MISSED OPPORTUNITIES FOR CARDIAC EVALUATION IN TERM NEWBORNS WITH HYPOXEMIA AT KNH-NBU: A CROSS-SECTIONAL STUDY

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DECLARATION

I declare that this thesis is my original work and has not been presented for the award of a degree in any other university.

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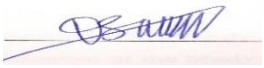
Signature:  **Date:** _June 29th 2023

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ABBREVIATIONS

CCHD: Cyanotic Congenital Heart Disease

CHDs: Congenital Heart Diseases

CI: Confidence Interval

CIN: Clinical Information Network

ECG: Electrocardiogram

ECHO: Echocardiogram

ERC: Ethics Research Council

IMCI: Integrated Management of Childhood Illness

KMTC: Kenya Medical Training College

KNH: Kenyatta National Hospital

LV: Left Ventricular

MO: Missed Opportunity

MR: Mitral regurgitation

NBU: Newborn Unit

PA: Pulmonary atresia

PO: Pulse Oximetry

PPHN: Persistent pulmonary hypertension of the new-born

UK: United Kingdom

UoN: University of Nairobi

WHO: World Health Organisation

OPERATIONAL DEFINITION OF TERMS

Missed opportunities: Situation where eligible children (those with pulse oximetry saturation less than 95%) were in a place with the ability to and should have had further cardiac evaluation but did not get evaluated. (18).

Short term clinical outcomes: Measurable changes in health, function or quality of life that result from the care given before discharge or death. e.g. Alive/dead, referred out, length of hospital stay at discharge.

Term new-born: equal or above 37 weeks of gestation.

Cardiac Abnormalities: structural or functional abnormalities of the heart as documented by the Paediatric cardiologist.

Cardiac Evaluation: Any of the cardiac evaluation with confirmed Echocardiogram; Chest X Ray, Echocardiogram and electrocardiography as reported by paediatric cardiologists.

Hypothermia: Axillary temperature below 36.5°C (97.7°F) as defined by WHO

Positive Screen: A pulse oximetry of less than 90 or pulse oximetry reading of less than 95 for the first reading, second and third one hour a part, preductal post ductal difference of more than 3% (16).

Incomplete data: Records missing one or more of the following. (Age, gender, single pulse oximeter reading, Birth Weight, condition at discharge; alive or dead)

ABSTRACT

Study Background: There are many children with congenital cardiac abnormalities who are either diagnosed late or miss an opportunity to be diagnosed and present their cases when they are too advanced for intervention. Many of these children present to practitioners yet they are not evaluated for congenital heart diseases and this constitutes missed opportunities for cardiac evaluation.

Objectives: To determine the proportion of term newborns with hypoxemia at 24 to 48 hours of life who missed further cardiac evaluation within the time of hospital stay.

Methodology: A retrospective cross-sectional study was carried out on records of term neonates with low pulse oximetry saturation of <95% at 24hours to 48hours of life and up to the date of discharge at the newborn unit, Kenyatta National Hospital- Kenya.

Data Analysis: The data was analysed using R software Version 4.1.2. Descriptive analysis was done on subjects' demographic data and missed opportunities. Factors associated with missed cardiac evaluation were analysed using odds ratios and a p value of <0.05 was considered significant. The proportion of missed opportunities for cardiac evaluation in term new-borns with hypoxemia was calculated where a 95% cut-off was used as per the Kenyan guidelines (16).

Results: A total of 736 term infants were assessed from the CIN database. Out of which206 infants were enrolled in the study. Based on the definition of missed cardiac evaluation, 89.3% (95% CI =84.8 – 92.7) subjects had missed opportunities for cardiac evaluation. Among neonates with missed opportunities (MO) for cardiac evaluation, 67.9% were male and 32.1% were female ($X^2 = 2.07$, $p = .1498$). The mean duration of hospital stay in days was 8.9 days (SD 15.2) for those who had echocardiogram done (22), TOF with PA was the only cyanotic cardiac lesion identified.

Conclusion: The study found 89% proportion of Missed opportunity for cardiac evaluation among term neonates with hypoxemia. There was disproportionately low representation of congenital cardiac abnormalities which are associated with high morbidity and mortality in neonatal period. TOF with PA was the only cyanotic cardiac lesion identified.

CHAPTER ONE

INTRODUCTION

1.1 Background of the Study

Neonatal assessment within 24 to 48 hours of birth is very crucial in identifying any red flags that may warrant further evaluation (1). Missed opportunities for further cardiac evaluation can result in morbidity and delays in diagnosis. Further, cardiac disorders associated with hypoxemia may be overlooked and as a result, the necessary interventions the infant requires may be missed or postponed and this can be fatal to the infant (1, 28). Well neonates with hypoxemia do not present with clinical signs, however, sick neonates with hypoxemia normally present with fast breathing, respiratory distress and cyanosis in severe forms of hypoxemia. Infants with cyanotic cardiac lesions present with respiratory distress from severe forms of hypoxemia and it is worth noting that a typical infant with CCHD has persistent hypoxemia despite supplemental oxygen (24).

For prompt diagnosis, the Kenyan guidelines (16) recommends that a level 6 facility should have a management level of care that consists of human resources who include a paediatric cardiologist, specialised nurses and diagnostic equipment that include; Echocardiogram machines. The guideline further recommends that infants should be screened using the pulse oximetry protocol (neonates with a pulse oximeter reading of less than 95%) and evaluated for critical cardiac lesions to prevent late diagnosis. Missed opportunities that characterise children who should have had further cardiac evaluation but did not get the evaluation with Pulse oximetry saturation of less than 95% creates significant incidences of readmission, organ damage and even death across the globe This gap may even be higher in countries like Kenya with limited resources. Nonetheless, there is limited data in Kenya on missed opportunities in the timely cardiac evaluation of term newborns with hypoxemia. Thus, the current study is useful in filling a significant gap in paediatrics.

New-born clinical examination and antenatal newborn screening are already accepted medical methods to help detect and timely evaluate cardiac defects. Nevertheless, studies have estimated significantly low detection rates with these methods(2). Certainly, hypoxemia detection utilising visual assessment of the colour of the newborn has considerable impediments and cardiac murmurs do not at all times present in cardiac malformation cases

(2). More studies show that 40% of newborns with missed diagnoses go into cardiogenic shock and 5% of newborns get diagnosed during autopsy (3-6).

Consequently, studies have observed that augmenting the clinical examination and antenatal newborn screening with routine pulse oximetry (PO) significantly improves early detection and timely diagnosis of cardiac malformations prior to severe cardiovascular collapse and contribute to positive neurological and cardiopulmonary outcomes in newborns (10, 11). Studies from Europe and the USA almost by consensus appear to promote the use of PO as a tool to detect cardiac malformations, especially in well newborns presenting with hypoxemia(12).

However, Kenyan guideline (2018) does not specify whether the screening is on well or sick neonates. The guidelines only recommend that all infants should be subjected to a simple screening by use of pulse ox after 24hrs. Any neonates with saturation <95% (13-15) and a preductal-post ductal difference of more than 3% should have further cardiac evaluation. (16).

Further, Mathur and Kurien (32) have examined PO Screening to detect Cyanotic congenital defects in sick newborns and considered abnormal PO results if <90% were noted. However, not many studies done in Kenya have looked at sick newborns where missed opportunities appear to be high and hence the need for the present study.

Anecdotal reports point to many children with low saturations not getting a further cardiac evaluation. This presents missed opportunities for cardiac evaluation in newborns who present a few hours to days after birth with hypoxemia which may result from Cyanotic congenital heart defects

Therefore, this current study seeks to fill a significant gap especially because there is a paucity of investigations on missed opportunities for cardiac evaluation in term newborns with hypoxemia within the African and especially the Kenyan context.

1.2 Statement of the Problem

Hypoxemia is a common feature in newborns representing a frequent indication for further cardiac evaluation. (4). The Kenyan guidelines state that all children with pulse oximetry reading of <95% should have cardiac evaluation. Other studies suggest that sick neonates with pulse oximetry <90% should have further cardiac evaluation. Anecdotal reports show that a number of newborns with a saturation of less than 95% miss to get a further cardiac evaluation.

This represents a missed opportunity to evaluate children for cardiac diseases that may present with cyanosis in the neonatal period such as Cyanotic heart diseases.

For prompt diagnosis, the Kenyan guidelines recommends that a level 5 and 6 facility should have a management level of care that consists of human resources who include a paediatric cardiologist, specialised nurses, cardiothoracic surgeon and a cardiac anaesthetist, diagnostic equipment that include; high specification echo cardiogram machine. The guideline further recommends that infants should be screened using the pulse oximetry protocol for Critical cardiac lesions to prevent late diagnosis.

However, missed opportunities for cardiac evaluation (children who should have had further cardiac evaluation but did not get the evaluation with Pulse oximetry saturation less than 95%) may be at risk of readmission, organ damage and even death. The missed opportunities for cardiac evaluation may be higher in countries like Kenya with limited diagnostic and human resources. Nonetheless, there is limited data in Kenya on missed opportunities in the timely cardiac evaluation of term newborns with hypoxemia. Thus, the current study is useful in filling a significant gap in paediatrics.

Findings from reviewed empirical literature help to underscore the magnitude of missed diagnoses of cardiac malfunctions among newborns and mostly screening capabilities of PO (14,16). However, these studies do not identify and analyse cardiac abnormalities in term neonates with hypoxemia at 24-48 hours who should get a cardiac evaluation as will be the case in the current study.

1.3 Scope of the Study

The study focussed on missed opportunities for cardiac evaluation in term newborns with hypoxemia in Kenya. The study considered term new-borns with hypoxemia <95% admitted to the newborn unit, Kenyatta National Hospital and will be a retrospective cross-sectional study that will cover a 2-year duration. Records of term neonates with hypoxemia admitted to the newborn unit at Kenyatta National Hospital from 1st January 2020 to 31st December 2021 constituted the study source.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This section reviews both the conceptual and empirical review of studies that touch on missed opportunities in cardiac evaluation in newborns with hypoxemia. We searched in PubMed and Cochrane library for literature on pulse oximetry and cardiac evaluation or cyanotic heart disease. The keywords used in the literature search included: oximetry, saturation, concentration, hypoxemia, echocardiography, chest x-ray, electrocardiogram, newborn, neonate, infant, term, missed opportunities, cardiac evaluation, cyanotic congenital heart disease, cardiac abnormalities, and heart dysfunction. Specifically, it considers the conceptual description of missed opportunities in newborn evaluation, hypoxemia in newborns, and cardiac evaluation in newborns. It then offers an empirical review of studies done, the methods used and some of the notable research gaps. It also presents the justification of the study, the significance of the study, both research questions and objectives and a summary of research gaps.

2.2 Conceptual and Empirical Literature Review

2.2.1 Missed opportunities in newborn evaluation.

Missed opportunities in healthcare have been defined as the lack of further care after a risk has been established in a patient by a health practitioner(17). Singh et al.(18) define missed opportunities as instances where *post-hoc* evaluation and consequent judgment show that alternative medical actions and decisions could have contributed to timely and effective diagnosis. For instance, a lack of evaluation of a child with suspected congenital cardiac malformations characterises a missed opportunity to effectively deal with cardiac challenges in a timely manner. The present study deals with missed opportunities in cardiac evaluation among new-borns with hypoxemia. Consequently, operationally, the present study defines missed opportunity as children (with Pulse oximetry saturation less than 95%) who should have had further cardiac evaluation but did not get the evaluation

Studies have been done to examine missed opportunities in the evaluation of newborns within the healthcare system. Pattinson (19) examined missed opportunities and avoidable factors in perinatal deaths among newborns in South Africa. The prospective cohort study used Perinatal

Problem Identification Programme (PPIP) to examine 232,718 live births over two years. The study found that missed opportunities that led to perinatal deaths in children were missed evaluation related at 36.7% and 28.7% at the urban and rural hospitals respectively. Further deaths as a result of newborn asphyxia were noted to be preventable at 63.2% if there were no missed opportunities to evaluate the newborns early. The study concluded that the keenness of health practitioners towards remediable health problems often missed made possible by further evaluation reduces perinatal deaths (19). This study is useful in examining missed opportunities in perinatal deaths but does not consider an investigation of missed opportunities in cardiac evaluation in term newborns within the Kenyan context.

Ng and Hokanson(20) sought to establish the cases of missed opportunities in diagnosing congenital heart disease among neonates that lead to readmission and deaths within the first two weeks following a live birth. The study used a prospective cohort study design to examine neonates who had been discharged without any cardiac issues within the period of 2002 and 2006; 340 203 babies were examined. Adverse events were associated with congenital heart disease in the event the diagnosis was cyanotic heart defects or left-sided obstructive lesion. The study found that congenital heart disease among the neonates led to 14 deaths out of the 340 203 babies examined (1: 24 684) two weeks following discharge. The study noted that from the deaths, hypoplastic left heart syndrome and coarctation of the aorta were the most prevalent diagnoses. Therefore, readmission and fatalities among neonates in Wisconsin just after two weeks following discharge occurred at a ratio of 1: 24 684 as a result of missed opportunities for further evaluation.

A similar study to that by Ng and Hokanson was done by Chang et al.(21)to examine missed opportunities of CCHD among 898 infants using a cohort study. The study noted that 50% of infants with missed diagnoses of CCHD eventually died at home within an average of 13.4 days after birth. Hypoplastic left heart syndrome and coarctation of the aorta were the most prevalent diagnoses. The study noted that in the California area, there were 20 cases of late diagnosis and 10 incidences of missed diagnosis each year. The study concluded that 30 infants in California died of CCHD after two weeks following discharge every year due to missed diagnosis and recommended the need for cardiac evaluation as an early intervention.

Further studies like those done by Eckersley et al.(7) have noted that newborns who should have undergone evaluation but did not with Pulse oximetry saturation of less than 95% and thus presented missed opportunities constituted 20% and 51% for critical and non-critical

cardiac malformation cases in New Zealand. Marek et al. (4, 8) in a study in Norway noted missed opportunities in 24% and 56% of critical and non-critical cardiac malformation cases. Bartos et al.(9)on their part noted 59% of missed opportunities among newborns with cardiac malformations in Turkey. All these studies show that there are missed opportunities in cardiac evaluation in newborns with hypoxemia but no study has been done yet within the Kenyan context.

It should be noted that these studies do not engage in examining missed opportunities in cardiac evaluation but missed diagnosis of congenital heart disease. Consequently, this study fills a significant research gap.

2.2.2Hypoxemia in New-borns

Hypoxemia in newborns is abnormally low oxygen levels in arterial blood presenting when the oxygen saturation levels are <95% when measured by a pulse ox and always a concern in a term neonate of above 37 weeks gestation (21,22). Hypoxemia is a circulation or breathing problem occurring at intracardiac, extracardiac and intrapulmonary levels(21). It indicates the presence of severe illnesses that include sepsis, pneumonia and cardiac abnormalities in Children (22,23). To that extent, Hypoxemia is a significant predictor of morbidity and mortality among newborns presenting with a variety of pathologies. According to Morgan et al., (36), hypoxaemia represents 17% to 43% of sick neonates admitted to Paediatric wards in Low and Middle-Income countries.

Studies have noted that Hypoxemia is difficult to detect based on clinical findings only (22). Further, the incapacity of health practitioners to timely detect Hypoxemia in newborns with critical cardiac lesions may significantly lead to fatalities (15). Pulse Oximetry (PO) is now considered a non-invasive, painless and reliable tool and plays an important role in screening for congenital heart malformations and is recommended to be used on all neonates before discharge

2.2.3 Cardiac Abnormalities in Hypoxemic New-borns

Moderate to severe cardiac defects occur in about 1% of all newborns (24, 25) and they are the second leading cause of death among infants in the first year of life, yet, prenatal screening and clinical examination pick only 50% of the affected neonates (1).

In most of these cases, the basic mechanism for hypoxemia involves largely right to left heart shunting of desaturated venous blood into the systemic arterial circulation. Cardiac

abnormalities presenting with hypoxemia in the early neonatal period are potentially life-threatening cyanotic cardiac lesions in which cardiovascular collapse is likely and compromised if not picked within 2 weeks (1). These are: Transposition of the great arteries (TGA), critical Coarctation of the aorta or Interruption of the aorta (COA/IAA), Hypoplastic left heart syndrome (HLHS), obstructed total anomalous pulmonary venous return (TAPVR), Tetralogy of Fallot with pulmonary atresia (TOF with PA), (1, 24, 26).

2.2.4 Cardiac Evaluation in Newborns

Evaluation is done based on the clinical judgement based on the assessment of oxygen saturation in the blood. Most newborns with cardiac defects do not present with a murmur but may be in a significant distress if there is pulmonary circulatory overload. It is also important to note that a typical newborn with a cyanotic heart defect has persistent hypoxemia despite supplemental oxygen (1, 24,27, 28). An initial evaluation would involve the use of Pulse Oximetry which has the potential to detect hypoxemia in newborns. The World Health Organization (WHO) Integrated Management of Childhood Illness (IMCI) guideline of 2014 apart from indicating that PO use is optional rather than mandatory, sets a threshold of <90% that shows Hypoxemia and thus requires timely hospital referral (28).

However, in Kenya, the Ministry of Health Guideline on Cardiovascular Disease Management (16) sets a threshold of <95% that shows Hypoxemia and thus requiring of immediate referral to a paediatric cardiologist. The <95% threshold is also supported by other medical scholars (13,16,30) including the AAP algorithm on oxygen saturation in either the right arm or one foot and this is the threshold that is adopted in the present study. PO should be done within 24-48 hours of life as a later screen can miss the opportunity for cardiac evaluation for severe forms of cyanotic heart lesions that are duct dependent. This cut-off is in keeping with some studies which estimated the median ductal closure to be 27 hours for boys and to be 45hours for girls (21). It is worth noting the significance of performance sites to prevent over-diagnosing hypoxemia as some studies have shown consistently lower readings when fingertip devices are used(22). Yet, some studies showed no significant effect on pulse oximeter sensitivity and specificity regarding the testing site (13, 17).

2.2.5 Pulse oximetry performance in screening of cyanotic congenital heart diseases

Some Studies like that of Mathur and (32) when examining PO in detecting Cyanotic congenital heart disease in sick newborns observed sensitivity, positive predictive value,

specificity, odds ratio (95% CI) and negative predictive value of pulse oximetry at 95.2%, 9.5, 52.4%, 22 (5.3, 91.4), and 99.5 respectively. The study thus concluded that PO is a useful tool to help detect cyanotic heart diseases in sick newborns.

Any positive screen is considered a sign of possible cardiac abnormalities (10) requiring immediate diagnostic evaluation by; Paediatric cardiology consultation, electrocardiogram (ECG), Chest-X-ray, or echocardiogram to determine the heart anatomy and function (10).

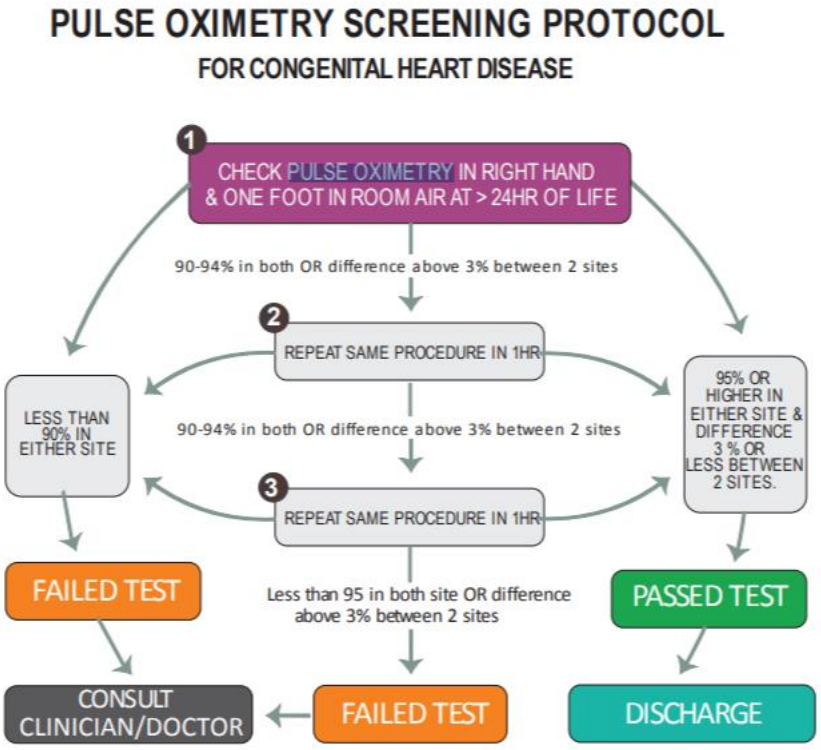


Figure 1:PO Screening Protocol by the Ministry of Health (2018). (16)

Therefore, all neonates with a pulse oximeter reading of less than 95% should have a further cardiac evaluation as per Kenyan guidelines.

2.4 Justification of the Study

A proportion of neonates with hypoxemia miss getting a further evaluation for cardiac disorders within 24 to 48 hrs. Timely recognition and evaluation reduce morbidity and mortality among neonates with hypoxemia resulting from cyanotic heart defects presenting a few hours to days after birth. The detection that can be accessed using PO has not yet been investigated in the Kenyan setup and this study thus fills a significant research gap.

The Kenyan guideline (2018) does not specify whether the screening should be done on well or sick neonates. The guideline recommends that all infants with pulse oximetry reading of <95% should have cardiac evaluation. Other studies suggest that sick neonates with pulse oximetry <90% should have further cardiac evaluation. Anecdotal reports show that, a number of new-borns with a saturation of less than 95% miss to get a further cardiac evaluation. This represents a missed opportunity to evaluate children for cardiac diseases that are associated with high morbidity and mortality during the neonatal period. This may present with cyanosis in the neonatal period such as in Cyanotic heart diseases. However, missed opportunities for cardiac evaluation (children with Pulse oximetry saturation of less than 95% who should have had further cardiac evaluation but did not get the evaluation) may be at risk of readmission, organ damage and even death. The missed opportunities for cardiac evaluation may be higher in countries like Kenya with limited diagnostic and human resources. Nonetheless, there is limited data in Kenya on missed opportunities in the timely cardiac evaluation of term newborns with hypoxemia. Thus, the current study is useful in filling a significant gap in paediatrics.

Timely evaluation of neonates with low pulse oximeter readings is recommended to rule out cardiac disorders. This may lead to early diagnosis and intervention which may in turn, lead to better outcomes. However, it is not clear how many of such children get the required cardiac evaluation after being found to have low oxygen saturation and thus missed opportunity for further cardiac evaluation. This study will identify missed opportunities for further cardiac evaluation for cardiac assessment as per the Kenya guidelines. Identifying the gaps in practice may lead to the development of interventions to improve the care provided at Kenyatta National Hospital. This study will determine the missed opportunities for cardiac evaluation in children who had documented pulse oximetry values of less than 95% and who should have had the cardiac evaluation as per the Kenyan guidelines.

2.5 Significance of the Study

This study will better awareness of the problem of both the system and paediatric practitioners and thereby provide room for health care improvement. Secondly, By assessing the proportion of Missed opportunities for cardiac evaluation, this finding will enable health care providers to deliver timely diagnosis and reduce early infancy mortality as recommended by Kenyan guidelines.

2.6 Research Question

i. What is the proportion of term newborns with hypoxaemia admitted in the newborn unit at Kenyatta National Hospital from 1st January 2020 to 31st December 2021 who missed cardiac evaluation?

ii. What are the cardiac abnormalities in term neonates admitted to the NBU with hypoxemia at 24-48 hours who get a cardiac evaluation?

2.7 Research Objectives

2.7.1 Primary objective

To determine the proportion of term newborns admitted to the New-born unit at Kenyatta National Hospital with hypoxemia at 24 to 48 hours of life who missed further cardiac evaluation before discharge/death recorded from 1st January 2020 to 31st December 2021.

2.7.2 Secondary Objective

i. To describe the sociodemographic and clinical characteristics of term newborns with hypoxemia at 24 to 48 hours of life at the time of screening in the Newborn unit at Kenyatta National Hospital recorded from 1st January 2020 to 31st December 2021.

ii. To describe the spectrum of cardiac abnormalities among of term newborns with hypoxemia at 24 to 48 hours of life admitted to the Newborn unit at Kenyatta National Hospital recorded from 1st January 2020 to 31st December 2021 and had echocardiograms done.

iii. To establish factors associated with missed opportunities for cardiac evaluation of term newborns with hypoxemia at 24 to 48 hours of life admitted to the Newborn unit at Kenyatta National Hospital recorded from 1st January 2020 to 31st December 2021.

CHAPTER THREE

METHODOLOGY

3.1 Study Design

This was a retrospective cross-sectional study carried out on records of term neonates with low pulse oximetry saturation of <95% at 24hrs to 48 hours of life and up to date of discharge.

3.2 Study Setting

The study was done at the newborn unit, Kenyatta National Hospital, Kenya. The hospital offers specialised care which is accessed from the intensive care units, renal units, cardiology units, accident and emergency, obstetric units, renal units and newborn units with a staff capacity and bed capacity that exceeds 6000 and 2000 respectively.

The newborn Unit (NBU) at KNH receives babies who are sick. Majority of neonates get admission on day one of life. Healthy newborns who need observation and abandoned babies are part of the newborn admitted. In the NBU unlike postnatal Wards with low-risk infants, infants undergo pulse oximetry measurement at admission and for days to weeks until discharge. There is also improved recording and documentation of data in the CIN (33). Basic check-ups are done by the health practitioners including doctors, nurses and nutritionists to check the health progress of the child and the mother. With the aforementioned, the study examined many of the cases that needed further evaluation occurring in NBU. They were identified by the health care workers in the unit and then further cardiac evaluation was requested for in this set-up.

The Clinical Information Network (CIN) is a clinical database established in 2013. It is a partnership between Wellcome Trust, Kenya Medical Research Institute and the University of Nairobi. CIN data collection activities obtained approval for its activities. It uses standardised paediatric admission forms which continuously captures routine patient data for all patients' admissions to NBU-KNH. KNH is one of hospitals participating in CIN database activities among other hospitals. Data was then entered by a data clerk into the REDcap Software after which the data was verified for quality and eventually exported to the database (33).

3.3 Study population

Records of term neonates with hypoxaemia admitted at KNH-NBU from 1st January 2020 to 31st December 2021 were studied.

The estimated number of all neonates in the CIN database over a 2-year period were 4000 while those with hypoxemia were 1080.

3.3.1 Sample size

According to the statistics from Clinical Information Network, there were initially 736 patients with low oxygen saturation (below 95) at less than 24 hours. However, it was expected that this number would decrease at 24 hours to 48 hours. The decrease was based on excluding patients whose oxygen saturation improved, those who experienced hypothermia, those with missing files and those who passed away before screening. A review of the 736 files was made and all eligible patients were enrolled into this study.

Assuming a population of 736 patients at 48 hours, the minimum sample size using Mugenda's (Mugenda & Mugenda, 2003) formula for single proportion would be:

$$n = \frac{Z\alpha^2 pq}{L^2}$$

Where:

n = is the minimum sample size for a statistically significant study

$Z\alpha$ = is the value for a two-sided confidence interval (1-α), $\frac{Z\alpha}{2}$=1.96

p= is the proportion of the population estimated to be at risk set at 0.5. A proportion of 0.5 will be used to generate study sample size since there is no existing literature of similar studies to approximate p.

q = is the proportion of the population not at risk (q = 1 – p)

L = is the precision of the estimate set at 0.05

Hence,

$$n = \frac{1.96^2 * 0.5 * 0.5}{0.05^2}$$

=384

Since the population was finite (N<10,000), the obtained sample size was adjusted using a Finite Population Correction factor (FPC):

$$n' = \frac{1}{\frac{1}{n}+\frac{1}{N}} = \frac{1}{\frac{1}{384}+\frac{1}{736}} = 252$$

If the study was to take a sample from the patients with hypoxemia, a sample size of 252 would be required to get the proportion.

However, in this study the whole population of neonates will be studied.

3.3.2 Inclusion criteria

Term neonates with low pulse oximetry saturation of <95% at 24hrs to 48hours of life and up to date of discharge were included.

3.3.3 Exclusion criteria

1. Neonates who were prenatally diagnosed and confirmed with CHD at birth.
2. Referrals with already established diagnoses of cardiac abnormalities
3. All preterm infants
4. Patients' files with incomplete data
5. New-borns with hypothermia

3.4 Data Collection Procedure and Strategy

The data collection tool was validated prior to data collection. This was done by assessing its reliability in collecting the prescribed data. In addition, training of the data collectors was done to ensure standardization.

Secondary data was obtained from clinical information network-(CIN) data and patients' files. The data collection process begun after approval from UoN/KNH-ERC. CIN data was purely secondary in nature and CIN data collection had already obtained Ethical approval for its activities hence no further consent was required from the clients. Data was abstracted from an existing electronic database (CIN) as per inclusion criteria using a standardised file abstraction form.

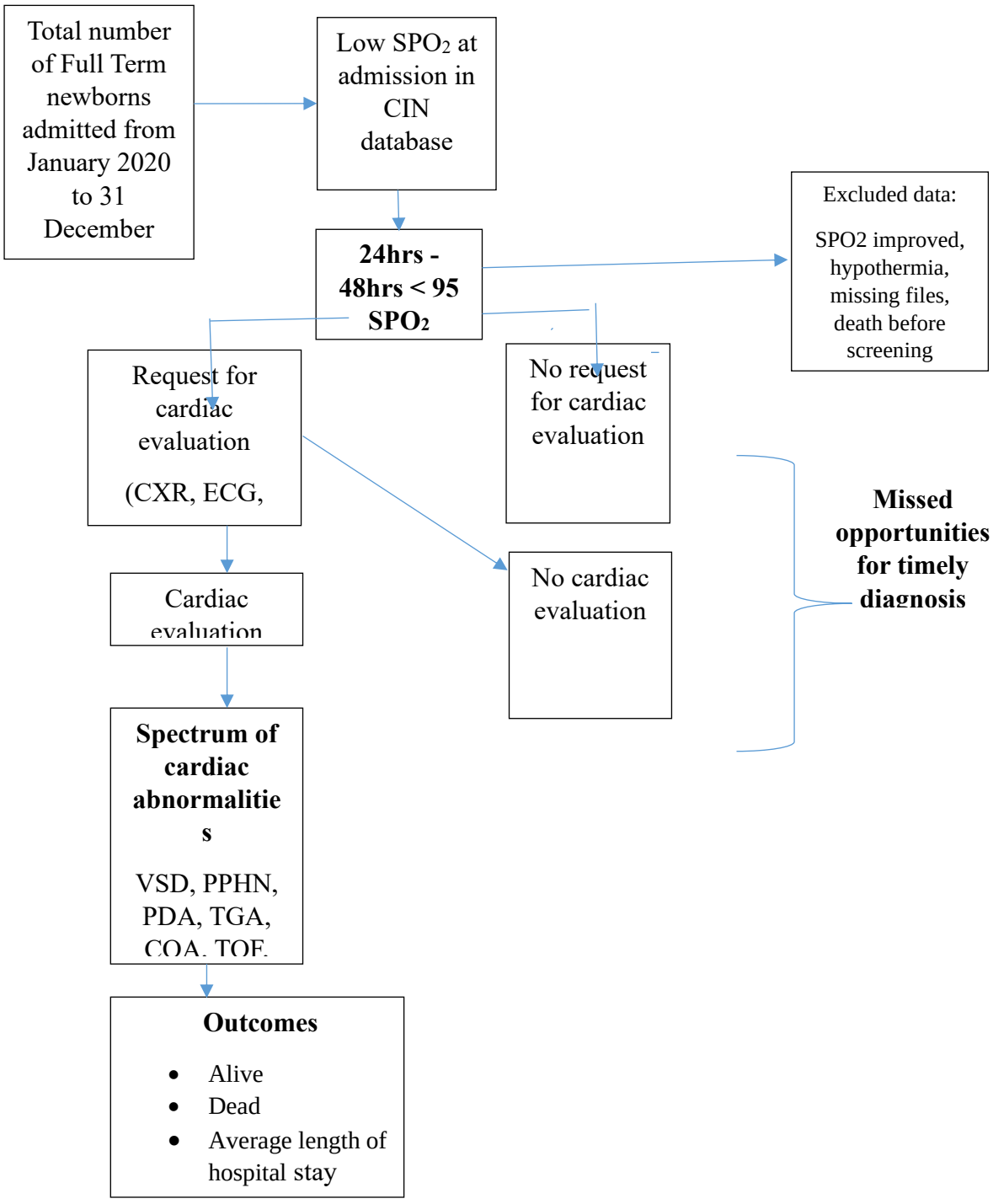
The data collection procedure was done by the principal investigator assisted by 2 trained research assistants with a bachelor's in Medicine, Nursing and Clinical Medicine qualification. The data collection began with the login into the CIN database whose credentials were provided by a data clerk. A prewritten search procedure of the CIN database was done for the term new-borns who were 37weeks gestation and above with hypoxemia recorded by a pulse oximeter,

admitted in the newborn unit from 1st January 2020 to 31st December 2021. The exclusion criteria was applied in the search to remove preterm, those with hypothermia and those with pre-existing cardiac diseases.

The file abstraction tool was filled for each record. Records with missing data were noted down after which physical tracking of the files from the Kenyatta National Hospital Records department was done. The missing data was completed from the physical file. Records were considered incomplete if more than 50% of the variables were missing i.e Missing dates, gender, only one reading of SPO2 recorded. The variables abstracted included neonatal biodata, maternal biodata, the presence or absence of cardiac evaluation and outcome. Missed cardiac evaluation opportunities were evaluated by checking the presence of written requests for intervention and the performance of the intervention itself. These included Pulse oximetry readings at 24, 48, 72 and 96 hours, echocardiography, chest x-ray and cardiology team review.

Outcome variables included proportion of neonates who missed an opportunity to get a cardiac evaluation, length of hospital stay and condition at discharge i.e alive or dead.

3.4.1 Study Flow Diagram



3.4.2 Sources of Bias with a retrospective cross-sectional study

Chronological bias was expected since the retrospective study period was 2 years. This bias was dealt with by choosing a time period with homogenous intervention. During this time, the standard of care of having all neonates on pulse oximetry was constant. Survival bias was present since some neonates may have died before cardiac evaluation done. Informed presence bias was also expected. Its mitigation measure was the fact that CIN data was collected for all neonates and not just the very sick subgroup.

3.5 Data Analysis

Data was entered into a secure spreadsheet software where Data cleaning was done. The data was then uploaded to R software Version 4.1.2. Descriptive analysis was done on subjects' demographic data and missed opportunities. Categorical data was analysed using frequencies and percentages while continuous data was analysed using appropriate measures of centrality (mean/median) and spread (SD/IQR) and tested for normality using the Shapiro-Wilk test.

The proportion of missed opportunities in cardiac evaluation in terms of new-borns with hypoxemia was calculated thus:

$$\% \text{ proportion} = \frac{\text{Number of term newborns with hypoxemia who did not get cardiac evaluation}}{\text{Total number of term newborns who had hypoxemia (sats<95\%)}} * 100$$

The proportion was calculated with a 95% cut off as per the Kenyan guidelines (16)

The inferential analysis was done to see if there is a statistically significant difference between those who missed opportunities for cardiac evaluation and those who did not. This helped determine if there are other patient characteristics that are associated with cardiac evaluation. A Pearson Chi-square test or Fishers exact test was used for categorical variables with the Fishers Exact test being used where cell values were less than 5. The independent samples T-test or Mann Whitney U test was used to test continuous data for parametric and non-parametric data respectively. The values of subsequent pulse oximetry readings were evaluated to see the trend of pulse oximetry from admission to 120 hours.

The various forms of cardiac evaluation were analysed descriptively by using proportion. Any possible delays in undertaking the cardiac evaluation was analysed using the median time from initial low pulse oximetry to the time the evaluation is ordered and done.

To evaluate the third objective addressing the possible associated factors, the odds ratios of the presence or absence of cardiac evaluation was calculated against selected variables. This was done for variables like length of stay and outcome at discharge.

3.5.2 Missing data

Records that were missing over 50% of the variables were considered incomplete records and were omitted from the analysis. The missing data was mainly in the requests for cardiac evaluation and in this study, we assumed that if is not recorded, it is not done.

The missing data was collected and quantified for each entry and variable. Possible relationships between the missing data and observed data was investigated descriptively to classify the type of missing data. Entries with the missing data was grouped and analysed against observed data using the Kruskal Wallis test for continuous data and Chi-Square for categorical data. The results were used to classify the type of missing data.

For non-outcome data that was Missing Completely at Random (MCAR) complete case analysis was done using pairwise deletion. Missing at Random data (MAR) was imputed by using statistical methods such as mean/median, best/worst observation carried forward or maximum likelihood method depending on the type of variable and direction of bias. Missing Not at Random (MNAR) data was handled using sensitivity analysis and consulting the ethics review board to ascertain if the volume was substantial.

No imputation was done for the outcome variables.

3.6 Ethical considerations

Approval to carry out the study was sought from KNH-UoN ERC and the Kenyatta National Hospital administration, CIN to allow access to the patient files. Confidentiality, anonymity, and privacy was fully guaranteed throughout the study. Covid-19 prevention guidelines as per the Ministry of Health were observed to control cross infection among research assistants.

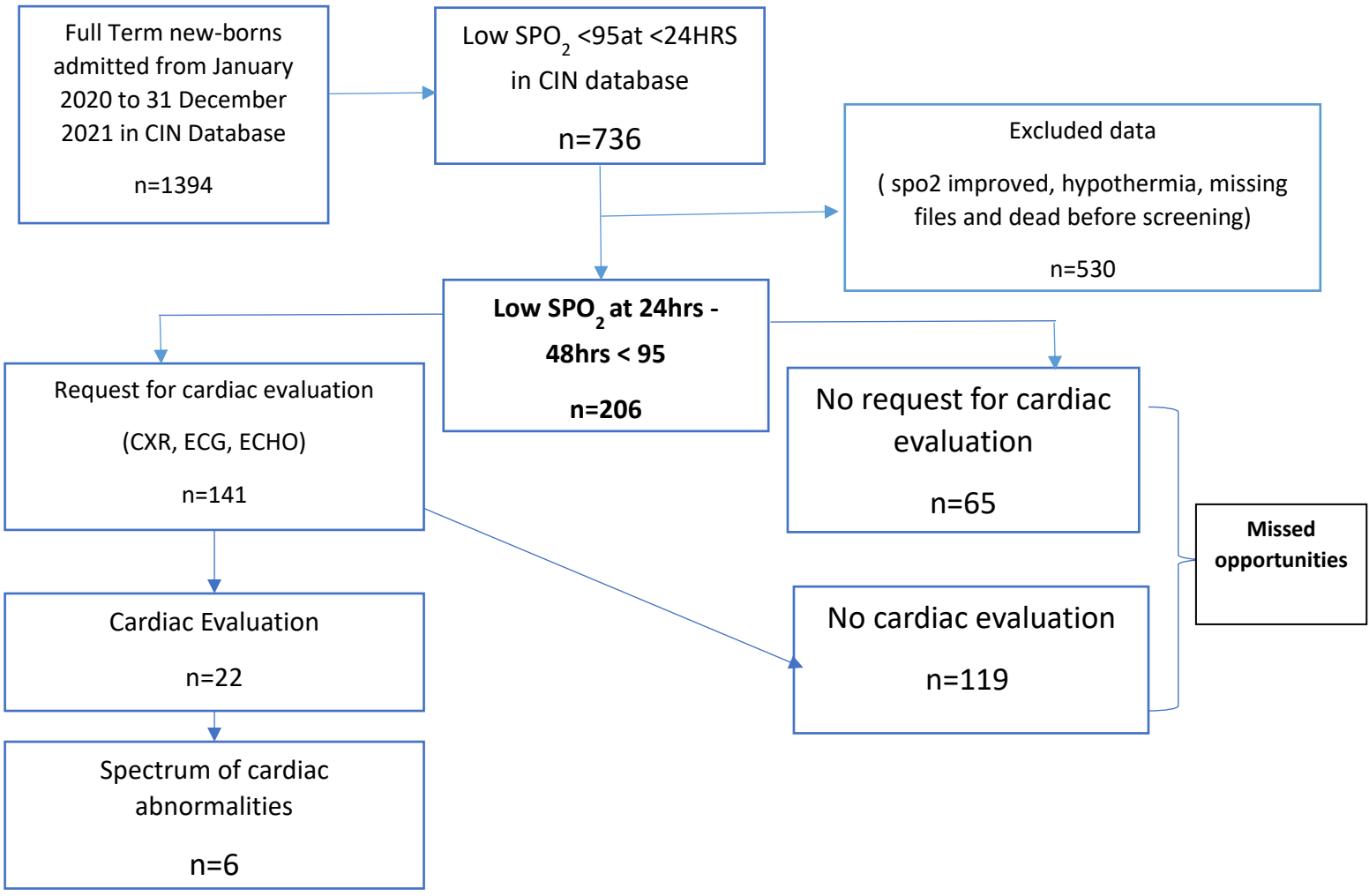
I sought the waiver of individual participant consent from the KNH-UoN ERC as this was a retrospective review of medical records.

4.0 Data Results

4.1.0 Introduction

The study investigated the proportion of missed opportunity for cardiac evaluation among term neonates with hypoxemia who were admitted to newborn unit at KNH from January 2020 to 31 December 2021 in CIN Database. A proportion of term newborns with hypoxemia at 24 to 48 hours of life who missed further cardiac evaluation within the time of hospital stay was studied. A total of 736 term infants with low spo2 in less 24hrs in CIN database were identified. Five hundred and thirty were excluded because they did not meet the study inclusion criteria. while 206 subjects were enrolled in the study as shown in the flow chart below:

4.1.1 Screening and Enrolment Flowchart



4.2 Sociodemographic and clinical characteristics of study participants

A total of 206 individuals were included in this study. The median age at admission was reported with the interquartile range (IQR). Among the participants, 136 (66.01%) were male, while 70 (33.9%) were female. The mode of delivery indicated that 77 (37.38%) cases were delivered through spontaneous vaginal delivery (SVD), whereas 129 (61.16%) cases were delivered via caesarean section (CS). The majority of deliveries took place at Kenyatta National Hospital, accounting for 158 (76.7%) cases, while 48 (23.3%) cases were referrals from other facilities. Regarding the admission unit, 23 (11.2%) cases were admitted to the neonatal intensive care unit (NICU), 78 (37.9%) to the high-dependency unit (HDU), 3 (1.5%) to the isolation ward, and 20 (9.7%) to Ward D. The indication for admission was not indicated in 82 (39.8%) cases.

Table 1:showing demographics characteristics of neonates with hypoxemia at 24-48 hours with/without missed opportunities for cardiac evaluation at KNH newborn unit from Jan2020 to Dec 2021

		Total N=206	**Neonates with no missed opportunities n= 22**	**Neonates with missed opportunities n=184**
Age at admission(median-IQR)			0 hours (24)	0 hours (36)
Sex	Male (%)	136(66.01)	11/50	125(67.9)
	Female (%)	70(33.9)	11/50	59(32.1)
Mode of Delivery	SVD (%)	77(37.38)	6 (27.3)	70(38.3)
	CS (%)	129(61.16)	16 (72.7)	113(61.4)
Place of Delivery	Kenyatta National Hospital (%)	158(76.7)	7(31.8)	151(73.3)
	Referral (%)	48(23.3)	15(68.2)	55(26.7)
Admission Unit	NICU (%)	23(11.2)	12(54.5)	11(7.1)
	HDU (%)	78(37.9)	4(18.2)	74(40.2)
	Isolation ward (%)	3(1.5)	0	3(1.6)

	Ward D (%)	20(9.7)	0	19(10.3)
	Not indicated (%)	82(39.8)	7(31.8)	75(40.8)
Mean duration of admission days			18.4(22.5)	
Mean birthweight in grams (SD)			3305 (675.63)	
Mean maternal age (SD)			29.5 (5.4)	
Number of ANC visits	<4 visits (%)	61(29.6)	4(18.1)	57(31)
	=>4 visits (%)	89(43.2)	11(50)	78(42.4)
Outcome at discharge	Alive (%)	150(72.8)	12(54.6)	138(76.7)
	Dead (%)	56(27.2)	10(45.5)	48(23.3)

4.2.1 sociodemographic characteristics.

Among neonates with missed opportunities (MO) for cardiac evaluation, 67.9% were male and 32.1% were female ($X^2 = 2.07$, $p = .1498$). Sex distribution in those with no missed opportunities (no MO) was split evenly at 50% for males and females. Caesarean section was the predominant mode of delivery at 61.4% and 72.7% for MO and no MO respectively but the chi-square test was not statistically significant ($X^2 = 0.59$, $p = .4391$). Among Neonates in the MO group, 73.3% were born at Kenyatta national hospital while the no MO group had 31.8% which is a statistically significant difference between the two groups. Neonates born at Kenyatta national hospital were 5.8 times more likely to miss cardiac evaluation ($OR = 5.88$, $2.28 - 15.19$ $p = .0003$).

The MO group had a mean birth weight of 3272 grams (SD 603.4) while the no MO group had a mean weight of 3305 grams (SD 675.6) ($T = -0.22$, $p = .8264$).

The mean duration of hospital stay was 8.9 days (SD 15.2) for the MO group and 18.4 days (SD 22.5) for the no MO group. The neonates with a duration admission of less than 7 days were 4.77 times more likely to miss cardiac evaluation ($OR = 4.77$, $1.85 – 12.30$ $p = .0013$).

Admitting Unit

The units where the MO neonates were initially admitted were in High dependent unit (HDU) (40.2%), NICU (7.1%), Isolation unit (1.6%), and Nursery D (10.3%). The units where the no MO neonates were initially admitted were in NICU (54.5%) and HDU (18.2%). The admission unit was not indicated in 40.8% of the MO group and 31.8% in the no MO group ($X^2 = 47.6$, $p = .0001$). 50.5% of the MO subjects were transferred to a second unit within the new born unit while 45.5% of the no MO subjects were internally transferred. The MO group had a further 3.8% admitted in a third unit while the no MO group had 27.3% ($X^2 = 18.3$, $p = .0001$).

The location of the neonate was analysed to see if there was any association with missed cardiac evaluation. Being admitted in the NICU decreased the odds of missing cardiac evaluation by 95% (*OR = 0.05, 0.02 – 0.15, p = .0001*) while being in the HDU increased the odds of missing cardiac evaluation by 203% (*OR = 3.03, 1.00 – 9.30, p = .0502*). Internal transfer to a second unit was statistically insignificant while an internal transfer to a 3rd unit reduced the odds of missing cardiac evaluation by 87% (*OR = 0.13, 0.04 – 0.42, p = .0006*).

4.2.2 Clinical Characteristics at Screening

The clinical characteristic at screening was analysed. In terms of symptoms, 1.1% of the MO subjects had parlour while the no MO had none. Cyanosis was recorded in 8.8% of the MO group and 27.3% in the No MO group which was statistically significant ($X^2 = 7.2$, $p = .0271$). Having cyanosis reduced the odds of missing cardiac evaluation by 73% (*OR 0.27, 95%CI 0.09 – 0.80, 0.183*). Both groups had a similar mean temperature of 36.7 C (*T = 0.32, p = .7538*). The mean heart rate in the MO group was 140 bpm (SD 18) and 146 bpm (SD 38) in the no MO group (*T = -0.69, p = .4939*). The mean respiratory rate in the MO group was 61 bpm (SD 16) while the no MO group was 68 bpm (SD 14) with a statistically significant difference (*T = -2.1, p = .0422*). Neonates with a respiratory rate of more than 60 breaths per minute had a 14% probability of missing cardiac evaluation (*OR = 0.17, 0.06 – 0.49, p = .0009*).

Table 2: showing Clinical characteristics of neonates with hypoxaemia at 24-48 hours with/without missed opportunities for cardiac evaluation at KNH new born unit from Jan 2020 to Dec 2021

	Neonates with missed opportunities	Neonates with no missed opportunities
Pallor count (%)	2(1.1)	0(0)
Cyanosis count (%)	16(8.8)	6(27.3)
Temperature mean (SD)	36.7(0.6)	36.7(0.4)

Heart rate mean (%)	140(18)	146(38)
Respiratory rate (%)	61(16)	68(14)
Mode Silverman score (%)	2(15.8)	5(18.2)

The clinical characteristics of the neonates were analysed for an association with missed cardiac evaluation. Apgar at 10 minutes and bradycardia were statistically insignificant.

Pulse Oximetry Readings

The mean pulse oximetry at 24, 48, 72 and 96 hours had a statistically significant difference between the two groups. The MO group had a higher 24 hour mean pulse oximetry reading of 85% (SD 11.1) while the no MO group having 80% (SD 11.1) (*T = 2.1, p = .0491*). The mean pulse oximetry at 48 hours was 89% (SD 4.9) in the MO group and 86% (SD 8.4) in the no MO group (*T = 2.2, p = .0351*). The MO group had a higher 72-hour mean pulse oximetry reading of 91% (SD 5.8) while the no MO group having 83% (SD 9.8) (*T = 3.4, p = .0017*).

Of all the neonates with initial hypoxemia, 132 had hypoxemia at 72 hours. The missed opportunity for cardiac evaluation beyond 72 hours was 114(86.4%).

Table 3:showing Hypoxemia and missed opportunities for cardiac evaluation beyond 72 hours

Parameters	24-48 hours	72 hours
Hypoxaemia neonates (Count)	206	132
Those with Missed Opportunity for cardiac evaluation (Count)	184	114
Percentage of missed opportunity for cardiac evaluation (%)	89.3%	86.4%

Supplemental Oxygen Usage

The supplemental oxygen usage at 48, 72, 96 and 120 hours had a statistically significant difference between the two groups. The MO group had a lower 24-hour supplemental oxygen usage of 28% while the no MO group had 50% ($X^2 = 4.5, p = .1032$). Oxygen usage at 24 hours decreased the odds of missing cardiac evaluation by 61% (*OR = 0.39, 0.16 – 0.97, p = .0422*).

The supplemental oxygen usage at 48 hours was 39.6% in the MO group and 68.2% in the no MO group ($X^2 = 6.8, p = .0339$). The MO group had a lower 72-hour supplemental oxygen usage of 30.1% while the no MO group having 63.6% ($X^2 = 10.3, p = .0055$). The supplemental

oxygen usage at 96 hours was 19.7% in the MO group and 40.9% in the no MO group ($X^2=6.4$, $p=.0395$). The supplemental oxygen usage at 120 hours was 12% in the MO group and 45.5% in the no MO group ($X^2=16.8$, $p=.0002$).

Table 4:Supplimental oxygen usage of neonates with hypoxemia at 24-48 hours with/without missed opportunities for cardiac evaluation at KNH newborn unit from Jan2020 to Dec 2021

	Neonates with missed opportunities n=184	Neonates with no missed opportunities n=22
Oxygen usage 24 hours (%)	48(28.2)	11(50)
Oxygen usage 48 hours (%)	72(39.6)	15(68.2)
Oxygen usage 72 hours (%)	55(30.1)	14(63.6)
Oxygen usage 96 hours (%)	36(19.7)	9(40.9)
Oxygen usage 120 hours (%)	22(12)	10(45.5)

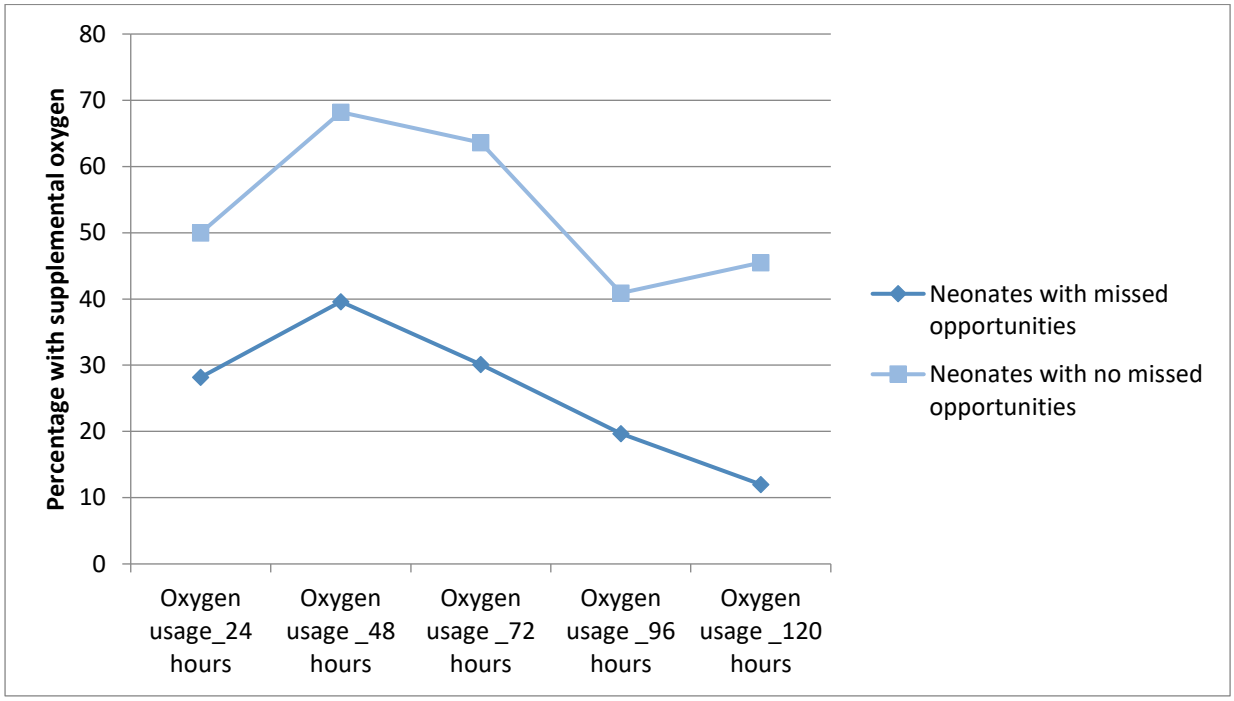


Figure 2: Supplemental oxygen usage of neonates with hypoxaemia at 24-48 hours with/without missed opportunities for cardiac evaluation at KNH new born unit from Jan 2020 to Dec 2021.

4.3 Proportion of term newborns admitted to the New-born unit at Kenyatta National Hospital with hypoxemia at 24 to 48 hours of life who missed further cardiac evaluation before discharge

Based on the definition of missed cardiac evaluation, 89.3% (95%CI=84.4 %to 92.8%) subjects had missed opportunities (MO) for cardiac evaluation while 10.7% (95CI=4.6% to19.2%%) subjects had no missed opportunity (No MO) for cardiac evaluation.

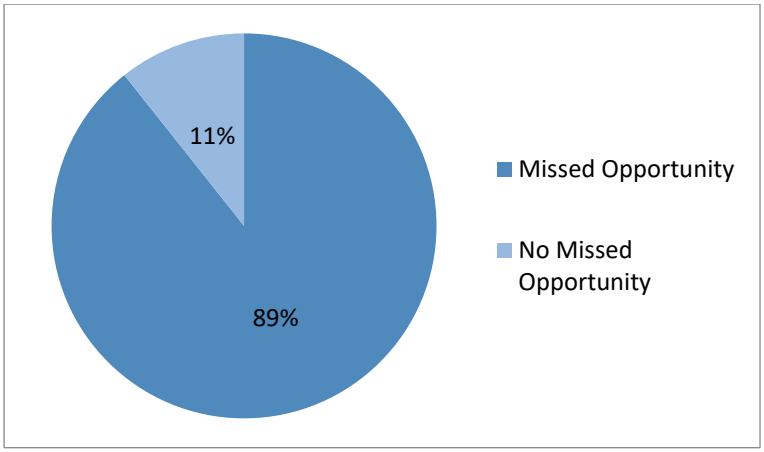


Figure 3: Pie chart of neonates with hypoxaemia at 24-48 hours with missed opportunities for cardiac evaluation at KNH newborn unit from Jan 20220 to Dec 2021.

4.4 Opportunities for Cardiac Evaluation

An analysis of the various cardiac evalaution methods that were requested for and performed was done. The chest xray was requested for 81(39.3%) subjects but it was done in 23(11.1%) of the subjects. Echocardiography was requested in 57(27.7%) of the total subjects but it was done on 23(11.1%) subjects. This was similar to cardiology review. An EKG was requested in 3(1.4%) subjects and performed in 1(0.5%) subject.

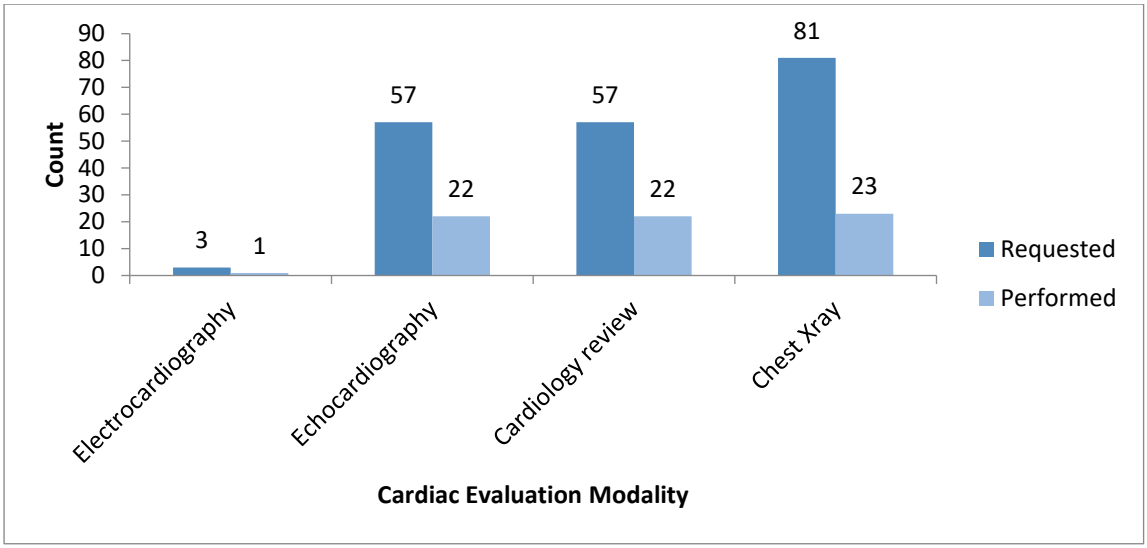


Figure 4: Cardiac evaluation modalities in neonates with hypoxaemia at 24-48 hours at KNH new born unit from Jan 2020 to Dec 2021.

4.5 Spectrum of cardiac abnormalities

The top 5 diagnoses in the MO group were Birth asphyxia (46%), meconium aspiration syndrome (30%), respiratory distress syndrome (28%), neonatal sepsis (18%), and transient tachypnoea of the newborn (13%). There were 11 (6%) subjects with a working diagnosis of congenital cardiac disease who missed cardiac evaluation.

Neonates who received the echocardiogram, 6/22 (27%) had cardiac lesions and 16 (73%) had no cardiac lesions (PPHN at 41%, sepsis at 14% while MAS, Birth Asphyxia and Tracheoesophageal fistula each had 1(4.5%)). Cardiac lesions types were; ASD 2/6 (33.3%), PDA 2/6 (33.3%), Hypertrophic Cardiomyopathy 1/6 (16.65) and TOF with pulmonary atresia. 1/6 (16.65%).

4.6 Factors associated with missed opportunities for cardiac evaluation.

Table 5: showing factors associated with missed opportunities for cardiac evaluation.

Domain		Odds ratio	95% Confidence Interval	P value
Neonatal Demographics	Sex(M)	2.12	0.87 - 5.17	0.0987
	Mode of Delivery (SVD)	1.65	0.62 – 4.42	0.3177

	Place of delivery (KNH)	**5.88**	**2.28 – 15.19**	**0.0003**
	Duration of admission (<7)	4.77	1.85 – 12.3	0.0013
Admission unit	**Straight admissiontoNICU**	**0.05**	**0.02 - 0.15**	**< 0.0001**
	Straight admission toHDU	**3.03**	**1.00 - 9.30**	**0.0502**
	Transfer to 2nd unit	1.02	0.42 – 2.47	0.9616
	Transfer to 3rd unit	**0.13**	**0.04 – 0.42**	**0.0006**
Clinical Characteristics	Apgar at 10(< 5)	0.82	0.17 – 3.89	0.8064
	Supplemental oxygen at 48 hrs.	**0.39**	**0.16 – 0.97**	**0.0422**
	Cardiac disease diagnosis	0.40	0.10-1.57	0.1905
	Tachypnoea Respiratory rate (> 60)	**0.17**	**0.06 – 0.4883**	**0.0009**
	Bradycardia Heart rate <100	0.23	0.02 – 2.65	0.2394
	Cyanosis	**0.27**	**0.09 – 0.80**	**0.0183**

Mortality

The outcome in the MO group was 138(76.7%) being discharged alive and 46(23.3%) being recorded as dead. The outcome in the no MO group was 12 (54.6%) as alive and 10 (45.5%) as dead. Neonates who had a cardiac evaluation were 2.5 times more likely to die compared to those with no cardiac evaluation *(OR 2.5, 95%CI 1.01 – 6.17, p .0467).*

5.0 DISCUSSION

5.1 Primary Outcome

All infants should be screened for critical cardiac lesions according to the 2018 Kenyan Guideline in order to make an early diagnosis of congenital heart diseases.

According to the criteria for missing cardiac evaluation (Eligible children with pulse oximetry saturation less than 95% in a place with the ability to and should have had further cardiac evaluation but did not get evaluated.), 89.3% of the participants had missed opportunities for cardiac evaluation. This was based on information from the CIN database, which held information about newborns admitted to the NICU at KNH. The Kenyan guideline recommendation did not state whether to test healthy or sick newborns. Due to the fact that the CIN database only contained information on neonates admitted to NICUs, our investigation was limited to analysing ill neonates.

5.1.1 Proportion of Missed Opportunity for Cardiac Evaluation

AAP guidelines among other guidelines and NB Marthur et al. recommends use of pulse oximetry screening for CCHD to aid in early detection and prompt diagnosis. The consensus appears to promote the use of Pulse oximeter as a tool to detect cardiac malformations, especially in well new-borns presenting with hypoxemia(12). Kenyan Guideline states that, all infants should be screened for critical cardiac lesions by use of pulse oximeter and further recommends a timely referral to a tertiary facility with specialised level of care that consists of paediatric cardiologist and specialised nurses among others and diagnostic equipment eg ECHO. Additionally, Ana Olga Mocumbi et al reported that paediatric cardiologists in sub-Saharan Africa deplored of the fact that there are many children with congenital cardiac abnormalities who are either diagnosed late or miss an opportunity to be diagnosed and present their cases when they are too advanced for intervention.

From the 206 abstracted records of study subjects with hypoxemia at 24hour to 48hour of life, 89.3% (95%CI =84.4% to 92.8%) subjects had missed opportunities for cardiac evaluation, while 10.7% (95%CI =4.6% to 19.2%) subjects had no missed opportunity for cardiac evaluation based on our study's definition of missed cardiac evaluation and the assumption that pulse oximetry protocol is performed for the eligible children in accordance with the Kenyan guideline. Whereas this period may include common respiratory illnesses like respiratory disease syndrome (RDS), and due to actual clinical practice in the Kenyan setup, it is

nonetheless remarkable that 86.4% of neonates with hypoxemia missed cardiac evaluation beyond the 72-hour mark during their hospital stay.

Since the database was unable to gather and track data from post-natal nurseries, our study population was restricted to NICU children. The prevalence mentioned earlier was high, which may be related to a rise in the number of false positives. This can be due to only one pulse oximetry reading recorded in majority of the subjects and thus unable to distinguish between the performance site being preductal or post ductal. In some types of CCHD linked to right-to-left shunting, pre- and post-ductal monitoring is essential.

Only 5 out of the 206 records had a preductal and post ductal measurement. All had SPO2 values below 90% three (3) had no request for cardiac evaluation, 1 had a cardiac evaluation request but not done and one (1) had a normal echocardiogram done. Despite some new-borns having pre and post ductal readings and clinically being tachypnoeic and cyanosed, they were either sent home to perform echocardiograms as an outpatient or no cardiac test request was made. This finding could have been contributed by human factors such as, training level of the staff, increased workload and inadequate sensitization on proper use of pulse oximetry screening protocol.

5.2 Spectrum of Cardiac Abnormalities

According to the percentage of newborns who had an echocardiography, 27% of them had cardiac lesions while 73% did not, however they had other lesions including PPHN (41%), sepsis (14%), MAS, Birth Asphyxia, and Tracheoesophageal fistula (4.5% each). Types of cardiac lesions were: ASD -33. %, PDA - 33.3%, TOF with pulmonary atresia and hypertrophic cardiomyopathy 16.65%. In contrast to higher numbers reported in developed nations where early detection and further heart evaluation are more likely to occur, TOF with PA was the only serious cardiac lesion discovered. This pattern may indicate that lesions like TGA, TAPVR, critical COA, and HLHS, which are linked to significant mortality and morbidity in the neonatal period, could be missed (due to single pulse ox determination), misdiagnosed, or die before cardiac evaluation.

5.3 Factors Associated with Missed Opportunities for Cardiac Evaluation

5.3.1 Place of Delivery

One notable difference was the place of delivery; 31.8% of the newborns in the no MO group and 73.3% of the neonates in the missed opportunities (MO) group for cardiac examination were born at Kenyatta National Hospital, respectively. This difference was statistically

significant. According to this, neonates delivered at Kenyatta National Hospital had a 5.8 times higher likelihood of missing cardiac assessment. After giving birth at a tertiary hospital like KNH, it is expected that you will benefit from having a cardiac evaluation. This was not observed in our study. However, our findings are consistent with Tubbs-Cooley et al. and Soohyun and Sun-Mi indicating that delivery in a tertiary care setting is associated with an increased risk of missed opportunities for neonatal care and follow-up, due to factors such as overcrowding, inadequate staffing, lack of training and education programmes and lack of resources (37,38, 41).

Neonates admitted straight to Neonatal Intensive Care Unit were less likely to miss cardiac evaluation compared to those admitted to the High Dependent Unit and other units within Newborn unit. These findings indicate that, unit of admission within the hospital plays a role in the likelihood of missing cardiac evaluation. Neonates in the NICU may have closer monitoring and supervision, leading to a higher likelihood of timely cardiac evaluation.

To reduce missed opportunities for cardiac evaluation, Maria N. Plana et al., recommend routine screening for CCHD in asymptomatic newborns before discharge from the well-baby nursery. This is especially important for babies who are referred late with CCHD to tertiary hospitals, regardless of the level of hospital care (15).

5.3.2 Duration of Admission

A neonate's likelihood of missing a cardiac examination increased by 4.77 times if their length of hospital stay was less than seven days. This is in line with earlier studies that found shorter stays in the neonatal intensive care unit (NICU) were linked to a higher likelihood of patients missing out on follow-up and care because they were believed to have minor illnesses. (39). This might also be due to the heavy workload, risks associated with NICU hospitalizations, like reinfections, and time healthcare professionals stay in the NICU. It decreases the likelihood to adequately evaluate and monitor every newborn.

5.3.3 Mode of Delivery and Sex

While Majani et al. have demonstrated that male newborns and neonates delivered by caesarean section were at low risk of missing opportunities for care and follow-up, sex and mode of delivery were not significantly linked with missed opportunities for cardiac examination in our study. This result was at contrast with research on the Indian community, which discovered a gender bias in the way male children were treated. To validate and comprehend the underlying relationships, more research is necessary. (40).

5.3.4 Clinical Characteristics

The presence of cyanosis was associated with a decreased likelihood of missing cardiac evaluation. The mean respiratory rate was found to be significantly lower in the group with missed opportunities for cardiac evaluation, and neonates with a respiratory rate above 60 breaths per minute were less likely to miss cardiac evaluation. It implies that increased respiratory rate and/or cyanosis are the most common symptoms in infants with CCHD.

At various time intervals, differences in pulse oximetry measurements between the groups with and without missed opportunities (MO) were shown to be statistically significant. These findings imply that the two groups of newborns used different amounts of supplemental oxygen, with the missed opportunity (MO) group consuming less oxygen throughout the study. With the exception of 24 hours, this difference is statistically significant at all time points. Also, it was observed that using supplemental oxygen at 24 hours reduced the likelihood of missing a cardiac evaluation by 61%. This implies that newborns who weren't getting supplemental oxygen may have been thought to be less ill and hence less likely to be referred for more testing. However, it is worth noting that the association between the unit admitting the neonates for the first time and missed cardiac evaluation was only statistically significant for neonates admitted to NICU and HDU. This suggests that other factors may be at play in the likelihood of missing cardiac evaluation.

5.3.5 Clinical Outcomes

According to the study, neonates who underwent a cardiac evaluation were more likely to die than those who did not (the possibility that the neonates who received a cardiac evaluation were more severely ill than those who did not). Finally, although a sizable percentage of participants (39.3%) had their chest x-rays requested, a much smaller percentage (11.1%) had them actually taken. Similar to how echocardiography was sought by 27.7% of study participants and completed by 11.1% of them, EKGs were requested by just (1.4%) of study participants and completed by an even smaller percentage (0.5%). These results imply that not all cardiac evaluation techniques requested were carried out on all patients. From the information given, it is unclear why this may be the case. However, this could be associated with increased workload with limited staff, and delay or no cardiac evaluation would prove detrimental for critical lesions making prompt management impossible. Additional context and information about the study, including the specific research question and study design, would be helpful in providing a more detailed discussion of the study.

5.4.0 Study strengths

1. This is the first study to provide understanding into the proportion of missed opportunity for cardiac evaluation in hypoxemic term neonates. This may lead to understanding where there are challenges in early diagnosis of CHDs.

2. This is a whole population study and hence picked all the missed opportunities. The retrospective nature of the study also strengthened the study by eliminating the Hawthorne effect that resulted in a behaviour change from the ongoing presence of a prospective study.

3. This study also identified other conditions causing hypoxemia in term infants

5.4.1 Study limitations

Pulse ox is a non-invasive tool with excellent results. However, it can result in inaccurate saturation reading in certain situations that require careful interpretation, especially in newborns with Hypothermia.

Incomplete data from the CIN and patients' files was also a limitation we encountered. These was dealt with by excluding them from the study.

Another limitation was due to the retrospective nature of the study: the causative factors of missed opportunities for further cardiac evaluation was not identified.

The study could not ascertain whether the health practitioners followed the Kenyan National Guidelines for Cardiovascular Disease Management Pulse oximetry protocol as recommended.

The single centre design of the study restricted the generalisability of the study to large referral hospitals with comparable infrastructure and staffing levels.

6.0 CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

1. The study found an 89% proportion of Missed opportunity for cardiac evaluation among term neonates with hypoxemia.
2. TOF with pulmonary atresia (PA) was the only cyanotic cardiac lesion identified, while acyanotic types were ASDs and PDAs in the population
3. Length of hospital stay, place of delivery showed a positive association with missed opportunities for cardiac evaluation among term infants with hypoxemia

6.2 Recommendations

To fully understand the factors that lead to missed opportunities for neonatal cardiac evaluation, more research is required. It would be useful to explore the potential impact of staffing levels, training, and protocols for monitoring and evaluation in different units within the hospital. Understanding these factors could help identify potential interventions for improving the timely identification and management of cardiac issues in neonates.

It is important to emphasize the value of more cardiologist consultations.

It is crucial to emphasize the value of follow-up testing as well as pre- and post-ductal testing for an initial abnormal screen.

Developing capacity: In the event of a positive pulse oximetry screen, neonatologists and neonatal fellows should be trained in bedside echocardiography as a tool for CCHD screening. As a result, there may be fewer referrals because of false-positive tests.

6.3 Dissemination

The findings accruing from this study was disseminated to the Department of Paediatrics & Child Health, University of Nairobi, KNH/UON ethics review committee, medical and academic audiences coupled with experts in the field and policymakers. Further, the findings may be published in relevant paediatric-based peer-reviewed journals.

6.4 Funding

The funding source of the study was exclusively from the researcher with no external funding.

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APPENDICES

Appendix I: Budget

No	Category	Description	qty	Unit cost	Total (KSh)
1	Proposal development	Printing and copies	4	1,500.00	6,000.00
		Internet and airtime costs	12	1,000.00	12,000.00
2	Data collection	Stationery	4	2,000.00	8,000.00
		Training Research assistants	2	1,000.00	2,000.00
		Allowance for RA for 3 months	2	3,000.00	6,000.00
3	Data entry	Data entry clerk	1	3,000.00	3,000.00
4	Data analysis	Statistician	1	15,000.00	15,000.00
5	Thesis write up	Printing drafts	3	1,000.00	3,000.00
		Printing thesis	1	3,000.00	3,000.00
6	Contingency	10% Contingency			5,800
Total					63,800.00

Appendix II: Work Plan

No	Activity	2021		2022											
		Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
1	Concept and proposal development and presentation														
2	Proposal submission for ethical review and approval														
3	Data Collection														
4	Data analysis and reporting														
5	Thesis writing and defence														
7	Final submission of thesis and examination														

Appendix III: DATA COLLECTION TOOL

MISSED OPPORTUNITIES FOR CARDIAC EVALUATION IN TERM NEWBORNS WITH HYPOXEMIA AT KNH-NBU

Study Identifiers

Abbreviated name		Date of Enrolment	
Study Number		Data collector	

Neonate Biodata

Date of birth		Time of birth	
Date of admission		Time of admission	
Date of discharge		Time of discharge	
Sex	M / F	Place of Delivery	KNH/Referral
Unit Date & Time	NICU HDU Nursery D Isolation room		
Mode of delivery	SVD/CS	BWT at Admission(gms)	
APGAR(1/5/10)	____/_____/_____	Outcome	Alive/Dead
Admission Diagnoses:		Discharge Diagnoses:	

Maternal Biodata

Age		Number of ANC	
Perinatal Infection	Yes/ No		

Results

PULSE OXIMETRY

Hour	0-24	24-48	48-72	72-96	96-120
Reading					
Oxygen status at time of reading	RA/ O_2	RA/ O_2	RA/ O_2	RA/ O_2	RA/ O_2
Site(RH/LH/RF/LF)					

Symptoms at Screening

Respiratory rate	Heart rate	Temperature	Pallor	Cyanosis	None

Silverman score at screening

Upper Chest movement	Lower chest retraction	Xiphoid retraction	Nasal Flaring	Grunting	Total

Cardiac Evaluation results

Cardiac Evaluations	Done? Yes/No	Date/ Time of Documented Request	Date/Time of Evaluation
Initial Pulse Oximetry		___/___/___ ___:___am/pm	___/___/___ ___:___am/pm
EKG		___/___/___ ___:___am/pm	___/___/___ ___:___am/pm
ECHO		___/___/___ ___:___am/pm	___/___/___ ___:___am/pm
Request for review by Cardiology team		___/___/___ ___:___am/pm	___/___/___ ___:___am/pm
Chest X-ray		___/___/___ ___:___am/pm	___/___/___ ___:___am/pm

CHEST XRAY

EKG

ECHO

OTHER COMMENTS

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8th July, 2022

Dr. Lydia Koila Mose
Reg. No. H58/37459/2020
Dept. of Paediatrics and Child Health
Faculty of Health Sciences
University of Nairobi

Dear Dr. Mose,

RESEARCH PROPOSAL: MISSED OPPORTUNITIES FOR CARDIAC EVALUATION IN TERM NEWBORNS WITH HYPOXEMIA AT KNH-NBU (P149/02/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P149/02/2022.** The approval period is 8th July 2022 – 7th July 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website **http://www.erc.uonbi.ac.ke**

Yours sincerely,

PROF. M. J. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chair, KNH- UoN ERC
The Dean, School of Medicine,UoN
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