University of Nairobi

THE INCIDENCE OF AND FACTORS ASSOCIATED WITH ADVERSE POST-OPERATIVE OUTOMES FOLLOWING OPEN SURGICAL LIGATION OF PATENT DUCTUS ARTERIOSUS AT THE KENYATTA NATIONAL HOSPITAL, KENYA

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF DEGREE OF MASTER OF MEDICINE (MMED) IN THORACIC AND CARDIOVASCULAR SURGERY OF THE UNIVERSITY OF NAIROBI

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H58/7952/2017

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STUDENT'S DECLARATION

I hereby declare that this study is my original work and to the best of my knowledge has not been presented for dissertation or examination at any other university. I further declare that all materials cited in this report which are not mine have been duly acknowledged.

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DEDICATION

To Anne, Ian, Samuel and Edna Takow

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LIST OF ABBREVIATIONS

CHD: Congenital heart disease

CLD: Chronic lung disease

CoA: Coarctation of the Aorta

DA: Ductus Arteriosus

hsPDA: haemodynamically significant PDA

ICU: Intensive Care Unit

IVH: Intraventricular haemorrhage

KNH: Kenyatta National Hospital

LPA: Left Pulmonary Artery

LVEF: Left ventricular ejection fraction

NDI: Neurodevelopmental Impairment

NEC: necrotising enterocolitis

PAH: Pulmonary arterial hypertension

PDA: Patent Ductus Arteriosus

PGE1: prostaglandin E1

PGE2 : prostaglandin E2

PGI1: prostaglandin I1

pO2: oxygen tension

PSI: Prostaglandin Synthetase Inhibitor

Qp:Qs: Pulmonic to Systemic blood flow

ROP: Retinopathy of prematurity

SSI: Surgical site infection

TOF: Tetralogy of Fallot

UoN: University of Nairobi

VATS: Video-Assisted Thoracoscopic Surgery

VSD: Ventricular Septal Defect

APGAR score: Appearance, Pulse, Grimace, Activity and Respiration score

OPERATIONAL DEFINITIONS

Chronic Lung Disease (CLD): chronic respiratory distress requiring supplemental oxygen or positive pressure ventilation

Haemodynamically significant Patent Ductus Arteriosus (hsPDA): a shunt magnitude with Qp:Qs ratio ≥1.5 or duct size of ≥1.5mm

Surgical Site Infection (SSI): Any infection of any severity affecting the thoracotomy or tube thoracostomy site or both

Haemodynamic support: intravenous administration of vasopressor or ionotropic medications

Ventilatory support: provision of supplemental oxygen either via invasive or non-invasive airway adjuncts

Length of hospital stay: Number of days spent in hospital from admission to discharge

Chest infection: any infection affecting the lung parenchyma which was absent prior to surgical ligation of PDA

Residual shunt: detection of a shunt of any magnitude on echocardiography at one month following surgical ligation of PDA

Hospital mortality: Death recorded while in hospital following PDA ligation

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ABSTRACT

Background

Open surgical ligation of patent ductus arteriosus (PDA) has been shown to be associated with adverse outcomes in some observational studies. However, new evidence is suggesting that open surgical ligation of a PDA may not increase adverse outcomes.

Objectives

To determine the incidence of, and factors associated with the occurrence of adverse post-operative outcomes after open surgical ligation of a PDA.

Methodology

We conducted a retrospective observational cohort study over a 10-year period using consecutive sampling method. Risk factors and predictors of adverse post-operative outcomes were analysed using cross tabulation and logistic regression analysis. Statistical significance was set at $P \leq 0.05$ at 95% confidence interval.

Results

The mean gestational age at birth was 36.72 ± 3.96 weeks. The median age at surgical ligation of PDA was 12 (IQR: 7, 22.5) months. Incidence of residual shunt at one-month post-operative was 15%. Chest infection within 3 weeks prior to surgical ligation and chest tube insertion correlated for adverse post-operative outcomes with Odds ratios of 4.1026 and 8.1535 respectively.

Conclusion

Open surgical ligation of the PDA is a relatively very safe procedure with minimal risk in our setup. The insertion of a chest tube before chest closure seemed to be associated with risk of the requirement for haemodynamic and ventilatory support. Chest infection within 3 prior to surgical ligation was predictive of hospital stay longer than 7 days.

INTRODUCTION

The foetal ductus arteriosus (DA) is a vascular conduit that connects the left pulmonary artery (LPA) to the proximal aspect of the descending thoracic aorta. The DA normally develops from the dorsal portion of the sixth aortic arch on the left. During intrauterine life, the DA shunts most of the maternally derived oxygen-rich blood from the foetal pulmonary artery to the foetal aorta, hence bypassing the high pulmonary vascular resistance in order to satisfy metabolic demands of the growing foetus.

Closure of the DA normally starts soon after birth and over 90% are completely closed within the first week of life in term pregnancies.(1) The DA closes to form the ligamentum arteriosum. The DA usually closes in two stages. The first (functional) stage is instigated by smooth muscle contraction and is usually completed with the first 10 to 20 hours after birth(2,3). The second (anatomic) stage is typically completed by 2 to 3 weeks after birth and involves the proliferation of fibrous tissue within the intima and necrosis of the media layers.(2,4) The closure or patency of the duct is mediated chiefly by variations in oxygen tension (pO2) and prostaglandins (PGE1, PGE2, PGI2). An increase in pO2 favours ductal closure while increasing prostaglandin levels favours ductal relaxation.(2,4,5)

Patent ductus arteriosus (PDA) occurs when the lumen of the duct persists beyond the early neonatal period resulting in the shunting of blood from the neonatal aorta into the neonatal pulmonary arterial tree causing pulmonary over-circulation(4). A PDA can exist singly or in co-existence with other malformations of the heart.

The clinical presentation of a PDA depends on the severity of left-to-right shunting (Qp:Qs ratio) which is a function of the transverse ductal diameter. A haemodynamically significant PDA (hs-PDA) will therefore have a high Qp:Qs ratio (Qp>Qs) and will most likely present with symptoms of pulmonary over-circulation and/or heart failure whereas a haemodynamically insignificant PDA may be asymptomatic.

Physical examination and echocardiography represent the foundations of diagnosis of PDA. A typical patient will present with poor weight gain, recurrent chest infections, respiratory distress, widened pulse pressure, hyperactive precordium and ‘machinery-like” murmur radiating from the pulmonic area to just below the mid-clavicle. Transthoracic doppler echocardiography is diagnostic and will usually demonstrate an accelerated, narrow jet flow that originates from the upper aspect of the descending thoracic aorta into the left pulmonary artery.(4)

Within the first year of life, an untreated isolated PDA can have mortality as high as 30%.(2) Depending on the age of the patient and availability of resources, treatment modalities can include the use of intravenous prostaglandin synthetase inhibitors (PSI), transcatheter occlusive devices, video-assisted thoracoscopic (VATS) PDA ligation or open surgical PDA ligation.

The ligation of PDA in preterm infants has been shown to be associated with adverse surgical outcomes such as bleeding, chylothorax, pneumothorax, left recurrent laryngeal nerve injury, inadvertent occlusion of the left main bronchus, left pulmonary artery and aorta(6,7). In 2021, Li et al studied the effect of gender, gestational age at birth, birth weight and APGAR score and the rates of occurrence of post-operative surgical complications (pneumothorax, bleedings, recurrent laryngeal nerve injury, hypotension, hypertension, periventricular leukomalacia, bronchopleural dysplasia, retinopathy of prematurity, necrotizing enterocolitis, respiratory support, hospital stay, hospitalization costs) in extremely premature infants in China(8). The proposed factors associated with adverse surgical outcomes that were analysed in this study included weight, pulmonary artery hypertension, chest infection within 3 weeks prior to surgical ligation of PDA and the insertion of a chest tube. It is not known if any of these factors increase the likelihood of the development of adverse post-operative outcomes as indicated above in our setting. This study was intended to provide data to bridge this knowledge gap.

Patent ductus arteriosus is one of the most common congenital heart conditions affecting preterm neonates. Adverse post-operative outcomes do not only increase the rates of morbidity and mortality but also tend to increase the length of hospital stays and consequently the total hospitalization costs. Adverse post-operative outcomes also have an indirect effect on other patients who may have to spend longer times on the waiting list for surgical ligation of PDA at KNH placing them at risk of worsening clinical condition.

LITERATURE REVIEW

EPIDEMIOLOGY

PDA is an acyanotic congenital heart disease (CHD) that accounts for about 10% of all CHDs in term neonates worldwide.(3) Similar prevalence rates have been documented across Sub-Saharan Africa(Table 1). It has been demonstrated that there is a male to female ratio of approximately 1:2 worldwide.(3–5,9) There is a far greater incidence of PDA among preterm neonates with some studies reporting ranges between 20% - 60%.(10) There exists an inverse proportionality between incidence of PDA and gestational age/weight.(9,11)

Table 1: Prevalence of PDA across select Sub-Saharan African Countries

Authors	Year of Publication	Country	Prevalence of PDA	Sample Size
Bannerman *et al*	1998	Zimbabwe	11.9%	286
Awori *et al*	2013	Kenya	10.7%	214
Mazhani *et al*	2020	Botswana	18%	377

The high incidence of PDA among preterm neonates and infants has been attributed to the lack of normal closure mechanisms as a result of immaturity.(9) Some risk factors demonstrated to increase the incidence of PDA include birth at high altitudes, intrauterine exposure to rubella, and genetic factors.(12)

PATHOPHYSIOLOGY

The patency of the lumen of the duct is affected mostly by both low pO_2 and high circulating levels of prostaglandins. PGE_2 is known to have the most profound effect on ductal smooth muscle relaxation. (13,14) Ductal smooth muscle relaxation is orchestrated via interaction of PGE_2 and its receptor EP4 resulting in the initiation of a sequence of events that ultimately bring about ductal vasodilation and eventually ductal patency. (9,15)

The consequences of a PDA on the respiratory and cardiovascular systems are related to the volume of the left to right shunt. Respiratory consequences are notably pulmonary congestion eventually leading to respiratory compromise and deterioration(11). Haemodynamic consequences are largely due to the phenomenon of ductal steal syndrome which may cause a decrease in the cardiac output with resultant impairment of perfusion of organs such as the brain, the kidneys and the bowel.(16)

SURGICAL MANAGEMENT OF hsPDA

There has been changing trends and controversies in the optimal timing and management of hsPDA among infants over the past decades with preference given to conservative and medical therapy.(17–19) With the advent of catheter based occlusive devices and improved neonatal ICU care, the trends are now shifting towards early ligation or treatment.(11,19–21)

Open surgical ligation is achieved usually via a left posterolateral thoracotomy through the 3rd or 4th intercostal space. The PDA could be singly, doubly or triply ligated using 2/0 silk, 2/0 ethibond or metal clips. Open surgical ligation can be done in the ICU or in the Operation Room (OR). Lee and colleagues in 2018 retrospectively studied a cohort study of 189 infants and reported that PDA ligations done in neonatal ICU were not associated with greater incidences of surgical site infections or mortality.(22)

OUTCOMES OF SURGICAL LIGATION OF hsPDA

Haemodynamically significant PDA (hsPDA) has been shown to be associated with substantial morbidity and mortality following open surgical ligation due to redistribution of blood flow preferentially to the lungs which may result in bronchopulmonary dysplasia (BPD), pulmonary haemorrhage, intraventricular haemorrhage (IVH), neurodevelopmental impairment (NDI), retinopathy of prematurity (ROP), metabolic acidosis as well as necrotising enterocolitis (NEC).(13,23–25).

In 2005, a retrospective cohort study of 98 infants who had open surgical ligation of PDA in 3 different tertiary hospitals in the United Kingdom, reported the respective incidences for BPD 77%, IVH 39%, NEC 26% and ROP 28%.(25) A meta-analysis conducted by Weisz *et al* (2014) among infants who underwent PDA ligation compared to other treatment options, opined that failure to correct pre-ligation confounders introduced risk of residual bias in interpreting data to conclude that PDA ligation increases the mortality and morbidity risks in infants who are preterm.(23) In a retrospective cohort analysis of preterm infants carried in Toronto, Canada, Weisz *et al* (2017) after correcting for confounders, concluded that surgical PDA ligation was linked with lower odds of in-hospital mortality and showed no difference in the development of CLD, ROP or NDI when compared to survivors who had pharmacological management.(24) Similar findings in the United Kingdom and Republic of Ireland have been reported by Warnock and colleagues in 2021 who described a post-operative complication of rate 20.5%(20), Naik-Mathuria et al (2008) in Houston, Texas(26), Lee et al (2020) in South Korea(27).

PDA ligation in preterm infants has been shown to be associated with adverse surgical outcomes such as bleeding, chylothorax, pneumothorax, left recurrent laryngeal nerve injury, inadvertent occlusion of the left main bronchus, left pulmonary artery and aorta.(6,7) A study in China analysed gender, gestational age at birth, birth weight and APGAR score and the occurrence of post-operative surgical complications such as pneumothorax, bleeding, recurrent laryngeal nerve injury, hypotension, hypertension, periventricular leukomalacia, bronchopleural dysplasia, retinopathy of prematurity, necrotizing enterocolitis, respiratory support, hospital stay, and hospitalization costs in extremely premature infants(8). Li et al reported a rate of 66.3% for the development of BPD post-ligation of PDA. There is paucity of research studies analysing outcomes of surgical ligation of PDA performed in Africa with a few reports from Nigeria(28), Tanzania(29), Ivory-Coast (30) and South Africa (31). No study was found in Kenya in the literature search at the time of writing this dissertation. These African studies were limited by their relatively small sample sizes ranging from 25 to 154 study participants.

The proposed factors associated with adverse surgical outcomes that were studied included low weight for age, presence of pulmonary artery hypertension, history of chest infection 3weeks prior to surgical ligation of PDA and the insertion of a chest tube. We also looked at short term post-operative outcomes notably: operative mortality; length of hospital stay; need for hemodynamic support; need for ventilatory support; surgical site infection; residual PDA (whether significant or not).

STUDY JUSTIFICATION AND RATIONALE

CHD is a substantial cause of mortality and morbidity among Kenyan infants and children. PDA is the second most common CHD in Kenya (10.7%) after ventricular septal defects (VSDs) which accounts for 18.7% of all CHD.(32)

With increasing availability of paediatric cardiology human resources and echocardiography services, coupled with the increasing trends in premature delivery and advances in NICU care, it could be logical to expect an increase in diagnostic accuracy and therefore the incidence of PDA among Kenyan infants and children.

It has also been observed that a significant length of time elapses between diagnosis and surgical ligation of PDA with infants and neonates waiting several weeks to months before admission for surgery at the KNH. This situation of prolonged exposure of the lungs to ductal blood shunting puts these children at risk developing severe pulmonary hypertension and Eisenmenger syndrome.

Complications and adverse post-operative outcomes after surgical PDA ligation have been observed to be on a rise in the cardiothoracic ward. These have a tendency to increase length of hospital stay thereby increasing bed occupancy rates in the cardiothoracic ward which does not help reducing time to surgical ligation for children on the surgical waiting list

It was therefore important to study the incidence and characterize the determinants of adverse post-operative outcomes after surgical ligation of PDA in out setting.

STUDY QUESTION

What are the risk factors associated with adverse post-operative outcomes following open surgical ligation of PDA in KNH?

STUDY OBJECTIVES

General Objective:

To determine the incidence of, and factors associated with adverse post-operative outcomes following open surgical ligation of PDA.

Specific Objectives:

- To determine the incidence of adverse post-operative outcomes following open surgical ligation of PDA
- To determine the factors associated with adverse post-operative outcomes following open surgical ligation of PA

CONCEPTUAL FRAMEWORK

The Figure 1 below depicts the conceptual framework of the study. It is thus hypothesized that certain pre-operative and intra-operative factors interplay to influence development of adverse post-operative outcomes following open surgical ligation of PDA.

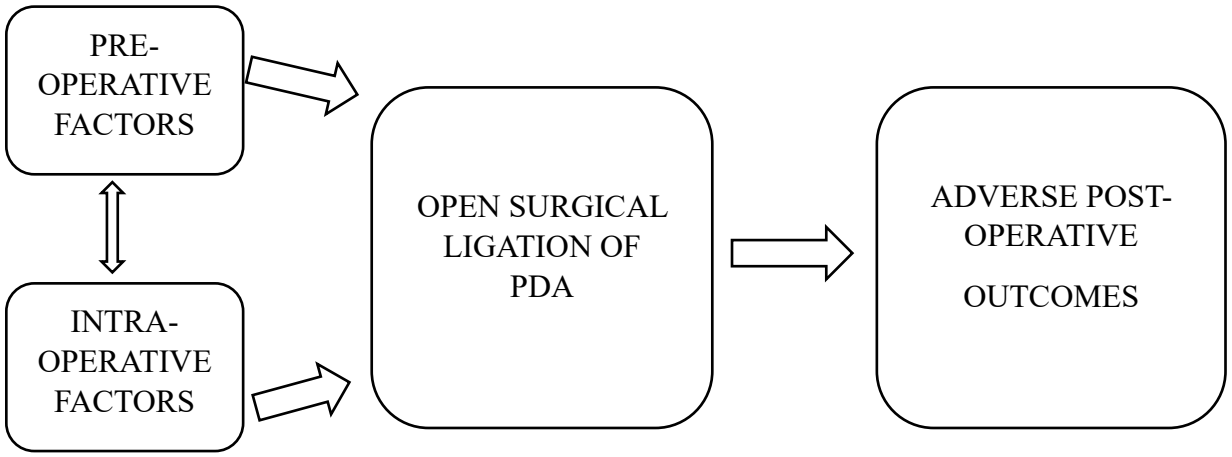

Figure 1: Conceptual framework

METHODOLOGY

STUDY DESIGN

The study design was a retrospective observational cohort study with the study population divided into two groups: control group and case group. The control group consisted of patients who were negative for any one of the independent variables while the case group consisted of subjects who were positive for any one of the independent variables.

STUDY SITE

The study was conducted at the Cardiothoracic Ward and Cardiothoracic Intensive Care Unit (ICU) of the Kenyatta National Hospital (KNH), located in Upper Hill, Nairobi, Kenya. It is the oldest and largest referral health facility for specialized medical and surgical care in the country with a bed capacity of over 1,800. It also serves as teaching hospital of the College of Health Sciences, University of Nairobi.

STUDY DURATION

The study was conducted over a period of ten (10) years using the medical records of patients who underwent open surgical ligation of PDA between January 2012 to December 2021.

STUDY POPULATION

The study population included all patients under the age of 5 years who underwent open surgical ligation of PDA at the Cardiothoracic Ward of KNH. The study population was divided into two groups: control group and case group. The control group consisted of patients who were negative for any one of the independent variables while the case group consisted of subjects who were positive for any one of the independent variables. Exposure referred to patients with either moderate or severe pulmonary arterial hypertension while non-exposure referred to patients with mild pulmonary arterial hypertension.

SAMPLE SIZE DETERMINATION

The sample size for this study was calculated using the following formula as indicated below:

$$N = \frac{[Z\alpha\sqrt{(1+1/m)p^*(1-p^*)}+Z\beta\sqrt{p1(1-p1)/m+p2(1-p2)}]2}{(p1-p2)2}$$

N = sample size

Zα = standard normal variate for level of significance (1.96)

m = number of control subject per experimental subject (1)

Zβ = standard normal variate for power or type 2 error (0.84)

p1 = probability of events in control group – estimated at 10.1%

p2 = probability of events in experimental group (20.5%) – using the prevalence of post-operative complications from reported by Warnock et al (20)

$$p^* = \frac{p2+mp1}{m+1}$$

Entering the above values into the formula yielded a total sample of 54 subjects per group, hence a total sample size of 108 subjects

SAMPLING TECHNIQUE

Sampling was based on consecutive sampling technique. Case files were obtained from the health information unit of KNH.

STUDY VARIABLES

- Independent Variables:
  - Pre-operative variables:
    - Weight
    - Severity of pulmonary arterial hypertension: mild (20-40mmHg), Moderate (41-55mmHg), Severe (>55mmHg)
    - Presence of chest infection within 3 weeks
  - Intra-operative variables:
    - Chest tube insertion before chest closure
- Dependent variables
  - Morbidity:
    - Haemodynamic support
    - Ventilatory support
    - Surgical site infection
    - Length of hospital stay
    - Residual shunt at 1-month post-operative
  - Mortality: hospital mortality

INCLUSION AND EXCLUSION CRITERIA

- Inclusion criteria: All patients who were less than or equal to five (05) years of age who underwent open surgical ligation of PDA at KNH during the study period.
- Exclusion criteria: Patients who underwent PDA ligation as part of intracardiac repair or staged procedures for complex CHD during the study period.

DATA COLLECTION

Data was collected by the principal investigator using a structured questionnaire (Appendix 1) and entered into an electronic data collection form created on EpiInfo™ version 7.2.5 platform on the principal investigator's personal computer in March 2023 at the health information unit of KNH.

DATA ENTRY, STORAGE AND MANAGEMENT

Data collected was entered into an electronic data entry form on EpiInfo™ version 7.2.5 (CDC, Atlanta, Georgia) for Microsoft windows on a password protected personal computer. Access to the data was restricted only to the principal investigator and supervisors.

DATA ANALYSIS

The data was analysed using the epidemiological statistical software EpiInfo™ version 7.2.5 (CDC, Atlanta, Georgia) for Microsoft windows.

Demographic data and patient characteristics were presented in pie charts, frequency tables and summary statistics. Continuous variables were presented as means, medians and standard deviations.

Incidence was calculated as the number of new patients with adverse post-operative outcomes over total number of cases with adverse surgical outcomes.

Relative risk was used to calculate determinants or risk factors of adverse post-operative outcomes. Logistic regression was used to calculate predictors. P-value was set at <0.05 at a confidence interval of 95%.

ETHICAL CONSIDERATIONS

Authorization to carry out this study was obtained from the KNH-UoN Ethics Research Committee. All data collected was anonymised and encrypted into EpiInfo™ version 7.2.5 (CDC, Atlanta, Georgia). Written consent was waived for this study as the case files were utilized for the same.

STUDY LIMITATIONS

Missing case files or data posed as limitation to this study

DISSEMINATION OF RESULTS

The results derived from this study were made available to the Department of Surgery, UoN Library and the Cardiothoracic unit of KNH for policy development and implementation. The research findings will be published in scientific conferences and peer-reviewed journals.

RESULTS

Overall, one hundred and thirty-three (133) records of patients who underwent open surgical ligation of PDA between January 2012 and December 2021 were screened. Thirteen (13) records met the exclusion criteria and were excluded from the study. A total of one hundred and twenty (120) records were therefore studied. The study participants were distributed according to their respective counties of birth as illustrated by the pie chart in Figure 2 below.

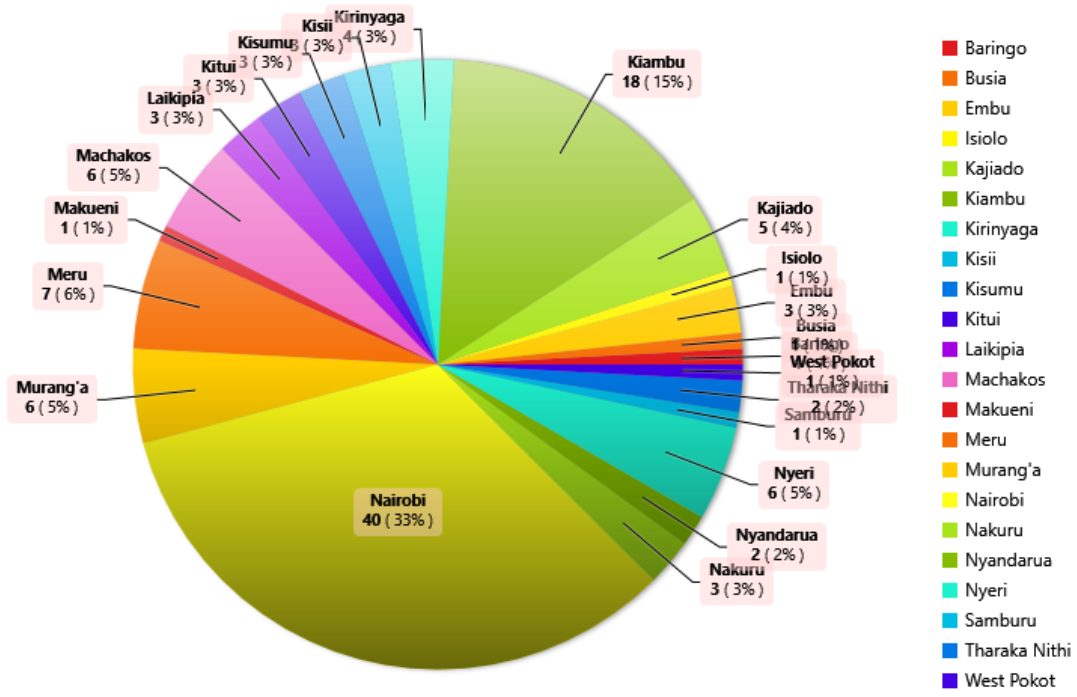

Figure 2: Distribution of study participants according to county of birth

Pre-Open Surgical Ligation of PDA Characteristics

The mean gestational age at birth was 36.72 ± 3.96 weeks. Over three quarters (78.33%) of the patients were born at term. The median age at echocardiographic diagnosis of PDA was 8 (IQR: 5, 17.5) months. The median age at surgical ligation of PDA was 12 (IQR: 7, 22.5) months. The median waiting time to surgery was 2 (IQR: 0, 4.5) months.

At open surgical ligation, the mean weight was 7.68 ± 3.30 Kg with 68.33% having weights less than 8kg at time of surgery. Table 2 summarizes the demographic and presurgical ligation characteristics of the study population.

Table 2: Demographic and pre-open surgical ligation of PDA population characteristics

Variable	n (%) [95%CI]
Gender	
Male	37 (30.83)
Female	83 (69.17)
Gestation at birth	
Extremely preterm (<28 weeks)	02 (01.67)
Very preterm (28 – 32+6)	12 (10.00)
Moderate to late preterm (33 – 36+6)	12 (10.00)
Term (≥37 weeks)	94 (78.33)
Severity of pulmonary arterial hypertension	
None or Mild (20 – 40mmHg)	72 (60.00)
Moderate (41 – 55mmHg) or Severe (>55 mmHg)	48 (40.00)
Weight at ligation	
0 – 5Kg	31 (25.83)
6 – 11Kg	72 (60.00)
12 – 17kg	17 (14.17)
Chest infection within 3 weeks before ligation	48 (40.00)

Post-Open Surgical Ligation of PDA Characteristics

The median length of hospital stay was 13 (IQR: 3, 23.5) days. No in-hospital mortalities were recorded and none of the patients developed surgical site infections. The incidence of the various adverse post-operative outcomes is as illustrated in Table 3 below. More than three quarters (78.33%) of the patients had a total length of hospital stay of at least one week following open surgical ligation. A quarter of the patients had residual PDA at one month after surgical ligation.

Table 3: Incidence of adverse post-operative outcomes following open surgical ligation of PDA

Variable	n (%) [95%CI]
Chest tube insertion before chest closure	20 (16.67)
Haemodynamic support	05 (04.17)
Ventilatory support	10 (08.33)
Length of hospital stay ≥ 7 days	94 (78.33)
Residual PDA at one-month post-ligation	18 (15.00)
Surgical site infection	0 (0.00)
In-hospital mortality	0 (0.00)

Risk factors and predictors of adverse post-operative outcomes

Two by two (2x2) cross tabulation and logistic regression analysis were performed to determine the risk factors and predictors of adverse post-operative outcomes respectively.

Risk Factors for Adverse Post-Operative Outcomes Following PDA Ligation

The analysis of the risk factors for adverse post-operative outcomes is presented in Table 4 below. The relative risk for requiring ventilatory support in patients who had a history of chest infection three weeks prior to open surgical ligation was calculated at 2.3787 (95% CI, p = 0.0267). Insertion of a chest tube was associated with a relative risk for ventilatory and haemodynamic support of 2.7500 (95% CI, p = 0.1042) and 2.5556 (95% CI, p = 0.4138) respectively. The relative risk for patients staying longer than a week in hospital was 2.1021 (95% CI, p = 0.0778) when echocardiographic diagnosis of PDA was made at age 6 months or less.

Table 4: Bivariate analysis of risk factors for adverse post-operative outcomes following open surgical ligation of PDA

Risk Factor	Outcome Variables	Relative Risk (RR)	95% Confidence Interval		P-Value
			Lower Limit	Upper Limit	
Chest infection (within three weeks prior to ligation)					
	Ventilatory support	2.3787	1.0498	5.3898	**0.0267**
	Residual shunt at 1 months	1.0000	0.4525	2.2097	1.0000
	≥1 week hospital stay	0.8095	0.4047	1.6193	0.7149
	Haemodynamic support	0.4894	0.0836	2.8638	0.6410
Chest tube insertion before chest closure					
	Ventilatory support	2.7500	1.1361	6.6564	0.1042
	Haemodynamic support	2.5556	0.8057	8.1060	0.4138
	≥1 week hospital stay	1.5674	0.4973	4.9402	0.6203
	Residual shunt at 1 month	1.0000	0.3261	3.0663	1.0000
Moderate or Severe PAH					
	Haemodynamic support	1.5333	0.7235	3.2497	0.6410
	Ventilatory support	1.0000	0.4525	2.2097	1.0000
	≥1 week hospital stay	0.9304	0.5563	1.5559	0.9639
	Residual shunt at 1 month	0.8095	0.4047	1.6193	0.7149
Echocardiographic diagnosis at ≤6 months of age					
	≥1 week hospital stay	2.1021	0.9211	4.7973	0.0778
	Haemodynamic support	1.1220	0.3730	3.3748	1.0000
	Ventilatory support	1.1282	0.5070	2.5106	1.0000
	Residual shunt at 1 month	0.5812	0.2366	1.4278	0.2985

Predictors of Post-Operative Adverse Outcomes Following Open Surgical Ligation of PDA

Logistic regression was used to calculated the odds ratio of predictors of adverse post-operative outcomes (Table 5). The odds ratio of patients having a hospital stay of at least one week were 4.1026 (95% CI, p = 0.0132) when chest infection was reported within 3 weeks prior to open surgical ligation of PDA and 2.3318 (95% CI, p = 0.2316) if a chest tube was inserted. The odds ratio for requiring haemodynamic support when a chest tube was inserted, with moderate or severe PAH was documented on echocardiography, or a weight at ligation of between 12 – 18Kg were respectively 8.1535 (95% CI, p =0.0634), 38708 (95% CI, p = 0.2026) and 3.0723 (95% CI, p = 0.3824). The insertion of a chest tube was associated with odd ratio of 4.8685 (95% CI, p = 0.0333) for ventilatory support. The odds ratio of having a residual shunt at one month after open surgical ligation when the weight at ligation was between 12 – 18kg was calculated at 3.7171 (95% CI, p = 0.1341).

Table 5: Predictors of adverse post-operative outcomes following open surgical ligation of PDA

Outcome variable	Predictor	Odds Ratio (OR)	95% Confidence Interval		P-Value
			Lower Limit	Upper Limit	
≥1 week hospital stay					
	Chest infection within 3 weeks	4.1026	1.3428	12.5343	**0.0132**
	Chest tube insertion	2.3318	0.5825	9.3349	0.2316
	Weight 12 – 18kg	0.8999	0.1076	7.5236	0.9225
	Moderate or severe PAH	0.7606	0.2869	2.0164	0.5822
Haemodynamic support					
	Chest tube insertion	8.1535	0.8897	74.7208	0.0634
	Moderate or severe PAH	3.8708	0.4827	31.0373	0.2026
	Weight (12 – 18Kg)	3.0723	0.2476	38.1180	0.3824
	Chest infection	0.4647	0.0371	5.8264	0.5525
Ventilatory support					
	Chest tube insertion	4.8685	1.1331	20.9185	**0.0333**
	Weight 12 – 18kg	1.7039	0.2050	14.1605	0.6218
	Chest infection	1.2412	0.2863	5.3806	0.7727
	Moderate or severe PAH	1.0927	0.2050	14.1605	0.6218
Residual shunt at 1 month					
	Weight 12 – 18Kg	3.7171	0.6670	20.7148	0.1341
	Chest tube insertion	1.1105	0.2780	4.4360	0.8821
	Chest infection	0.9917	0.3139	3.1335	0.9887
	Moderate or severe PAH	0.8351	0.2811	2.4810	0.7457

DISCUSSIONS

Geographical Demographics

The geographical demographics of the study population study showed that more than half (57%) of the study participants were referrals from the following three counties combined: Nairobi (33%), Kiambu (18%) and Meru (6%). These rates could indicate, in part, the proximity of these counties to the Kenyatta National Hospital thus encouraging relatively early referral and echocardiographic diagnosis of PDA; but also, a greater concentration of echocardiographic services and paediatric cardiologists in the aforementioned counties. This finding however raises concerns about potential significant delays in the establishment of definitive diagnosis of PDA in patients who are born in counties remote to KNH.

Pre-Surgical Ligation Characteristics

The results also pointed out that over 83 of the study participants were females while 37 were males giving a female to male ratio of approximately 2:1. This ratio is the same as the ratio of 2:1 from previous studies reported in other parts of the world(3–5,9).

More than three quarters (78.33%) of the study participants were born at term (≥37 weeks). It is known that one of the major risk factors for the development of PDA is prematurity(9). This finding could mean that other causal factors different from prematurity were major contributors to the occurrence of PDA in this study population(12).

The echocardiographic diagnosis of PDA is typically made within the first month of life. In this study, the median age at echocardiographic diagnosis of PDA was 8 (IQR: 5, 17.5) months. A previous study conducted by Awori et al in 2007(33) had reported a mean age at echocardiographic diagnosis of congenital heart disease at 18.6 ± 25.6 months. This represents a significant decrease by over 10 months in the overall time to echocardiographic diagnosis. This could possibly translate into considerable improvements in management pathway favouring early referrals to paediatric cardiologist outpatient clinics. At the time of echocardiographic diagnosis, about two-thirds of the study population had normal or mild pulmonary arterial hypertension. A probable explanation to this finding could be due to presence of PDAs which are haemodynamically insignificant hence causing minimal symptoms.

Controversies exist over the optimal timing for PDA ligation with literature suggesting better post-operative outcomes with early ligation within 3 – 4 weeks of life(17–21) or at latest the before completion of the third month of life (34–36). In our study, the median age at surgical ligation of

PDA was 12 (IQR: 7, 22.5) months as opposed to a mean age at surgical ligation of 64.3 ± 80.8 months reported by Mohammed et al in a similar study in Nigeria (28). The difference in median age at open surgical ligation between our study and that reported by Mohammed et al (2021) is based on the difference in study population characteristics. The latter study included participants older than 5 years.

The median interval time from the echocardiographic diagnosis to open surgical ligation was 2 (IQR: 0, 4.5) months. This finding was significantly different from that reported in a previous study done in 2007 at KNH by Awori et al, who found out that the mean interval time from echocardiographic diagnosis to surgical creation of a modified Blalock-Taussig Shunt for certain congenital heart disease was 8.0 ± 11.8 months(33). Our study thus could indicate that there has been a significant improvement in the efficiency of the management pathway of congenital heart disease in children and infant as evidenced by shortening of the interval time by 6 months. Hence, these children are now receiving surgical care earlier than later.

We reported a 40% prevalence rate of chest infection within 3 weeks before surgical ligation. This could also explain delays to surgical closure of PDA as such infections must be cleared before the execution of the surgical procedure.

In this study, the median age and the median weight at surgical ligation were respectively 12 months and 7.68kg respectively. Plotting these values on a standard WHO weight-for-age for boys or girls revealed that overall, the study population had an estimated weight-for-age value less than the 15th percentile. This finding indicates a high rate of under nutrition amongst this high risk population; highlighting the burden of congenital heart disease on the nutritional status of children under five years in Kenya country where the prevalence of malnutrition is estimated at 26%(37).

Post-Open Surgical Ligation of PDA Characteristics

In this study, we noted that there was no record of either surgical-site infection or in-hospital mortality in the study population. The 0% mortality is significantly different from reports published by Ban who documented in-hospital mortality rates between 6.5 and 8.1%(20,31). This finding could be translated as to consider the performance of open surgical ligation of PDA in our setup as a relatively very safe procedure with extremely minimal risk of intra-operative or in-hospital death.

On the other hand, the incidence of morbidity related to open surgical ligation of PDA was noted to be associated with chest tube insertion (16.67%), ventilatory support (08.33%), haemodynamic support (04.17%) and residual shunt (less than 3mm) at one-month after ligation (15%). The rate of residual shunt after ligation of PDA in our study is more than double that reported by Sudhakar in

2018 which was estimated at 6%(38). The higher rate of residual PDA in this study possibly indicates suboptimal occlusion of the PDA in the first instance or re-canalization of a totally occluded PDA. Further research into the phenomenon of residual shunting after PDA ligation is required to decipher which of the two hypothesis is responsible.

The median length of hospital stay was 13 (IQR: 3, 23.5) days with the majority of patients (78.33%) having hospital-stays longer than 7 days, measured from the time of admission to the time of discharge from the hospital. This finding differed significantly from that reported in 2021 in Nigeria by Mohammed et al who reported a mean hospital stay of 8 ± 2.1 days(28). This relatively prolonged hospital-stay, following a relatively safe and low risk procedure could partly be explained by the fact that 40% of study population were managed for chest infections concomitantly while being optimized for surgery.

Risk Factors for Adverse Post-Operative Outcomes Following Open Surgical Ligation of PDA

The risk factors for adverse post-operative outcomes following open surgical ligation of PDA were calculated from contingency tables by determining the relative risk ratios. Chest infection within 3 weeks prior to surgical ligation had a statistically significant relative risk (2.3787, p = 0.0267) for the need of ventilatory support following surgical ligation of PDA.

Insertion of a chest tube correlated with the need for haemodynamic and ventilatory support with respective relative risk ratios of 2.5556 (p=0.4138) and 2.7500 (p=0.1042) though these correlations were not statistically significant. This relationship could be partly answered by the notion that very sick patients might be exposed to haemodynamic instability and ventilatory failure as opposed to less sick ones.

Echocardiographic diagnosis of PDA made at age 6 months correlated with longer hospital-stay of more than 7 days. A possible explanation to this correlation is the observation that a significant number of younger infants with PDA in our set up tend to present with frequent severe lower respiratory tract infections and are managed for severe pneumonia; hence are diagnosed with PDA only when symptoms fail to respond promptly with optimal antibiotic therapy.

Predictors Of Adverse Post-Operative Outcomes Following Open Surgical Ligation of PDA

Logistic regression analysis was used to determine the predictive factors of adverse post-operative outcomes following open surgical ligation. Chest infection within 3 weeks prior to surgical ligation and insertion of chest tube were both predictive of a hospital-stay longer than 7 days with Odds ratios

of 4.1026 and 2.3318 respectively. However, the only the Odds ratio of chest infection within 3 weeks were statistically significant. Both the presence of chest infection and chest tube will tend to increase morbidity and could explain their predictive property for prolonged length of hospitalization.

The insertion of a chest tube before chest closure seemed to be associated with risk of the requirement for haemodynamic and ventilatory support with Odds ratios of 8.1535 and 4.8685 respectively though both values were not statistically significant. Chest tube insertion was practices differs among surgeons in our facility with a majority of surgeons inserting a chest tube before chest closure only when open surgical ligation was considered complicated (presence of air leaks, chylothorax, arrested bleeding). Hence there is a possibility that patients requiring haemodynamic and ventilatory support are at a relatively higher risk of requiring chest tubes for management of relatively common conditions like pneumothorax or chylothorax (6,7). This association between chest tube insertion and adverse outcomes was not different from the findings of a non-blinded randomized controlled trial reported by Kebba et al (2016) in Uganda(39). Kebba et al reported that insertion of a chest tube was associated with unfavourable post operative outcomes including but not limited to surgical site infection. Further research might be necessary to gain an in-depth understanding on outcomes following routine chest closure with or without chest tube insertion.

Moderate or severe pulmonary arterial hypertension was also observed to be associated with the need for haemodynamic support (Odds ratio = 3.8708). Though this finding was not statistically significant, it however underlines the need for keen haemodynamic monitoring of patients after open surgical ligation of PDA.

A body weight ranging between 12 – 18kg was associated with a residual shunt (less than 3mm) at one month following open surgical ligation of PDA though this relationship was not statistically significant. A possible explanation to this finding could be that higher weights could be associated with thicker ductal walls which may interfere with complete luminal occlusion on ligation of the PDA. The occurrence of residual shunt following surgical ligation of PDA has been attributed to either sub-optimal occlusion or re-canalization of a previously totally occluded PDA.(38)

CONCLUSION

In summary, open surgical ligation of the PDA is a relatively safe procedure with minimal operative mortality risk in our setup. The incidence of a residual shunt (less than 3mm) at one-month following open surgical ligation was found in 15% of patients.

Chest infection within 3 weeks prior to ligation, insertion of a chest tube post-operatively and echocardiographic diagnosis at 6 months were risk factors for the occurrence of adverse post-operative outcomes.

The presence of chest infection reported within 3 weeks before open surgical ligation of PDA was predictive of hospital stays longer than 7 days.

Identification of these high-risk groups is useful to counsel families regarding the reasonable outcomes following open surgical ligation of PDA.

RECOMMENDATIONS

1. Randomized trial to evaluate outcomes following chest tube before chest closure after open PDA ligation.
2. Study on the optimal time for open PDA ligation after recovery from chest infection.
3. Prospective cohort study to evaluate the outcomes between device closure and open surgical ligation of PDA
4. A randomized trial to accurately study the timing of open surgical ligation of PDA in our context

REFERENCES

1. Nagasawa H, Hamada C, Wakabayashi M, Nakagawa Y, Nomura S, Kohno Y. Time to spontaneous ductus arteriosus closure in full-term neonates. Open Heart. 2016;3:1–7.

2. Kouchoukos N, Blackstone E, Hanley F, Kirklin J. Patent Ductus Arteriosus. In: Kirklin/Barratt-Boyes Cardiac Surgery. Fourth. Philadelphia: Elsevier Saunders; 2013. p. 1343–59.

3. Kliegman R, Geme II J, Blum N, Tasker R, Shah S, Wilson K, et al. Patent Ductus Arteriosus. In: Nelson Textbook of Pediatrics. 21st ed. Philadelphia: Elsevier; 2020. p. 2382–4.

4. Yuh D, Yang S, Vricella L, Doty J. Patent Ductus Arteriosus. In: Johns Hopkins Textbook of Cardiothoracic Surgery. Second. McGraw Hill; 2014. p. 1001–8.

5. Mery C, Turek J. Patent Ductus Arteriosus. In: Review of Cardiothoracic Surgery. Chicago: Thoracic Surgery Residents Associaion; 2011. p. 204–5.

6. Harris L, Krishnamurthy R, Browne L, Morales D, Friedman E. Left main bronchus obstruction after patent ductus arteriosus ligation: An unusual complication. Int J Pediatr Otorhinolaryngol. 2012;76:1855–6.

7. Madhan P, Brown S, Kukady A, Samarakkody U. Surgical closure of patent ductus arteriosus in preterm low birth weight infants. Congenit Heart Dis. 2009;34–7.

8. Li Q, Han T, Yang Y, Zhou G, Wang H. Age at Surgical Ligation of Patent Ductus Arteriosus Affects Prognosis in Extremely Premature Infants. Iran J Pediatr. 2022;32(1).

9. Dice JE, Bhatia J. Patent Ductus Arteriosus: An Overview. J Pediatr Pharmacol Ther. 2007;12(3):138–46.

10. Hajjar M, Vaksmann G, Rakza T, Kongolo G, Storme L. Severity of the ductal shunt: a comparison of different markers. Arch Child Fetal Neonatal Ed. 2005;90(5):F419–22.

11. Soliman RM, Mostafa FA, Abdelmassih A, Sultan E, Mosallam D. Patent ductus arteriosus in preterm infants; experience of atertiary referral neonatal intensive care unit: prevalence, complications, and management. Egypt Pediatr Assoc Gaz. 2020;68(34):1–9.

12. Gittenberger-de Groot A, Moulaert A, Hitchcock J. Histology of the persistent ductus arteriosus in cases of congenital rubella. Circulation. 1980;62:183–6.

13. Hermes-De Santis E, Clyman R. Patent ductus arteriosus: pathophysiology and management. J Perinatol. 2006;26(1):S14–8.

14. Van Overmeire B, Chemtob S. The pharmacologic closure of the patent ductus arteriosus. Semin Fetal Neonatal Med. 2005;10(2):177–84.

15. Ivey KN, Deepak S. The paradoxical ductus arteriosus. J Clin Invest. 2006;116:2863–5.

16. Benitz W, Committee on Fetus and Newborn, American Academy of Pediatrics. Patent ductus arteriosus in preterm infants. Pediatrics. 2016;137(1):2015–3730.

17. Lokku A, Mirea L, Lee SK, Shah PS, Canadian Neonatal Network. Trends and Outcomes of Patent Ductus Arteriosus Treatment in Very Preterm Infants in Canada. Am J Perinatol. 2017;34(05):441–50.

18. Park J, Yoon SJ, Han J, Song IG, Lim J, Shin JE, et al. Patent ductus arteriosus treatment trends and associated morbidities in neonates. Sci Rep. 2011;11(10689):1–7.

19. Wang H, Jain A, Weisz DE, Moraes TJ. Trends in patent ductus arteriosus ligations in neonates and changesin outcomes: A 10-year multicenter experience. Pediatr Pulmonol. 2021;56(10):3250–7.

20. Warnock A, Szatkowski L, Lakshmanan A, Lee L, Kelsall W. Surgical management of patent ductus arteriosus in pre-term infants - a british paediatric surveillance study. BMC Pediatr. 2021;21:1–8.

21. Tort M, Ceviz M, Sevil F, Becit N. Surgical Treatment for Patent Ductus Arteriosus: Our Experience of 12 Years. Cureus. 2021;13(4):1–9.

22. Lee LK, Woodfin MY, Vadi MG, Grogan TR, Ross PJ, Applegate II RL, et al. A comparison of postoperative outcomes with PDA Ligation in the OR versus the NICU: a retrospective cohort study on the risk of transport. BMC Anesthesiol. 2018;18(199):1–11.

23. Weisz DE, McNamara PJ. Patent Ductus Arteriosus Ligation and Adverse Outcomes: Causality or Bias? J Clin Neonatol. 2014;3(2):67–75.

24. Weisz DE, Mirea L, Resende MH, ly L, Church PT, Kelly E, et al. Outomes of Surgical Ligation after Unsuccessful Pharmacotherapy for Patent Ductus Arteriosus in Neonate Born Extremely Preterm. J Pediatr. 2017;1–8.

25. Lee LlC, Tillet A, Tulloh R, Yates R, Kelsall W. Outcome following patent ductus arteriosus ligation in premature infants: a retrospective cohort analysis. BMC Pediatr. 2005;6(15):1–6.

26. Naik-Mathuria B, Chang S, Fitch ME, Westhoff J, Brandt ML, Ayres NA, et al. Patent ductus arteriosus ligation in neonates: preoperative predictor of poor operative outcomes. J Pediatr Surg. 2008;43:1100–5.

27. Lee JH, Lee HJ, Park HK, Ahn ja H, Kim HS, Jang HJ, et al. Surgical ligation of patent ductus arteriosus in preterm neonates weighing less than 1500g: a 9-year single centre experience. J Cardiothorac Surg. 2020;15(144):1–9.

28. Mohammed II, Ahmad JI, Nurein TO, Ishaq NA, Aliyu I. Management of patients with patent ductus arteriosus: Challenges and outcomein low-resource settings. Sahel Med J. 2021;24:129–33.

29. Nyawawa E, Ussiri E, Njelekela M, Mpoki U, Nyangassa B, Wandwi W, et al. Surgical Experience with Closure of an Isolated PDA at Muhimbili Cardiothoracic Unit in Dar es Salaam, Tanzania. COSECSA/ASEA. 2013;18(2):127–36.

30. Yangni-Angate H, Ayegnon G, Meneas C, Diby F, Yapobi Y. Patent ductus arteriosus in adults: Surgical experience in Ivory-Coast. Ann Afr Med. 2007;6(1):34–5.

31. Banieghbal B. Physiological marker and surgical ligation of patent ductus arteriosus in neonates. Afr J Paediatr Surg. 2016;13:109–13.

32. Awori M, Ogendo S. The Spectrum of Paediatric Congenital Heart Disease at The Kenyatta National Hospital: Implications for Surgical Care. Ann Afr Surg. 2013 Jan;10(1):8–10.

33. Awori M, Ogendo S, Gitome S, Ong'uti S, Obonyo N. Management pathway for congenital heart disease at Kenyatta National Hospital, Nairobi. East Afr Med J. 2007;84(7):312–7.

34. Onakpoya U, Ogunrombi A, Aladesuru A, Okeniyi J, Adenekan A, Owojuyigbe A. Trans-thoracic open ligation of the persistent ductus arteriosus in Ile-Ife, Nigeria. Niger J Cardiol. 2015;12:8–12.

35. Fonseca E, Georgiev S, Gorenflo M, Loukanov T. Patent ductus arteriosus in preterm infants: Benefits of early surgical closure. Asian Cardiovasc Thorac Ann. 2014;22:391–6.

36. Actis Dato G, Cavaglia M, Actis Dato AJ, Bardi G, Rizza M. Patent ductus arteriosus. Follow-up of 677 operated cases 40 years later. Minerva Cadioangiol. 1999;47:245–54.

37. UNICEF. UNICEF Kenya Country Programme 2022-26 [Internet]. 2020. Available from: www.unicef.org/kenya

38. Sudhakar B. Percutaneous transcatheter closure of a distorted residual patent ductus arteriosus post surgical ligation using retrograde wiring and femoral arterio-venous loop technique - a case report. IHJ Cardiovasc Case Rep CVCR. 2018;2(3):208–10.

39. Kebba N, Mwambu T, Oketcho M, Izudi J, Obuku E. Chest closure without drainage after open patent ductus arteriosus ligation in Ugandan children: A non blinded randomized controlled trial. BMC Surg. 2016;16(69).

40. Cochran W. Sampling Techniques. John Wiley & Sons; 1977.

APPENDICES

APPENDIX 1: Data collection tool

THE INCIDENCE AND DETERMINANTS OF POST-OPERATIVE OUTOMES FOLLOWING OPEN SURGICAL LIGATION OF ISOLATED PATENT DUCTUS ARTERIOSUS AT THE KENYATTA NATIONAL HOSPITAL, KENYA

Date:_____

Serial Number:_____

A. Demographics
    a. Sex: M or F
    b. Age at birth:____weeks
    c. Age at echographic diagnosis of PDA:_____weeks
    d. Age at surgical ligation of PDA:_____weeks
    e. County of birth_____
B. Patient characteristics
    a. Pre-operative data:
        i. Weight:____kilograms
        ii. Chest infection within 3 weeks: YES / NO
        iii. Pulmonary arterial hypertension: a) Mild/Moderate b) Severe
    b. Intra-operative data
        i. Chest tube insertion: YES / NO
    c. Post-operative data
        i. Morbidity:
            1. Hemodynamic support: YES / NO
            2. Ventilatory support: YES / NO
            3. Surgical site infection; YES / NO
            4. Total length of hospital stay: ____days
            5. Residual shunt at 1 month post op: YES / NO
        ii. Mortality:
            - In-hospital death: YES / NO

9% Confirmed

APPENDIX 2: Plagiarism check report

THE INCIDENCE OF AND FACTORS ASSOCIATED WITH ADVERSE POST-OPERATIVE OUTOMES FOLLOWING OPEN SURGICAL LIGATION OF PATENT DUCTUS ARTERIOSUS AT THE KENYATTA NATIONAL HOSPITAL

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