardiac intervention in early first year.

7 CONCLUSION AND RECOMMENDATION

7.1 Conclusion

The five year survival probability in this study was 84.8% and the log rank (Mantel cox) shows there is no statistically significance difference on survival probability between sex of children managed with CHD(X2 = 1.474 at 95% CI, P = 0.225). Cox regression analysis identified covariates significantly associated with mortality as weight at admission (AHR 19.023; P = 0.004), types of interventions (AHR73.016; P = 0.007), pre-operative condition (AHR 65.097; P =0.0001), family history of heart disease (AHR 10.81; P = 0.003), maternal history of substance use (AHR 46.67; P = 0.001) and maternal history of viral infection (AHR 52.034; P< 0.0001).

Results of this study can give an insight into the survival status and associated factor of under-five children with CHD provide baseline data for future detailed studies, as there was very little data available in the past. Donors, policymakers, and volunteer health professionals were recommended to return to delivering the precious cardiac interventions for free to vulnerable developing societies. Therefore; the attention should be given for those predictor variables and cardiac interventions to improve the overall survival probability of children born with CHD in developing countries.

7.2 Recommendations

Although many children with CHD were dies while waiting for surgical intervention; those managed with cardiac intervention had improved survival probability. Based on the findings from this study the principal investigator would like to recommend different stakeholders the following recommendations.

To the federal minister of health

To address treatment options for congenital heart disease and promote survival, federal minister of health should focus on policies related to congenital heart disease.

The number of specialize cardiac centers provide specialized cardiac intervention for CHD patients should be increased in developing countries like Ethiopia to minimize under-five mortality. Protocol to encourage antenatal and early postnatal screening for congenital heart disease should be prepared.

To TASH and Ethiopia child heart fund-ECC

Since both institutions are the public referral institutions, the number of health professionals provides cardiac intervention in both institutions should be increased and equipped to decrease waiting time for cardiac intervention.

To health care providers

Early screening, referral and early cardiac intervention should be the priority to be given to increase survival status of children born with congenital heart disease at all level of health institutions.

To future researchers

Future researchers shall do a longitudinal prospective cohort study to include variables that are impossible to include in a retrospective analysis, such as the influence of severe CHD, antenatal diagnosis, dietary problems, and environmental factors.

REFERENCES

[1] Z. Mandalenakis *et al.*, "Survival in children with congenital heart disease: Have we reached a peak at 97%?," *J. Am. Heart Assoc.*, vol. 9, no. 22, Nov. 2020, doi: 10.1161/JAHA.120.017704.

[2] W. Africa, U. A. Susan, T. P. Nnena, and O. B. Edewele, "Prevalence of congenital heart diseases among primary school children in the Niger Delta Region of," *JCCM*, vol. 4, pp. 144–149, 2019, doi: DOI: dx.doi.org/10.29328/journal.jccm.1001056.

[3] M. N. Mat Bah, M. H. Sapian, M. T. Jamil, A. Alias, and N. Zahari, "Survival and Associated Risk Factors for Mortality Among Infants with Critical Congenital Heart Disease in a Developing Country," *Pediatr. Cardiol.*, vol. 39, no. 7, pp. 1389–1396, Oct. 2018, doi: 10.1007/s00246-018-1908-6.

[4] H. Yan *et al.*, "Prevalence of Congenital Heart Disease in Chinese Children With Different Birth Weights and Its Relationship to the Neonatal Birth Weight," *Front. Pediatr.*, vol. 10, May 2022, doi: 10.3389/fped.2022.828300.

[5] M. S. Zimmerman *et al.*, "Global, regional, and national burden of congenital heart disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017," *Lancet Child Adolesc. Heal.*, vol. 4, no. 3, pp. 185–200, Mar. 2020, doi: 10.1016/S2352-4642(19)30402-X.

[6] M. E. Oster, K. A. Lee, M. A. Honein, T. Riehle-Colarusso, M. Shin, and A. Correa, "Temporal trends in survival among infants with critical congenital heart defects," *Pediatrics*, vol. 131, no. 5, May 2013, doi: 10.1542/peds.2012-3435.

[7] N. D. Pace, M. E. Oster, N. E. Forestieri, D. Enright, J. Knight, and R. E. Meyer, "Sociodemographic Factors and Survival of Infants With Congenital Heart Defects," *Am. Acad. pefiatrics*, vol. 142, no. 3, pp. 1–13, 2018, doi: ddoi. org/ 10. 1542/ peds. 2018-0302.

[8] Y. Liu *et al.*, "Global birth prevalence of congenital heart defects 1970 – 2017 : updated systematic review and meta-analysis of 260 studies," *Int. J. Epidemiol.*, vol. 0, no. 0, pp. 1–9, 2019, doi: 10.1093/ije/dyz009.

[9] D. A. Angaw, R. Ali, A. Tadele, and S. Shumet, "The prevalence of cardiovascular disease in Ethiopia : a systematic review and meta ‑ analysis of institutional and

community ‐ based studies," *BMC Cardiovasc. Disord.*, pp. 1–9, 2021, doi: 10.1186/s12872-020-01828-z.

[10] W. Wu, J. He, and X. Shao, "Incidence and mortality trend of congenital heart disease at the global, regional, and national level, 1990-2017," *Medicine (United States)*, vol. 99, no. 23. Lippincott Williams and Wilkins, 2020. doi: 10.1097/MD.0000000000020593.

[11] A. T. Tankeu *et al.*, "Prevalence and patterns of congenital heart diseases in Africa : a systematic review and meta-analysis protocol," *BMJ*, vol. 7, pp. 1–5, 2017, doi: 10.1136/bmjopen-2016-015633.

[12] O. Access, "Mission-based cardiac surgery and catheter treatment of coarctation of aorta in the young and older children: a facility based review of cases in Addis Ababa," vol. 8688, pp. 1–13, 2019, doi: 10.11604/pamj.2019.34.160.19406.

[13] T. Hurisa, H. Megersa, and T. Tsegaye, "Delayed in Diagnosis of Congenital Heart Disease and Associated Factors Among Pediatric Patients in," *C. Am. J. Heal. Res.*, vol. 10, no. 3, pp. 51–62, 2021, doi: 10.11648/j.ajhr.20221003.12.

[14] M. Cardio *et al.*, "Prevalence of Factors Associated with Congenital Heart Disease," *Multidiscip Cardio Ann. Press*, vol. 10, no. 60, pp. 0–4, 2020, doi: 10.5812/mca.106026.Research.

[15] C. D. Varela-chinchilla, D. Edith, and P. A. Trinidad-calder, "Congenital Heart Disease : The State-of-the-Art on Its Pharmacological Therapeutics," 2022.

[16] S. Zaidi and M. Brueckner, "Genetics and Genomics of Congenital Heart Disease," *Circulation Research*, vol. 120, no. 6. Lippincott Williams and Wilkins, pp. 923–940, Mar. 17, 2017. doi: 10.1161/CIRCRESAHA.116.309140.

[17] S. Ali *et al.*, "The burden of cardiovascular diseases in Ethiopia from 1990 to 2017: Evidence from the Global Burden of Disease Study," *International Health*, vol. 13, no. 4. Oxford University Press, pp. 318–326, Jul. 01, 2021. doi: 10.1093/inthealth/ihaa069.

[18] F. Talargia, G. Seyoum, and T. Moges, "Congenital heart defects and associated factors in children with congenital anomalies," 2018. [Online]. Available: https://www.researchgate.net/publication/328232568

[19] J. I. E. Hoffman, "Review Article The global burden of congenital heart disease," *Cardiovasc. J Africa*, vol. 24, no. 4, pp. 141–145, 2013, doi: 10.5830/CVJA-2013-028.

[20] T. Aliku *et al.*, "Profile of congenital heart disease and access to definitive care among

children seen at Gulu Regional Referral Hospital in Northern Uganda : a four-year experience," *J. Congenit. Cardiol.*, vol. 0, no. 9, pp. 5–10, 2021, doi: doi.org/10.1186/s40949-021-00064-0 (2021).

[21] A. Muntha and T. Moges, "Congenital Cardiovascular Anomalies among Cases of Down Syndrome: A Hospital Based Review of Cases in TikurAnbessa Specialized Hospital, Ethiopia," *Ethiop. J. Health Sci.*, vol. 29, no. 2, pp. 165–174, Mar. 2019, doi: 10.4314/ejhs.v29i2.3.

[22] S. C. (Chidre. H. B. Kloesel et al., J.A DiNardo, *Cardiac Embryology and Molecular Mechanisms of Congenital Heart Disease*, vol. 123, no. 3. Boston, MA, 2017. doi: 10.1213/ANE.0000000000001451.Cardiac.

[23] M. C. R. J. Martin, A. Fanarof, "Fanaroff and Martin ' s Neonatal-Perinatal Medicine," in *Diseases of the Fetus and Infant*, ELEVENTH E., A. A. F. Richard J. Martin, Ed. Philadelphia,: Elsevier, Inc, 2019, p. Chapter 71-78. [Online]. Available: https://www.elsevier.com

[24] B. Zheleva and J. B. Atwood, "The invisible child : childhood heart disease in global health," *Lancet*, vol. 6736, no. 16, pp. 15–16, 2016, doi: 10.1016/S0140-6736(16)32185-7.

[25] M. E. Oster, S. W. Aucott, J. Glidewell, J. Hackell, and N. Carolina, "Lessons Learned From Newborn Screening for Critical Congenital Heart Defects," vol. 137, no. 5, 2016, doi: 10.1542/peds.2015-4573.

[26] B. Han, Y. Tang, X. Qu, C. Deng, X. Wang, and J. Li, "Comparison of the 1-year survival rate in infants with congenital heart disease diagnosed by prenatal and postnatal ultrasound A retrospective study," *Med. (United States)*, vol. 100, no. 4, Jan. 2021, doi: 10.1097/MD.0000000000023325.

[27] N. E. Thomford *et al.*, "Clinical Spectrum of congenital heart defects (CHD) detected at the child health Clinic in a Tertiary Health Facility in Ghana: a retrospective analysis," *J. Congenit. Cardiol.*, vol. 4, no. 1, Dec. 2020, doi: 10.1186/s40949-020-00034-y.

[28] J. K. Triedman and J. W. Newburger, "The Future of Cardiovascular Biomedicine Trends in Congenital Heart Disease The Next Decade," pp. 2716–2733, 2016, doi: 10.1161/CIRCULATIONAHA.116.023544.

[29] Z. Mandalenakis, A. Rosengren, K. Skoglund, G. Lappas, P. Eriksson, and M. Dellborg,

"Survivorship in children and young adults with congenital heart disease in Sweden," *JAMA Intern. Med.*, vol. 177, no. 2, pp. 224–230, Feb. 2017, doi: 10.1001/jamainternmed.2016.7765.

[30] K. E. Best and J. Rankin, "Long-term survival of individuals born with congenital heart disease: A systematic review and meta-analysis," *J. Am. Heart Assoc.*, vol. 5, no. 6, Jun. 2016, doi: 10.1161/JAHA.115.002846.

[31] D. Bonnet, "Impacts of prenatal diagnosis of congenital heart diseases on outcomes," *Translational Pediatrics*, vol. 10, no. 8. AME Publishing Company, pp. 2241–2249, Aug. 01, 2021. doi: 10.21037/tp-20-267.

[32] S. G. Jivanji, S. A. Qureshi, B. Reel, and S. Lubega, "Congenital heart disease in East Africa," *Frontiers in Pediatrics*, vol. 7, no. MAY. Frontiers Media S.A., 2019. doi: 10.3389/fped.2019.00250.

[33] B. Nigussie and H. Tadele, "Heart Failure in Ethiopian Children: Mirroring the Unmet Cardiac Services," *Ethiop. J. Health Sci.*, vol. 29, no. 1, pp. 811–818, Jan. 2019, doi: 10.4314/ejhs.v29i1.2.

[34] M. Tsegaye, "Survival Status of Infants With Congenital Anomalies in The Selected Hospitals, Addis Ababa, Ethiopia: A Retrospective Cohort Study," Addis Ababa, Ethiopia, 2021. [Online]. Available: Addis Ababa University portal/Libriary

[35] Chung-Yi Li, "Association of maternal chronic disease with risk of congenital heart disease in offspring," *CMAJ*, pp. 1–9, 2016, doi: 10.1503/cmaj.160061/-/DC1.

[36] A. A. Alabdulgader, "Survival analysis: Prenatal vs. postnatal diagnosis of HLHS.," *J Invasive Noninvasive Cardiol*, vol. 1, no. 2, p. 12, 2018, [Online]. Available: http://www.alliedacademies.org/journal-invasive-non-invasive-cardiology/

[37] K. Taylor *et al.*, "Effect of maternal prepregnancy/early-pregnancy body mass index and pregnancy smoking and alcohol on congenital heart diseases: A parental negative control study," *J. Am. Heart Assoc.*, vol. 10, no. 11, pp. 0–18, 2021, doi: 10.1161/JAHA.120.020051.

[38] M. E. Oster *et al.*, "A population-based study of the association of prenatal diagnosis with survival rate for infants with congenital heart defects," *Am. J. Cardiol.*, vol. 113, no. 6, pp. 1036–1040, Mar. 2014, doi: 10.1016/j.amjcard.2013.11.066.

[39] H. Jicinska *et al.*, "Does First-Trimester Screening Modify the Natural History of

Congenital Heart Disease?: Analysis of Outcome of Regional Cardiac Screening at 2 Different Time Periods," *Circulation*, vol. 135, no. 11, pp. 1045–1055, Mar. 2017, doi: 10.1161/CIRCULATIONAHA.115.020864.

[40] A. Raissadati, H. Nieminen, J. Haukka, H. Sairanen, and E. Jokinen, "Late Causes of Death After Pediatric Cardiac Surgery: A 60-Year Population-Based Study," *J. Am. Coll. Cardiol.*, vol. 68, no. 5, pp. 487–498, Aug. 2016, doi: 10.1016/j.jacc.2016.05.038.

[41] L. D. Botto, A. E. Lin, T. Riehle-colarusso, S. Malik, and A. Correa, "Seeking Causes : Classifying and Evaluating Congenital Heart Defects in Etiologic Studies," vol. 727, no. August, pp. 714–727, 2007, doi: 10.1002/bdra.20403.

[42] I. D. of Licensing, "IBM SPSS Categories 26," *IBM Corp.*, pp. 0–48, 2019.

[43] A. J. G. Lawrence S.Meyers , Glenn C. Gamst, *Performing data analysis using IBM SPSS*, 1st Ed. Sacromento, California: (Jon Siley & Sons, Inc. Newjersey Canada), 2013.

ADDIS ABABA UNIVERSITY COLLEGE OF HEALTH SCIENCES, SCHOOL OF ALLIED HEALTH SCIENCES, DEPARTMENT OF NURSING AND MIDWIFERY POSTGRADUATE PROGRAM

Appendix-I: Hospital data extractor format

Code	Variables		Response		Skip pattern
QID	Identification	Code			
		Hospital			
Section 1	**Socio demographic**				
101	Maternal	Residency	1. Urban 2. Rural	3. Unknown	
		Monthly income			
		Economic status	1 Below average 2 Average 3 Above average		
		Level of education	1 Cannot read and write 2 Primary level 4 Secondary Complete 3 College diploma 4 Bachelor degree 5 Unknown		
		Employment status	1. Government Employee 2. Self employed 3. House wife		
102		Date of delivery	DD/MM/YYYY		
103		Maternal Age			
104	Child	Sex	1. Male 2. Female	3. Ambiguity	
105		Gestational age(Weeks)	1. 28 to 31 6/7 2. 32 to 33 6/7 3. 34 to 37	4. > 37 wks 5. Unknown	
106		Birth weight(g)	1. < 1500g 2. 1500g to 2499g 3. 2500g to 3999bg	4. >=4000g 5. Unknown	
		Weight at admission	1. . 5kg		

			2. >5kg		
107		APGAR Score at 1min	1. <7 2. >= 7 3. Unknown		
108		APGAR Score at 5 min	1. < 7 2. >= 7 3. Unknown		
		Order of birth	1. 1st Birth 2. 2nd Birth 3. 3rd and above		
109	Date of Admission		DD/MM/YYYY		
110		Age at admission	1. Within 24 hour 2. Within first 7 days 3. 8 to 28 days 4. First 1st to 6th months	5. 6th to 12th months 6. 12th to 24th months 7. 24th to 36th months 8. 36th to 48th months 9. 48 to 59th months	
Section 2	**Clinical Characteristics**				
201	Comorbidities	1. Yes 2. No			If No skip to, 203
202	If Yes, Types of comorbidities	1. Upper respiratory tract infection 2. Pneumonia 3. Severe PHT			
203	Type of CHD	1. Hypo plastic left heart syndrome 2. HLHS 3. Tetralogy of Fallot (TOF) 4. Transposition of great arteries (TGA) 5. Pulmonary atresia (PA) 6. Tricuspid atresia (TA) 7. Persistent truncus arteriosus (PTA) 8. Total anomalous pulmonary venous 9. return (TAPVR) 10. Coarctation of the aorta (CoA),	12. Ebstein anomaly (EA), 13. Interrupted aortic arch (IAA) 14. Single ventricle (SV). 15. Aortic stenosis (AS) 16. Atrial septal defect (ASD) 17. Patent ductus arteriosus (PDA) 18. Pulmonary artery stenosis (PS) 19. Ventricular septal defect (VSD). Other Specify.....		

		11. Double outlet right ventricle (DORV)		
	CHD Lesion group	1. Lesion group 1 2. Lesion group 2 3. Lesion group 3 4. Lesion group 4 5. Lesion group 5 Lesion group 6		
	Severity Type	1. Critical 2. Non		
	Type of intervention	1. Medical 2. Surgical 3. Catheterization		
	Preoperative condition	1. Poor Pre-op(Requiring resuscitation, Acidosis) Good preoperative		
Section 3	**Other Related Characteristics**			
301	Time of Diagnosis	1. Prenatal 2. Postnatal	3. Unspecified	If 3 skip to 304
302	If prenatal	1. At first trimester 2. At second trimester	3. At third trimester	Skip to 304
303	If postnatal	1. Within 24 hour 2. Within the First week of life	3. Within the First month 4. After the first month....specify in month.....	
304	Clinical finding at presentation (presenting symptom)	1. Dyspnea 2. Cyanosis 3. Coughing 4. Murmur 5. Pallor	6. Heart failure 7. Other specify 8. All exist 9. Unknown	
305	Method of diagnosis	1. Prenatal U/S 2. Echocardiography	3. Pulse Oximeter 4. Unknown	
306	Genetic predisposition /Family Hx of CHD	1. Yes 2. No		If no, skip to 310
307	If Yes, is who?	1. Maternal CHD 2. Paternal CHD	3. Sibling with CHD	
308	Maternal Substance use	1. Yes 2. No		If No, skip to 312
309	History of Maternal Viral	1. Yes		If No, skip

	Infection	2. No		to 314
310	If Yes, type	1. Rubella 2. Syphilis	3. Toxoplasmosis 4. Others (specify)	
Section 4	**Outcome variables**			
501	Survival status	1. Death 2. Survived	3. Censored	If 2 & 3, skip to 508
502	If Death, Date of death	Write DD/MM/YYYY format		
503	If Censored, how?	1. Loss to follow 2. Transferred to other place/Institution		
504	Date of Censoring	DD/MM/YYYY		
505	Condition at discharge	1. Improved 2. Deteriorate 3. Unknown		
506	Date of discharge	DD/MM/YYYY		