# AN AUDIT OF THE USE OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE IN NEONATES WITH RESPIRATORY DISTRESS, ADMITTED TO THE NEWBORN UNITS OF FOUR COUNTY AND SUB-COUNTY HOSPITALS IN KENYATTA: (A Cross-Sectional Observational Study)

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## DECLARATION

I, **Dr. Jane Nyawira Magondu**, certify that this research dissertation is my original work and has not been presented for the award of a degree in any other university.

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## DEDICATION

I dedicate this dissertation to the Almighty God and to my beloved mother, brother, children, and friends, whose support and encouragement have been unwavering.

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## LIST OF ABBREVIATIONS AND ACRONYMS

| | |
|---|---|
| bCPAP - | Bubble Continuous Positive Airway Pressure |
| BiPAP - | Bi-level Continuous Positive Airway Pressure |
| bNCPAP - | Bubble Nasal Continuous Positive Airway Pressure |
| CI - | Confidence Intervals |
| CIN - | Clinical Information Network |
| CPAP - | Continuous Positive Airway Pressure |
| CPHD - | Centre for Public Health and Development |
| ENaC - | Epithelial Sodium Channels |
| ERC - | Ethics and Research Committee |
| FiO2 - | Fraction of inspired oxygen |
| FRC - | Functional Residual Capacity |
| HFNC - | High Flow Nasal Cannula |
| KID - | Kid's Inpatient Database |
| KEMRI - | Kenya Medical Research Institute |
| KNH - | Kenyatta National Hospital |
| KPA - | Kenya Paediatric Association |
| KS - | Kolmogorov Smirnov |
| KWTRP - | Kenya Medical Research Institute Wellcome Trust Research Programme |
| LMICs - | Low and Middle-Income Countries |
| MAS - | Meconium Aspiration Syndrome |
| MoH - | Ministry of Health |
| MTRH- | Moi Teaching and Referral Hospital |
| NACOSTI - | National Commission for Science, Technology, and Innovation |
| NAR - | New-born Admission Records |

NBUs - New Born Units

NCPAP - Nasal Continuous Positive Airway Pressure

NEST - New-born Essential Solutions and Technologies

nHFOV - Nasal High-Frequency Oscillation Ventilation

NIPPV - Non-Invasive Positive Pressure Ventilation

OR- Odds Ratio

PPHN - Persistent Pulmonary Hypertension of the Newborn

QQ Plot - Quantile vs Quantile Plot

RDS - Respiratory Distress Syndrome

REDCap - Research Electronic Data Capture

RNA - Ribonucleic Acid

SERU - Scientific and Ethics Review Unit

SDG - Sustainable Development Goals

SP - Surfactant Protein

SpO2 - Oxygen saturation

SVD- Spontaneous Vertex Delivery

TTN - Transient Tachypnea of the Newborn

UON - University of Nairobi

US - United States

VLBW - Very Low Birth Weight

WHO - World Health Organization

## OPERATIONAL DEFINITIONS

**Adverse outcomes:** Death, chronic lung disease as evidenced by oxygen dependence on day 28, need for mechanical ventilation

**Clinical Information Network (CIN) – Neonatal:** A database developed as a partnership between Kenya Medical Research Institute (KEMRI), the Ministry of Health (MoH), The Kenya Paediatric Association (KPA), and several public hospitals across the country. The CIN-Neonatal network collects standardized routine data on newborn admissions.

**Continuous Positive Airway Pressure (CPAP)**: A non-invasive form of ventilation that continuously delivers positive end-expiratory pressure to maintain alveoli open at the end of expiration, hence improving oxygenation and ventilation.

**Gestational age**: the period of time between conception and birth as a measure of pregnancy age from last normal menstrual period.

**Grunting:** An expiratory sound produced due to sudden closure of the glottis during expiration in an attempt to maintain the Functional Residual Capacity (FRC) and prevent alveolar collapse

**Low birth weight**: Defined by World Health Organization (WHO) as weight at birth of < 2500 grams.

**Nasal flaring:** Widening of nostrils as a compensatory mechanism that increases the diameter of the upper airway and hence reduces resistance and work of breathing.

**Neonates**: Infants aged 0-28 days old

**Preterm**: A baby born before 37 weeks of gestation are completed. Preterm births can be further classified based on gestational age: extremely preterm (<28 weeks), very preterm (28 - <32 weeks) and moderate to late preterm (32 - <37 completed weeks of gestation)

**Respiratory distress**: One or more signs of increased work of breathing, such as tachypnea, nasal flaring, chest retractions, or grunting.

**Respiratory Distress Syndrome**: A condition of pulmonary insufficiency that commences at or shortly after birth due to deficiency of surfactant. It is characterized by features of early respiratory distress comprising tachypnea, cyanosis, grunting and retractions.

**Retractions:** The use of accessory muscles of respiration in the neck, rib cage (intercostal), sternum, or abdomen that occurs when there is increased airway resistance coupled with poor lung compliance.

**Silverman Anderson Score:** A score of the severity of respiratory distress that measures five parameters including upper chest retraction, lower chest retraction or indrawing, xiphoid retraction, nasal dilatation (flaring) and expiratory grunt.

**Tachypnea:** Respiratory rate more than 60 breaths per minute in a neonate. This is measured by counting the respiratory rate over one minute.

## ABSTRACT

**Background:** Neonatal respiratory distress is the most frequent indication for admission to the newborn unit (NBU). International and Kenyan guidelines advocate for the early use of Continuous Positive Airway Pressure (CPAP) as a standard of care. CPAP machines have been introduced in several county and sub-county hospitals in Kenya but implementation of CPAP therapy has not been well documented in these less-resourced facilities. We set out to audit the use of CPAP in neonates with features of respiratory distress in these hospitals. Specifically, we sought to describe the criteria used to initiate, wean, and stop CPAP therapy, patient monitoring, patient outcomes, and factors associated with adverse outcomes.

**Methodology:** A hospital-based, retrospective, cross-sectional observational study conducted in the NBUs of four purposively selected secondary-level public referral facilities. We included all neonates admitted with features of respiratory distress, and among them, those managed on CPAP from January 2020 to December 2022. Data were obtained from the Clinical Information Network (CIN) database, patient files, and facility CPAP records. Variables of interest were descriptively reported in proportions, medians, and interquartile ranges. Measures of associations were summarized as odds ratios. The outcomes of interest were survival to discharge, need for mechanical ventilation, death, and chronic lung disease. Factors associated with these adverse outcomes were analyzed using a multivariate regression model.

**Results:** A total of 23,119 neonates were admitted to the selected NBUs from January 2020 to December 2022. 6,469 (28%) had features of respiratory distress, with CPAP use in 1,211/6469 (18.7%). For those managed on CPAP, all 259 available patient records were audited. 160/259 (62%) were male, 136/259 (53%) had a low birth weight < 2500 grams, 178/259 (69%) were premature and 184/259 (71%), had a diagnosis of RDS. 193/259(75%) were discharged alive, 61/259 (24%) died and 5/259 (1.9%) were referred for mechanical ventilation. The median time to initiation of CPAP from admission was 13.8 hours (IQR: 3.8-35.6 hours) with a median duration of

CPAP use of 2 days (IQR: 1.0-3.0 days). The median number of monitoring observations in the first 24 hours while on CPAP were 4 (IQR: 2-8) respiratory rate, 5(IQR: 3-8) heart rate, and 5(IQR: 3-8) oxygen saturation (SpO2) observations. Only 10 /259(3.9%) had documented weaning of FiO2 by 10% up to 30% and 8/259 (3.1%) had documented weaning of CPAP pressure by 1 cm to a minimum of 5 cm of water before cessation of CPAP. Silverman Anderson Score (SAS) was only indicated in 17/259 (6.6%) of the records. Male gender, prematurity, low birth weight, hypothermia, and maternal diabetes were associated with higher odds of death in patients on CPAP but these were not statistically significant. Neonates with neonatal sepsis had a 67% reduction in the odds of death (OR 0.33, 95% CI [0.12, 0.79]), after adjusting for other confounders at multivariate analysis likely due to antibiotic use.

**Conclusion:** Use of CPAP was low with only 18.7% (95% CI [17.8, 19.7]) of neonates with features of respiratory distress managed on CPAP. There was delayed initiation, inadequate monitoring, improper titration, weaning, and cessation of CPAP therapy. There was understaffing as well as lack of adequate monitoring equipment in the study sites. Concerted efforts need to be put into training health workers, guideline implementation, and adequate monitoring and staffing.

# CHAPTER ONE

# 1.0 BACKGROUND AND LITERATURE REVIEW

## 1.0 Introduction

In the initial hours and days of life, a neonate has to quickly adapt to life in the extra-uterine environment. During this crucial period, they are susceptible to developing respiratory distress (1). Respiratory distress occurs in 7% of all term newborns (2,3) and 30% of preterms(3). It contributes to all three of the most common causes of global neonatal deaths: prematurity, perinatal asphyxia, and neonatal sepsis (4). Respiratory disorders are the most frequent indications for admission to the newborn unit in term and preterm infants, and a leading cause of early neonatal mortality and morbidity, (5) and studies have shown that neonates with respiratory distress have a 2-4 fold higher risk of death (6). Some of the conditions that lead to respiratory distress in neonates include prematurity, neonatal sepsis, perinatal asphyxia, meconium-stained liquor, pulmonary haemorrhage, caesarean section delivery, multiple gestation, gestational diabetes, premature rupture of membranes, maternal chorioamnionitis, oligohydramnios, congenital structural lung abnormalities, congenital heart disease among others (1,2).

The clinical signs and symptoms of respiratory distress in this population include tachypnea (respiratory rate > 60 breaths per minute), nasal flaring, grunting, retractions (subcostal or lower chest wall, intercostal, suprasternal), cyanosis, apnea, bradypnea (respiratory rate < 30 breaths per minute), irregular (seesaw) breathing, stridor, wheeze, and hypoxia (5).

Prematurity remains the most significant risk factor for respiratory distress in neonates, in which case it is referred to as Respiratory Distress Syndrome (RDS). Preterm birth complications account for close to a third of all neonatal deaths globally, with RDS due to primary surfactant deficiency being the most frequent cause of these avertable deaths (5). In low and middle-income countries (LMICs), mortality rates from RDS are as high as ten times more than in developed countries (8) In addition, long-term morbidity in preterm patients with RDS includes bronchopulmonary dysplasia and other chronic lung diseases, cerebral palsy, and childhood epilepsy (8).

Regardless of the cause, respiratory distress can progress to respiratory failure, cardiorespiratory arrest and death if not recognized and managed promptly (2). Respiratory support in form of non-invasive ventilation [Continuous Positive Airway Pressure (CPAP), Non-invasive positive pressure ventilation (NIPPV), high flow nasal cannula (HFNC), and nasal high-frequency oscillation ventilation (nHFOV)], invasive mechanical ventilation and surfactant administration are routinely used in high-income countries(9,10). However, these costly interventions require a high level of expertise and this may not be economically sustainable and feasible for LMICs (7). In this regard, low cost CPAP devices have been developed and are being implemented on an increasingly larger scale in LMICs, to reduce the high burden of morbidity and mortality in neonates(7,11–14).

Various international guidelines including those from The World Health Organisation (WHO), The European Consensus and the American Academy of Paediatrics advocate for the early use of Continuous Positive Airway Pressure (CPAP) as a standard of care in managing neonatal respiratory distress(2,15,16). The Kenyan Basic Paediatric protocols and Comprehensive newborn guidelines include guidance on CPAP use in our setting(17,18). Its use is associated with reduced progression to respiratory failure, reduced rates of mechanical ventilation, and death (4,8,19).

Bubble CPAP provides a simple, safe, and cheaper way of delivering CPAP in LMICs with varying levels of effectiveness ranging from 42% to 85%(20). In this type of CPAP, the air pressure is regulated and set by immersing the end of the expiratory limb in water. The level of depth of the expiratory tube in the water determines the pressure in the system. This pressure maintains the alveoli patent, prevents atelectasis and improves the functional residual capacity (FRC), in support of the neonates' breathing(7). A systematic review of Bubble CPAP implementation in Sub-Saharan Africa demonstrated that when it is utilized well, it could lessen by 30-50%, the need for mechanical ventilation, without increasing mortality(21)

In Kenya, between July 2014 and April 2016, the Centre for Public Health and Development (CPHD) implemented a program to train health care workers as well as provide CPAP equipment and accessories to 13 hospitals. Additionally, through the Newborn Essential Solutions and Technologies (NEST 360°) initiative, 13 public hospitals have received CPAP machines as well as other medical technologies since January 2020.

A few studies have been carried out in NEST 360° implementing countries such as Malawi, Tanzania, Kenya, and Nigeria. Most of these studies were in tertiary level facilities where CPAP was piloted. These studies showed that the barriers to implementation of CPAP in these countries included inadequate and/or unreliable supply of CPAP equipment and accessories, staffing shortages, inadequate staff training, rigid division of roles among health care providers and caregivers' hesitancy(22–25).

There is a paucity of data regarding the use of CPAP in Kenya, especially in secondary level facilities, that have recently received CPAP machines. These facilities typically do not have neonatologists or neonatal nurses. In addition, they often lack equipment for effective monitoring as part of the issues that generally plague the Kenyan health system. This study sought to audit the current practice in the implementation of CPAP in these secondary level facilities, seeking to identify the gaps in CPAP use, application of local guidelines and impact of scaling up of CPAP. It will serve to inform guideline implementation and capacity building.

## 1.1 Literature review

### 1.1.1 Aetiology and Pathophysiology of Respiratory Distress in Neonates

The causes of neonatal respiratory distress are diverse and multi-systemic ranging from airway obstruction and malformations to pulmonary, cardiovascular, neurological and systemic causes. Pulmonary causes may be due to developmental/congenital abnormalities. More commonly, they arise as complications during the transition to extra-uterine life, including Transient Tachypnea of the Newborn (TTN), Respiratory Distress Syndrome (RDS), Meconium Aspiration Syndrome (MAS), neonatal pneumonia, persistent pulmonary hypertension of the newborn (PPHN) and pulmonary haemorrhage, among others (1,2,5).

Respiratory distress may also arise due to cardiac conditions in the newborn including congenital heart defects, cardiac failure, conduction or rhythm abnormalities, pericardial effusions and tamponade. Neuromuscular conditions such as hypoxic-ischemic encephalopathy, neonatal meningitis, obstructed hydrocephalus, spinal muscular atrophy and neonatal myasthenia gravis, can also present with respiratory distress. Furthermore, systemic disorders such as sepsis, acidosis, hypoglycaemia, anaemia, inborn errors of metabolism and electrolyte abnormalities, may also present with respiratory distress (1,2).

Respiratory Distress Syndrome (RDS) specifically is a condition that results from deficiency or dysfunction of surfactant in the immature lungs of premature neonates. Surfactant is a substance that lines the alveoli and reduces surface tension, hence preventing the collapse of the alveoli at the end of expiration. The deficiency causes alveolar collapse, atelectotrauma, atelectasis, decreased lung compliance, altered ventilation and perfusion, and subsequent increased work of breathing(5,8). Surfactant usually reaches optimum level by 35 weeks of gestation and therefore neonates born before this gestation are at increased susceptibility to neonatal RDS (26).

In the 2015 European perinatal health report, the rate of respiratory distress syndrome among preterm neonates born at 24-25 weeks was 92%, 88% at 26-27 weeks, and 57% at 30-31 weeks of gestation (27). RDS usually presents at birth or shortly thereafter (within 4 hours) followed by clinical progression with increasing severity over the first two days of life. This clinical course can be altered by timely exogenous surfactant administration and early use of continuous positive airway pressure (CPAP). If RDS is left untreated, it alters lung function and results in progressive hypoxemia, respiratory failure, and death.

Regardless of the cause, the initial stage of respiratory failure is marked by attempted compensation. There is increased oxygen demand and increased work of breathing to maintain respiratory airflow, despite decreased lung compliance(2).

### 1.1.2 Epidemiology of respiratory distress in neonates

Respiratory distress in neonates is a noteworthy cause of morbidity and mortality in the world, occurring in 7% of all newborns with a varied regional distribution (2). It accounts for a significant number of neonatal intensive care patients and is the most common cause of respiratory arrest in neonates(28,29) . It is more common among premature (30%) and post term (21%) than among term newborns (4.2%) (3). The prevalence of neonatal respiratory distress is considerably higher in LMICs in comparison to the developed world. In addition, the case fatality rate for neonatal respiratory distress in LMICs is unacceptably high at 20% (4). In a 2011 epidemiological survey across 20 hospitals in China, 580 /17406 (3.3%) of the neonates had respiratory distress, with an average gestational age of 33 weeks (30). In a 2019 study of 6120 neonates at a teaching hospital in India, the overall respiratory distress prevalence was 4.4% (3). In contrast, a cross-sectional descriptive study of 625 newborns admitted to a Nigerian Teaching hospital over 2 years from 2012, found that 164 (26.2%) of them had respiratory distress (31)

As a subset of respiratory distress, respiratory distress syndrome (RDS) incidence is also variable. RDS mostly affects preterm babies, but also occurs in 6.8% of term and near term newborns with respiratory distress (28). The general prevalence of RDS in the United States is roughly 1%, with 20,000-30,000 babies developing RDS annually and contributing to 2.3% of all infant deaths (8). The reported prevalence of RDS is 18.5% in France, 4.2% in Pakistan and 20.5% in China (28).

In a 2018-2019 study of 2280 hospitalized newborns in Nigeria and Kenya, the burden of all respiratory conditions in neonates was found to be 35.8% with a high risk of mortality (32). In a multisite retrospective cohort study on neonatal mortality in Kenyan hospitals over 2 years from April

2018 to March 2020, involving 40,183 neonates, RDS accounted for 18% of overall admissions and was the most common disorder (37%) in those patients less than 2000 grams (33). This represents a significant local disease burden.

### 1.1.3 Non-invasive respiratory support in neonatal respiratory distress

Several modalities of non-invasive respiratory support have been used in neonates with respiratory distress. They include high flow nasal cannula (HFNC), non-invasive positive pressure ventilation (NIPPV), bi-level CPAP (BiPAP), CPAP, and nasal high-frequency oscillation ventilation (nHFOV)(9,10). A 2020 systematic review and network meta-analysis of 35 studies, that included 4078 neonates across various neonatal intensive care units, showed that NIPPV was more effective in reducing the need for mechanical ventilation than CPAP. NIPPV was also associated with a lower risk of pulmonary air leaks, bronchopulmonary dysplasia or death, compared to CPAP (9). However, these interventions are mostly unavailable and not feasible for use in LMICs due to high cost, shortage of specialized staff and lack of expertise.

In addition, studies on low-cost CPAP use in LMICs have shown that CPAP is an effective and safe therapy in preterm neonates with respiratory distress in these settings. It lessens in-hospital mortality, minimizes referrals and the need for mechanical ventilation (13,14).

Nasal CPAP (NCPAP) maintains continuous inspiratory and expiratory pressure, splints the airway, and reduces resistance to airflow, thus preventing airway collapse. The continuous positive pressure recruits and distends the alveoli hence improving pulmonary compliance. In this way, CPAP increases the functional residual capacity (FRC), facilitates better ventilation and lung perfusion, and reduces the neonates' oxygen requirement. It also increases the contractility of the diaphragm and maintains the stability of the chest wall, hence modulating the respiratory rate. Furthermore, CPAP promotes surfactant production and preservation, reduces alveolar oedema, and facilitates growth of the lung. It thus significantly lowers neonatal morbidity and mortality (7).

CPAP works through the delivery of humidified gas under continuous controlled positive pressures, via an interface, to a spontaneously breathing patient (Figure 1).

***Figure 1:*** Image of a bubble CPAP machine (34)

The CPAP system consists of three components. The first component is an inspiratory circuit through which gas flows continuously. It is connected to a source of oxygen. An oxygen blender allows the gas to be supplied according to the appropriate Fraction of inspired oxygen (FiO2), while a flow meter controls the flow rate of the inhaled gas. A humidifier moisturizes and in some devices warms the inhaled gas. The second component is the interface device that connects the CPAP circuit to the neonate's airway. Nasal prongs are the most widely used interface. The final component is the mechanism for generating positive pressure in the circuit. Positive pressure can be achieved by inserting the expiratory limb in water or 0.25% acetic acid solution to the desired depth (5 cm), or by variable flow CPAP or high flow nasal cannula (7). Immersing the expiratory limb of a respiratory circuit in an underwater seal, generates bubbles with patient exhalation, (bubble CPAP) (4) (Figure 2).

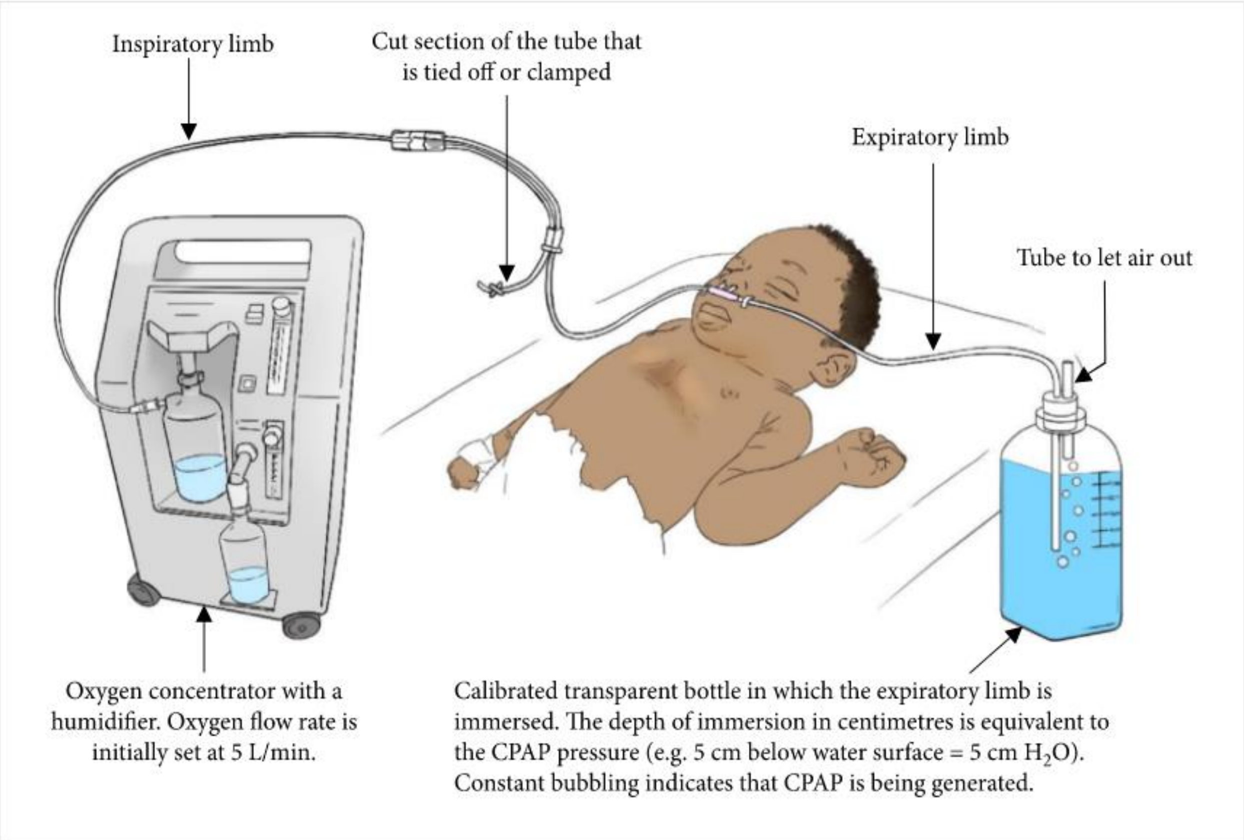


***Figure 2****:* An illustration of an improvised bubble CPAP system**(7)**

As a mode of NCPAP, bubble NCPAP (bNCPAP) has been introduced and operated by clinical staff of different cadres in various New-born Units in Africa after short durations of training in LMICs (7,12–14,21,35). These low-cost bubble CPAP devices may be as efficacious as the commercial CPAP machines used in higher-income countries (7,13,14,21). Nevertheless, the successful implementation and impact on health outcomes of this intervention depends on the availability, health infrastructure, and presence of skilled health personnel (7,36).

### 1.1.4 Use of nasal Continuous Positive Airway Pressure in Neonates

In a tertiary hospital in Blantyre, Malawi in 2012, a prospective non-randomized control study to evaluate the effectiveness of a low-cost bubble CPAP system was conducted, among 87 newborns (62 bCPAP, 25 controls), weighing > 1 kg, with severe respiratory distress. There was a 71% (44/62) survival rate among neonates with severe respiratory distress who received low-cost bCPAP, compared to 44% (11/25) among those managed on standard oxygen therapy. Among the Very Low Birth Weight neonates who received bCPAP therapy, 65.5 % (19/29), survived to discharge, compared to 15.4% among the controls. Close to two-thirds, 64.6% (31/48) of neonates with respiratory distress syndrome (RDS) receiving bCPAP survived to discharge compared to 23.5% (4/17) of controls. About 60% of newborns with sepsis who received CPAP survived to discharge, while none in the control group survived. In this study, it was established that using low-cost bubble CPAP in the management of neonatal respiratory distress improved survival by 27% (14).

Following the introduction of CPAP in 26 government hospitals in Malawi, from 2013 to 2015, an observational study was carried out involving 2651 neonates with respiratory distress, to evaluate CPAP usage and outcomes in NBUs. There was higher survival to discharge for all neonates admitted with respiratory distress (48.6% vs 54.5%; $P = .012$) and RDS (39.8% vs 48.3%; $P = .042$). Neonates with normal mean body temperatures during CPAP therapy had the highest survival rates (65.7% for those treated with CPAP and 60.0% for those diagnosed with RDS) (37). A follow-up study was carried out in 23 government district hospitals in Malawi between 2016 and 2017, following the national scale up of a nurse-led CPAP program. In this study, 362 neonates with respiratory distress and weighing 1-1.3 kg were analysed. Survival of neonates weighing 1-1.3 kg and treated with CPAP improved to 30.1%, compared to neonates of the same weight band treated with oxygen during the baseline (17.9%) and implementation (18.3%) periods (23).

In Uganda, a retrospective study of CPAP use in Very low birth weight (VLBW) neonates (weight < 1500 g) was carried out at a regional referral hospital, for two distinct periods from 2015 to 2017. The neonate admission records of 377 patients (188 pre-bCPAP period, 219 post-bCPAP period) were reviewed. In general , there was a 44% decline in mortality associated with RDS (OR 0.56, 95% CI 0.36–0.86; p = 0:01 ) (11).

In 2017 in a tertiary facility in Tanzania, a randomized control trial recruited and randomized 48 preterm patients with RDS into those managed on bCPAP, and those on conventional oxygen (25 vs 23 respectively). The neonates in the bCPAP group had 30% higher survival, lower risk of death and shorter hospital stay, compared to the oxygen therapy group (20).

A study of 118 preterm neonates was carried out in Kijabe Hospital in Kenya (a secondary level facility), in two 18-month periods from 2007 to 2011, before and after introduction of bCPAP. There was a higher survival-to-discharge rate of 85% compared to 61% pre-implementation of CPAP and lower rates of referral of preterm infants with RDS after introduction of bCPAP (4% vs. 17%) (12). Subsequently, more public facilities in Kenya have introduced and scaled up CPAP use since 2014 with CPAP available in twenty-two government hospitals to date. Additionally, the Ministry of Health (MoH) of Kenya recommended CPAP use in newborns with respiratory distress and developed a national guideline on the same in 2016 (8).

In 2018, a quality improvement initiative was carried out in Nakuru County Referral Hospital to increase the proportion of neonates with respiratory distress treated with bCPAP from 2% to 25% by January 2019. It involved change in organization of infrastructure, staff training and development/implementation of treatment protocols. 405 infants were included in the pre-initiative group, with 2% bCPAP use while 1157 infants were included in the post-initiative group, with

100/567 (17.6%) of those with respiratory distress treated with bCPAP. This demonstrated that it was possible to build capacity for the use of bCPAP to treat neonates with respiratory distress a low-resource setting(19).

To explore the experiences of using CPAP in neonatal care among healthcare workers and identify factors that would lead to successful scale-up, a qualitative study was carried out to across 19 secondary and tertiary level hospitals in Kenya, from September 2017 to February 2018. The main barriers reported were inadequate infrastructure, shortage of skilled staff and inadequate knowledge and training of staff. The key facilitators reported were positive patient outcomes after CPAP therapy and partnership with patient caregivers. The study identified key challenges that threaten safe and sustainable use of CPAP. The authors recommended optimal staff training and availing of enough infrastructure and resources to support its use(24).

There is however paucity of data on the implementation of CPAP in the country and more so in secondary level facilities, which are the focus of this study.

### 1.1.5 Criteria for initiation, patient monitoring, and weaning CPAP in neonates

According to the Kenyan Basic Paediatric Protocols of 2016 and Comprehensive Newborn Protocols of 2021, CPAP is indicated for the management of respiratory distress in neonates(17,18). Both of these guidelines were also updated and launched in November, 2022. They contain additional guidelines on CPAP use in neonatal respiratory distress (40,41). CPAP is indicated in neonates with respiratory distress who are at or above 28 weeks of gestation, and birth weight greater than 1000 grams, with an Apgar score of more than 4 at 5 minutes, and a Silverman Anderson Score of more than 4 (Table 1). It is deferred if uncontrollable seizures, floppy infant or apnoeic or gasping respiration (Figure 3). CPAP should be commenced prophylactically in neonates between 28- and 30-

weeks gestation or weighing 1000-1300 grams. It is used as rescue therapy in neonates above 30 weeks gestation with respiratory distress (respiratory rate > 60 breaths per minute, grunting, nasal flaring, sternal or intercostal recession, and severe lower chest wall indrawing), SpO2 less than 90% despite a clear airway and heart rate more than 100, after 15 minutes of standard oxygen therapy (Figure 4) (18)

Additional guideline revision of the Comprehensive Newborn Care Protocols in 2022 provides further guidance on CPAP monitoring, weaning, recognition of CPAP failure and complications as well as recommended preventive and corrective actions. It also provided for CPAP use in those below 28 weeks or below 1000 grams if resources are available (18).

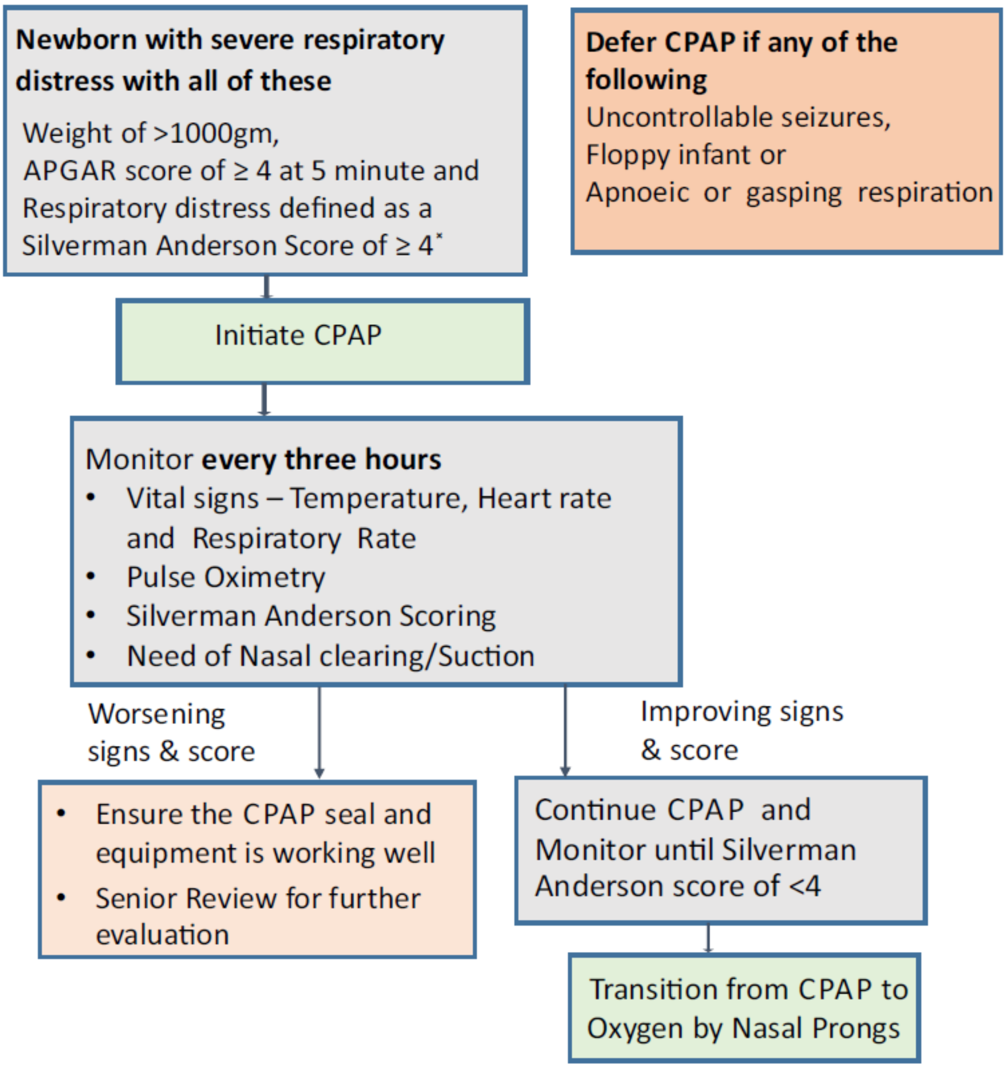


***Figure 3:*** CPAP Protocol, Kenya Basic Paediatric Protocols, 2016 (17)

***Table 1:*** Silverman Anderson Score

| Silverman- Anderson Score | | | |
|---|---|---|---|
| **Feature** | **Score 0** | **Score 1** | **Score 2** |
| Chest Movement | Equal | Respiratory Lag | Seesaw Respiration |
| Intercostal Retraction | None | Minimal | Marked |
| Xiphoid Retraction | None | Minimal | Marked |
| Nasal Flaring | None | Minimal | Marked |
| Expiratory Grunt | None | Audible with Stethoscope | Audible |

**Ministry of Health, Republic of Kenya, Basic Paediatric Protocols, 2016,** (17)

A score of 0: no respiratory distress, 1-3: mild respiratory distress, 4-6: moderate respiratory distress, ≥7: impending respiratory failure, 10: severe respiratory distress.

The key to the success of CPAP therapy is early initiation and other concurrent measures such as medication, warmth, feeding and other essential newborn care, as well as intensive monitoring. According to the Comprehensive Newborn Care guidelines, CPAP is initiated at a Fraction of Inspired Oxygen (FiO2) of 50%, total flow of 6 litres/minute, oxygen flow at 3 litres/minute, and CPAP water level of 6 cm. The FiO2 is titrated upward or downward by 20% (0. 5 litres/ minute) every 60 seconds until an oxygen saturation (SpO2) of 90-95% is achieved. The patient's heart rate, respiratory rate, SpO2 is reassessed at 15 minutes, 1 hour, and then 3 hourly whenever CPAP settings are adjusted. The water level can be increased by 1 cm every 3 hours to a maximum of 8 cm of water if SpO2 is more than 90% but the patient still has severe respiratory distress. As the neonate stabilizes, oxygen is weaned down before weaning down the pressure. Pressure is weaned by 1 cm every 3 hours until 5 cm. CPAP is then stopped if the neonate is stable at FiO2 of 30%, with a CPAP of 5 cm of water and SpO2 of 90-95% (18).

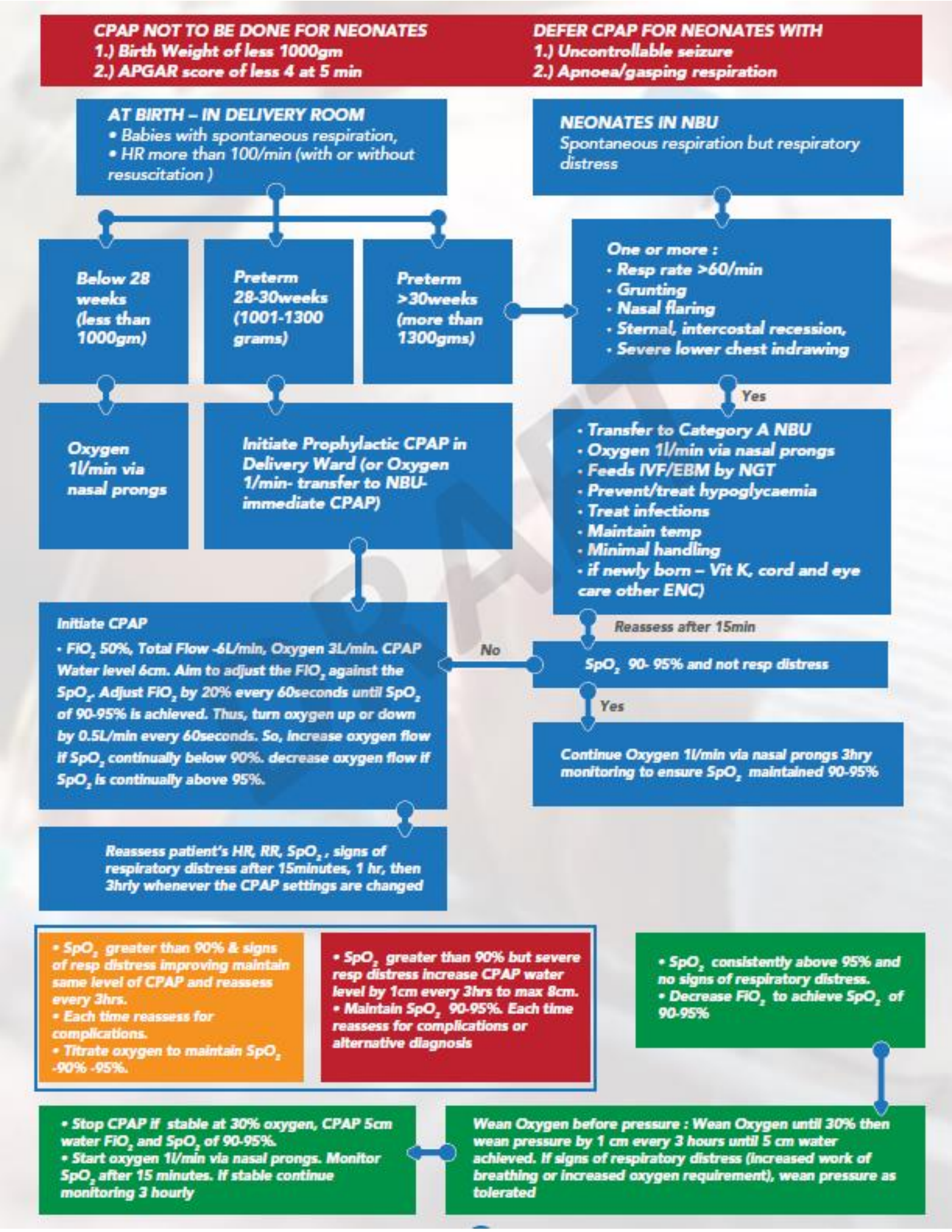


***Figure 4:*** CPAP protocol, Kenya Comprehensive Newborn Care Protocols, 2021(18)

An audit study of 72 neonates on CPAP was carried out in Kenyatta National Hospital NBU in 2022. The study showed poor overall documentation on CPAP use and monitoring. FiO2 was documented in 56 (77.8%), PEEP in 48 (66.7%), pulse oximetry in 71 (98.6%) There was no documentation on the position of the head nor the nasal prong size/position in all the neonates. Documentation on weaning of CPAP was done in 33 (45.8%) and it was gradual and successful in 17 (23.6%). Appropriate CPAP use as per the Kenyan guidelines was found to be 75.2% (42)

### 1.1.6 Outcomes of neonates who receive CPAP for management of respiratory distress

Oxygen therapy with CPAP is used to improve oxygenation and carbon dioxide elimination in neonates, reducing prolonged oxygen dependency. This technology serves to reduce airway resistance, improve and increase Functional Residual Capacity (FRC), prevent alveolar collapse, prevent muscle fatigue, increase lung expansion, reduce excessive respiratory effort, and maintain surfactant production and function. It also maintains airway patency and increases its diameter, provides better ventilation-perfusion matching, stimulates lung growth, and reduces the risk of infection and local airway trauma (7).

Side effects of CPAP are usually mild and are related to air leaks or pressure around the mask/interface. This results in dry mucus membranes, erythema or rash of the skin, nasal excoriations, cartilage injuries, septal distortion, and in more severe cases, pressure ulcers on the skin or nasal septum. Sodium chloride nasal drops, and the use of humidified air can reduce side effects. Other complications include over distention of the lungs, pneumothorax, gastric distension, increased pulmonary vascular resistance, infection, and even mortality (7,43).

### 1.1.7 Factors associated with adverse outcomes in neonatal respiratory distress

#### 1.1.7.1 Prematurity

Globally, the World Health Organization (WHO) estimates that 15 million babies are born premature annually translating to 1 in every 10 babies born (44,45). In a recent systematic review and meta-analysis of the impact of RDS and birth asphyxia exposure on the survival of preterm neonates in East Africa, the pooled mortality rate among preterms was found to be 19.2%, with a 3-fold increased risk of death in those preterms with RDS (46). In 2013, Wagura et al. carried out a study in Kenyatta National Hospital(KNH) and found the prevalence of premature births as 18.3% (95% CI: 14.1,22.5) (47). The Incidence of Respiratory distress syndrome and associated mortality was high among preterm neonates. A prospective descriptive study to determine short-term outcomes of preterms with RDS was done in 2015 at Moi Teaching & Referral Hospital (MTRH), Eldoret, Kenya. This study enrolled 94 premature neonates with RDS. CPAP was utilized in 62.8% (95% CI: 52.2, 72.5), while the rest were managed on conventional oxygen via nasal prongs and none of them received surfactant. Mortality at day 10 was 61% (0.61 95% CI: 0.51, 0.71) (48).

#### 1.1.7.2 Perinatal asphyxia

Perinatal asphyxia is defined as failure to initiate or maintain spontaneous breathing at birth. Asphyxia and the development of respiratory distress have a positive association. Severe birth asphyxia causes acute lung injury that decreases production and secretion of surfactant. Hypoxia, acidosis, and hypotension due to myocardial dysfunction have been shown to reduce the production of surfactant. Increased pulmonary capillary permeability results in plasma protein extravasation into the alveolar space, which in turn inactivates surfactant. Furthermore, reperfusion injury after oxygen supplementation leads to further depletion of surfactant by excessive free oxygen radicals. Severe asphyxia significantly increases mortality in neonates with respiratory distress and prolongs their hospital stay (49).

#### 1.1.7.3 Gender

A scoping review published in 2017 showed a significant disparity in respiratory morbidity and mortality by gender, with more males affected(50). Several factors contribute to these differences. For instance, surfactant production occurs earlier in female lung development than in male fetuses. In addition, epithelial sodium transport channels (ENaC) crucial for alveolar fluid clearance, are expressed in higher numbers in female foetuses compared to males. Sex hormones have also been shown to have an impact on fetal lung development. Androgens have been shown to inhibit surfactant production while estrogen favours type II pneumocyte proliferation and surfactant production (50,51). In a 2014 retrospective case control study of 615 term neonates with RDS at a Beijing Hospital, the relative risk of RDS was 2.6 times greater in males than in females (OR: 2.641; 95% CI: 1.721–4.053) (49).

#### 1.1.7.4 Mode of delivery and low birth weight

Elective caesarean section without labour is related to respiratory distress. One recent meta-analysis showed a 1.7-fold increase in the probability of respiratory distress in babies born via caesarean section without labour (52). The absence of the physiologic events that accompany spontaneous labour such as a surge in endogenous catecholamines and steroids has been shown to increase the risk. One study found an absence of endogenous prostaglandins in the absence of labour causes pulmonary hypoperfusion leading to persistent pulmonary hypertension(PPHN) and respiratory distress (53,54). A 5-year review of birth cohorts in the US showed an adjusted odds ratio for neonatal mortality of 1.69 (95% CI 1.35-2.11) for caesarean delivery without labour, compared with planned vaginal deliveries. This translated to a 69% higher risk of death in this cohort (55). In addition, respiratory distress is also more likely in babies born with low birth weight (49).

#### 1.1.7.5 Hypothermia

Preterm neonates with hypothermia have a two-fold increase in developing respiratory distress compared to those who are normothermic(56). Cold stress causes sequelae such as tissue hypoxia and acidosis, which in turn reduce surfactant production. A 2018 retrospective analysis evaluating the effect of hypothermia on outcomes of 65 neonates diagnosed with RDS found that not one of the neonates with a mean temperature under 35.8°C survived to discharge, despite the treatment modality offered for RDS (56).

#### 1.1.7.6 Maternal diabetes and macrosomia

The incidence of respiratory distress is higher in infants of diabetic mothers, due delayed pulmonary maturity despite the apparent macrosomia. Hyperglycaemia in the foetus results in the stimulation of insulin, insulin-like growth factors and growth hormone. Insulin inhibits the differentiation of type 2 pneumocytes, which produce surfactant. Hyperinsulinemia also inhibits surfactant biosynthesis, because insulin inhibits the accumulation of surfactant protein messenger Ribonucleic Acid (RNA), therefore down-regulating their production. Infants born to diabetic mothers are at a higher risk of preterm delivery compared to normoglycemic mothers, thus at a higher risk of surfactant deficiency (57). The neonatal mortality rate in infants of diabetic mothers is more than five times that of infants of non-diabetic mothers, irrespective of the gestational age and birth weight (58). A 2018 meta-analysis of 24 studies showed an association between maternal diabetes and the risk of neonatal RDS, with a pooled odds ratio (OR) of 1.47 (95% CI 1.24–1.74) (59).

#### 1.1.7.7 Sepsis

Sepsis is a potentially fatal condition that occurs when the immune system exhibits an exaggerated response to infection. It may present with respiratory distress in neonates. Furthermore, sepsis and the resultant inflammation causes a secondary surfactant deficiency due to lung injury, decreased synthesis and secretion of surfactant as well as inactivation of surfactant (29,31,49). Therefore, all neonates with respiratory distress should be screened for sepsis.

#### 1.1.7.8 Familial predisposition

Rare genetic disorders may contribute to respiratory distress including genetic absence of Apoproteins, which leads to deficiency in surfactant protein (SP)-B and SP-C. Mutations in the adenosine triphosphate binding cassette gene (ABCA) result in the poor lamellar body formation, altered phospholipid metabolism and thus inactive surfactant. Mutations in surfactant transporter genes (ABC transporter 3) have been documented with severe and often fatal forms of respiratory distress (60).

#### 1.1.7.8 Multiple gestation

Preterm births are seen in 50-60% of twin pregnancies, 90% of triplets and almost 100% of quadruplet pregnancies(54). One study showed respiratory distress occurred in 23% of triplets, 65% of quadruplets, and 75% of quintuplets (61). The average twin gestation is 35 weeks and this reduces to 33 weeks and 30 weeks in triplets and quadruplets respectively(62). Prematurity results in primary surfactant deficiency. Additionally, there is an increased rate of caesarean section among this population. In a multicenter analysis of the KIDs inpatient database in the US, over 22 million neonatal records spanning 15 years were analyzed for multiple gestation outcomes compared to singleton births. This study established that neonates born in multiple gestations have higher mortality and longer hospital stay unlike singleton births (63).

### 1.1.8 Nursing ratios

Nurses play a central role in care of small and sick newborns in the NBU.  Several interventions are carried out for this neonates such as nasogastric tube feeding, administration of intravenous fluids and medications, oxygen therapy and CPAP among others. According to the American Academy of Pediatrics guidelines for Perinatal Care, the internationally recommended ratios of newborn to nurses is 4:1 for basic or continuing care; 2-3:1 for stable babies requiring intervention; and 1:1 for high-dependency care (64). In contrast there are major staff shortages in many facilities in Kenya with documented neonatal patient to nurse ratios as high as 15:1(65). This affects the quality of care offered as including proper titration of CPAP therapy and monitoring.

### 1.1.9 CPAP equipment requirements

The recommended number of CPAP machines in a district level facility is 2-4 per high care beds in secondary level facilities according to the UNICEF toolkit for setting up Special Care Newborn units(66). Continuous monitoring of SPO2 is the ideal standard of care for patients on NCPAP to allow careful titration of FiO2 and pressures(67)

# CHAPTER TWO

# 2.0 STUDY JUSTIFICATION

## 2.1 Study justification

Before the introduction of the New-born Essential Solutions and Technologies (NEST) 360 bundle, the majority of NBUs in secondary referral hospitals had none or just one functional CPAP machine and were thus managing neonatal respiratory distress with conventional oxygen therapy (33). The equipment delivered included CPAP machines, oxygen concentrators, oxygen splitter, pulse oximeters, suction machines, phototherapy machines, light meters and radiant warmers. Initial training was carried out on the use of these technologies, with continued training and technical support by NEST. However, many of these facilities do not have access to neonatologists or neonatology nurses. Registered nurses, paediatricians, medical officers, and clinical officers offer CPAP therapy in these facilities (33). The effective use of NCPAP requires adequate training, staffing, and close patient monitoring. This involves titration of oxygen concentration as well as the institution of correct pressures while monitoring oxygen saturation and patient clinical response to treatment. Adequate management of neonates with respiratory distress on nasal CPAP may reduce morbidity and mortality significantly (7,13,14).

With this recent introduction of CPAP machines at some county and sub-county hospitals in Kenya, there has been a change in the management of respiratory distress. However, the implementation of CPAP and the patient outcomes have not yet been well documented. This study sought to understand the uptake and implementation of CPAP technologies as well as patient outcomes in secondary-level facilities that are often less resourced in terms of staff and equipment. We evaluated in four of the recipient hospitals, the criteria used for initiation and cessation of nasal CPAP in neonates, monitoring of patients, and patient outcomes. The aim was to inform better implementation of clinical guidelines and best practice for CPAP across the wider network within the Kenyan Health System.

## 2.2 Research Questions

1. What proportion of neonates admitted to the Newborn Units under study have respiratory distress?
2. What is the prevalence of CPAP use in neonates with respiratory distress, the criteria used for initiation, monitoring and weaning of CPAP?
3. What are the patient outcomes and factors determining adverse patient outcomes in the neonates admitted with respiratory distress and managed on CPAP in participating hospitals?

## 2.3 Objectives

### 2.3.1 Primary objectives

To audit the use of nasal continuous positive airway pressure in neonates with respiratory distress admitted to the newborn units in participating hospitals, and to describe the criteria used by healthcare workers to initiate, wean, and stop CPAP as well as patient monitoring during CPAP therapy.

### 2.3.2 Secondary objectives

1. To determine outcomes of neonates who receive nasal CPAP for management of respiratory distress.
2. To determine factors associated with adverse outcomes in the neonates admitted with respiratory distress who are managed on CPAP in participating hospitals.

# CHAPTER THREE

## 3.0 STUDY DESIGN AND METHODOLOGY

### 3.1 Study design

A retrospective, hospital-based, cross-sectional observational study that utilized inpatient neonatal data from January 2020 to December 2022, at the newborn units of four secondary-level county referral facilities.

### 3.2 Study area description

The study was conducted in Newborn Units at Mama Lucy Kibaki Hospital, Bungoma County Referral Hospital, Machakos County Referral Hospital and Kiambu County Referral Hospital. The four sites were selected by purposeful sampling with regional consideration as well as considering the number of newborn admissions. The sites are all secondary-level referral facilities that have a combined average admission of 7000 neonates per year. The average monthly admissions per hospital are shown in Table 2 below.

These are among the 13 sites that received bundles of technologies via the NEST 360 collaboration between the Ministry of Health and development partners and are part of the Clinical Information Network (CIN). Each of the facilities each had one CPAP machine prior to the NEST donations.

CIN has two linked networks namely, CIN-Paediatrics (CIN-Paeds) and CIN-Neonatal. CIN-Neonatal generates data from 24 county-level hospitals in Kenya from standardized newborn admission and discharge records (33,68). The average number of monthly admissions, staffing, bed space, and time of joining CIN for the four study sites are further described in Table 2 below. The equipment delivered to the four sites is described in

Table 3.

***Table 2:*** Study sites average monthly admissions, staffing, bed space, time of joining CIN

| **Information** | **Mama Lucy** | **Bungoma** | **Machakos** | **Kiambu** |
|---|---|---|---|---|
| Average monthly newborn admissions | 165 | 108 | 180 | 185 |
| Year when the site joined CIN | June 2017 | November 2018 | March 2018 | October 2018 |
| Staffing | | | | |
| Nurses – day shift: | 4 | 2 | 5 | 3 |
| Nurses – night shift: | 3 | 1 | 3 | 2 |
| Clinical Officers: | 0 | 0 | 7 | 3 |
| Medical Officers: | 0 | 1 | 1 | 0.5 |
| Paediatricians: | 1 | 1 | 1 | 1 |
| Neonatologist | 1 | 0 | 0 | 0 |
| Bed capacity* | 30 | 40 | 53 | 40 |
| Cots: | 15 | 17 | 53 | 39 |
| Incubators: | 8 | 10 | 7 | 8 |

Source: NEST 360 report

*Note*. *Bed capacity = (Total number of beds/cots, radiant warmers & incubators)

Medical Officers/Pediatricians; where 0.5, they spend 50% in newborn units and 50% in Paediatric wards

***Table 3:*** Equipment delivered by NEST to the study sites

| Hospital | Date delivered | CPAP | Oxygen concentrator | Oxygen Splitter | Pulse oximeter | Suction machine | Phototherapy machines | Light meter | Radiant warmer |
|---|---|---|---|---|---|---|---|---|---|
| Mama Lucy | 20/1/2020 | 3 | 3 | 3 | 3 | 2 | 4 | 1 | 2 |
| Bungoma | 30/10/2020 | 2 | 4 | 2 | 2 | 4 | 3 | 1 | 2 |
| Machakos | 23/11/2020 | 3 | 4 | 3 | 3 | 3 | 5 | 1 | 2 |
| Kiambu | 22/3/2021 & 23/4/21 | 4 | 1 | 3 | 3 | 3 | 3 | 1 | 2 |

**Source:** NEST 360 report

### 3.3 Study population

All medical records of neonates (0-28 days) admitted to the Newborn Units of the selected facilities from January 2020 to December 2022, with features of respiratory distress including a diagnosis of respiratory distress syndrome were identified and analysed to determine baseline demographics and summary statistics from the CIN-Neonatal database. In addition, facility medical records were sought for all neonates managed on CPAP. Only 259 records (medical files) of neonates managed on CPAP were available and were further analyzed for criteria used, monitoring, and outcomes. The rest of the files were unavailable due to archiving and loss of files.

#### 3.3.1 Inclusion criteria

The study included medical records of:

- Neonates less than 28 days old who had been admitted to the newborn units in the study facilities
- Neonates with features of respiratory distress or a diagnosis or respiratory distress syndrome.

- Neonates with respiratory distress of any aetiology who were managed with nasal CPAP.

### 3.3.2 Exclusion criteria

The study excluded medical records of:

- Extreme pre-term babies less than 28 weeks gestation and/or birth weight less than 1000 grams.
- Neonates with severe congenital malformations and especially those with airway and respiratory malformations such as cleft lip and palate, diaphragmatic hernia, and tracheoesophageal fistula.
- Neonates with severe birth asphyxia with an Apgar score less than 4 at 5 minutes who have respiratory distress after delivery.
- Neonates with uncontrolled seizures, prolonged apnea, or gasping respirations at the time that CPAP was to be commenced.

## 3.4 Sample size determination

Fischer's formula was used to calculate the sample size.

$$n = \frac{Z^2 p (1-p)}{d^2}$$

Where;

n = desired sample size

Z = standard normal value corresponding to 95% confidence interval (1.96)

d= desired degree of precision (0.05)

p= proportion of neonates with respiratory distress managed with CPAP in a county level facility in Kenya, documented at 17.6 in 2018(19)

Based on the formula, the sample size was calculated as follows:

$$n = \frac{1.96^2 \times (0.176) \times (0.824)}{0.05^2} = 223$$

All eligible neonates (6,469) admitted to the selected facilities with features of respiratory distress were included among whom 1,211 neonates were managed on CPAP. We were able to retrieve and audit 259 medical records of neonates managed on CPAP from the 4 study sites (Mama Lucy Kibaki Hospital, Bungoma County Referral Hospital, Kiambu County Referral Hospital, and Machakos County Referral Hospital). The rest of the records were not available due to archiving and records losses.

### 3.5 Sampling procedure

All available medical records of eligible neonates were obtained and included in the study.

### 3.6 Recruitment and consenting procedures

The study analysed anonymised patient data on the CIN-Neonatal database with ethical permission sought for the same. Authorization was sought from hospital management of the facilities under study, to undertake secondary data collection and analysis from patient files and hospital CPAP records (Appendix 1) and to carry out a facility audit (Appendix 2)

### 3.7 Variables of interest

- Patient demographics (age, sex, birth weight, gestation, mode of delivery)
- The percentage of neonates admitted to NBUs with a diagnosis or RDS or features of respiratory distress (one or more signs of increased work of breathing, such as tachypnea (Respiratory rate >60 per minute), nasal flaring, chest retractions, head nodding, grunting or sPO2< 90.
- The proportion of neonates with respiratory distress who are managed with nasal CPAP
- Day of life at initiation on NCPAP, duration of treatment on nasal CPAP, and duration of hospital stay

- Time to reduction in tachypnea to <60 breaths per minute and time to increase in Oxygen saturations to >90%
- Need for mechanical ventilation as evidenced by
  - Increased work of breathing such as tachypnea, grunting, sternal and intercostal recession
  - Oxygen requirement of more than 40% to maintain SpO2 between 90-95% in 8 cm water level of CPAP
  - A rapid rise in oxygen requirement (an increase of 10% FiO2 to maintain SpO2 of 90-95% within a 3-hour period
  - Recurrent apnoeic episodes requiring stimulation (39)
- Oxygen dependence by day 28 of life
- Mortality rates in patients with respiratory distress who were managed with nasal CPAP and those managed on conventional oxygen
- Factors associated with adverse outcomes in the neonates such as prematurity, perinatal asphyxia, hypothermia, maternal diabetes, macrosomia, multiple gestation, and neonatal sepsis.

## 3.8 Study outcomes of interest

### 3.8.1 Primary outcomes of interest

Prevalence of CPAP use amongst neonates with respiratory distress and the criteria used to initiate, monitor, wean and stop CPAP.

### 3.8.2 Secondary outcomes of interest

Document factors associated with adverse outcomes in the neonates admitted with respiratory distress, who are managed on CPAP in participating hospitals.

### 3.9 Data collection tools, procedures and data management

This study involved two sets of data, (a) newborn demographic, diagnosis, and outcome data and (b) CPAP treatment data.

Data were obtained from the Clinical Information Network (CIN) - Neonatal database, on patient demographics (age, sex, birth weight) as well as diagnosis. Neonates with features of respiratory distress were also identified from the neonatal admission register. For some key data that was not available within the CIN dataset such as CPAP start and stop dates, vitals monitoring, and criteria for weaning of CPAP, a structured data collection tool was used to collect these supplementary data from patient records and facility CPAP records (*Appendix 3*).

#### 3.9.1 New-born demographic, diagnosis, and outcome data from CIN-Neonatal database

Newborn data is routinely collected in the network of participating hospitals' newborn units for all newborn admissions at discharge, whether alive, dead, or referred (33,68). Trained Health Records and Information Officers capture this data from patient files in a standardized tool and format with the guidance of standard operating procedures. Data are abstracted into a structured electronic tool that resembles New-Born Admission Records (NAR), monitoring, and exit forms (33). The NAR was co-developed by newborn care experts and providers and is endorsed by the Ministry of Health in Kenya. The purpose-designed standardized electronic data capture tool is created and hosted in Research Electronic Data Capture (REDCap) platform within KEMRI Wellcome Trust Research Programme's servers in Nairobi, Kenya . REDCap is a secure, web-based software platform designed to support data capture for research studies, providing:

- An interface for validated data capture
- Audit trails for tracking data manipulation and export procedures
- Automated export procedures for seamless data downloads to routine statistical packages

- Procedures for data integration and interoperability with external sources (69,70).

The tool collects demographics, baby and mother's history, examination, diagnoses, treatments, supportive care, nurse monitoring, and discharge data. The design of the tool incorporates data quality checks such as validation for data types per field, out-of-range checks, and skip patterns among others. Extended data quality checks are done through customized error-checking scripts programmed in R statistical software on a routine basis to ensure and enhance data quality (68).

CIN data is stored both in each hospital's locally hosted REDCap database as well as at web-based REDCap servers at KEMRI Wellcome Trust Research Programme – Nairobi. Access to these databases and servers is very controlled and limited (via passwords) to only authorized data collectors and data managers and study principal investigators. A remote backup is also implemented to safeguard against data loss. Identifying data is not collected from individual patient files (71).

### 3.9.2 Nasal CPAP treatment data

To supplement the study population's CIN sourced dataset, a structured data collection tool was designed and used to collect CPAP treated data from the four hospitals' NBU patient medical records and CPAP books retrospectively. These data included: CPAP start and stop dates, vitals monitoring (temperature, heart rate, oxygen saturation, and respiratory rate), and criteria for weaning CPAP among others. (*Appendix 3*). The collected data was then compared to the Kenyan guidelines that specify the timing and procedure of CPAP initiation, frequency of monitoring, titration of FiO2 and CPAP pressure (water level), weaning and cessation as described in section 1.1.5 above.

Inpatient numbers (IP) and unique record identification (ID) numbers from the CIN database for all newborns previously admitted with features of respiratory distress and managed using nasal CPAP were identified and used for patient files retrieval. Supplementary data was abstracted from these files into a pre-designed MS Excel spreadsheet by the both the study PI and four trained Health Records and Information Officers. Where information was missing from the patient files, CPAP registers and other NBU records were used. These data were merged with the initial CIN dataset using unique IPs and IDs to create one master dataset using R programming in preparation for analysis.

### 3.10: Study Personnel

The principal investigator and three trained research assistants collected data at the various facilities. These assistants were informed on the purpose of the study and the study tools and procedures. They also underwent a pilot data collection exercise to ensure, quality data collection.

### 3.11 Ethical considerations

Ethical and regulatory approvals were sought and obtained from the KNH Ethics and Research Committee (KNH/UON ERC- No. P202/03/2022) (Appendix 5) and the National Commission for Science, Technology, and Innovation (NACOSTI) (License: NACOSTI/P/21/11580) (Appendix 6).

This study was part of a larger body of research work already approved by KEMRI Scientific & Ethics Review Unit (SERU) PROTOCOL NO. KEMRI/SERU/CGMR-C/229/4203 (Appendix 7) and NACOSTI License No: NACOSTI/P/21/11580 (Appendix 8Appendix 8). An application was made to the KEMRI-Wellcome Trust Data Governance Committee, for authorization to use the CIN database for this study. A letter of support is included in Appendix 9. I also sought approvals from respective county medical directors and the hospital management at the facilities under study. The various approvals are attached in the appendices (Appendix 10-15).

The confidentiality of study participants (neonates under study) was ensured by the use of unique identification codes. The evaluation process did not directly interact with the participants, as this was a retrospective study using patient records.

A full explanation of the study was provided to selected hospitals and they were provided with the study protocol and reassured of the confidential nature of the research. In addition, the hospital names were anonymized during reporting. Only aggregated data was disseminated and specific information from each facility was kept confidential. As per the SOP, all data collected were anonymised and no personal identifiers were collected

### 3.12 Data management and analysis

The master dataset (described in the data collection procedures) was abstracted onto a Microsoft Excel Spreadsheet and exported into R version 4.2.2 for analysis. Complete case analysis for continuous and categorical data such as age, birth weight groups, gestation categories, respiratory distress prevalence, proportions of CPAP use, and outcomes among other indicators was descriptively reported in percentages and through measures of central tendency statistics (median with interquartile ranges, IQR). Tabular and graphical descriptions and statistical commentary were used to present the summaries. Missing values were reported alongside available data. The denominator for each variable excluded the neonates with missing information for the corresponding variable. Statistical significance was estimated at a p-value less than 0.05 and 95% Confidence Intervals (CI) reported alongside.

In the respiratory distress and CPAP-treated sample population data, two statistical models were fitted to provide estimates for two main outcome measures a) outcome at discharge and b) length of hospital stay. For newborn outcome at discharge analysis, we fitted a binary logistic regression (not alive (dead) – 1, alive – 0,) model while adding covariates in a forward stepwise manner. These co-variates were selected apriori due to literature indicating that these variables were associated with adverse newborn outcomes. The co-variates were gender, age at admission, time to admission, birth weight, prematurity, perinatal asphyxia, hypothermia, maternal diabetes, macrosomia, multiple delivery, and sepsis. Pearson's correlation coefficient tests for continuous variables and chi-square tests of independence among categorical independent variables involved in the model were conducted. Variables that showed high collinearity and inter-dependence, respectively, were dealt with appropriately from the model to improve the integrity of the estimates and statistical power of the model. Odds ratios and corresponding 95% confidence interval for each predictor variable in the model were reported.

Independent variables from the bivariate model such as sex, gestation age, birth weight, and day of initiation of CPAP among others were populated into the multivariate model while paying attention to collinearity. A logistic regression model was fitted. Model significance and factors associated with an increase or decrease in the average length of hospital stay are reported alongside adjusted $R^2$ values, p values and 95% confidence intervals.

### 3.13 Control of Bias and errors

Information bias was reduced by assessing the data entered on the computer daily to ensure validity of the data. Data was entered from file records in the monitoring charts, clinical notes and the CPAP books to minimize missing information.

### 3.14 Study timeline

The study was carried out over three months after ethical approval in October 2022 and subsequent NACOSTI, county and hospital approvals in November to December 2022.

CHAPTER FOUR

# 4.0 RESULTS

## 4.1 Primary objective: Overall neonatal admissions and outcomes, Respiratory Distress proportions and CPAP use.

A total of 23,119 neonates aged 0 to 28 days were admitted to the NBUs of the four hospitals under study (Kiambu County Referral Hospital, Mama Lucy Kibaki Hospital, Machakos County Referral Hospital, and Bungoma County Referral Hospital) between January 2020 and December 2022. Of these, 19,955/23,119 (86%) were discharged alive, 2771/23,119 (12%) died, 361/23,119 (1.6%) were referred, 19/23,119 (<0.1%) were reported to have absconded and 13/23,119 (<0.1%) of the files had missing documentation on the outcome. Of the 72 neonates who were in hospital for more than 28 days from birth, 8/72 (11%) required oxygen on day 28 of life, an indicator of chronic lung disease (

Table ***4***).

Among all the admitted neonates, 6,469 /23,119 (28%) had features of respiratory distress among who, 1,211/6469 (18.7%) were managed on CPAP (**Error! Reference source not found.**). However, 49/23,119(0.2%) of all the admitted neonates had missing information regarding CPAP use. H1 had the highest proportion of CPAP use at 43.8% (620/1416) of all neonates with respiratory distress admitted to the facility. In contrast, CPAP use was documented in 19.3% (231/1195) of neonates with respiratory distress in H2, 12.1% (152/1252) in H3 and 8.0% (208/2606) in H4. Of the overall 1,211 neonates managed on CPAP, 259 medical record retrieved for audit from the four facilities. The rest of the files could not be retrieved due to archiving. The breakdown per hospital is represented in

Table ***4*** below with hospital names anonymized as H1, H2, H3, and H4.

***Table 4:*** Newborn admissions, proportion with Respiratory Distress, CPAP use and outcomes in participating hospitals from January 2020 to December 2022

| **Characteristic** | **Overall, N = 23,119[1]**<br>**n (%)** | **H1, N = 3,698[1]**<br>**n (%)** | **H2, N = 7,255[1]**<br>**n (%)** | **H3, N = 6,506[1]**<br>**n (%)** | **H4, N = 5,660[1]**<br>**n (%)** |
|---|---|---|---|---|---|
| **Respiratory Distress** | 6,469 (**28%**) | 1,416 (38%) | 1,195 (16%) | 1,252 (19%) | 2,606 (46%) |
| **CPAP use in those with Respiratory Distress** | | | | | |
| *Yes* | 1,211 (**18.7%**) | 620 (**43.8%**) | 231 (**19.3%**) | 152 (**12.1%**) | 208 (**8.0%**) |
| *No* | 21,859 (95%) | 3,072 (83%) | 6,993 (96%) | 6,346 (98%) | 5,448 (96%) |
| *Missing* | 49 (0.2%) | 6 (0.2%) | 31 (0.4%) | 8 (0.1%) | 4 (<0.1%) |
| **Outcome** | | | | | |
| *Alive* | 19,955 (**86%**) | 2,718 (73%) | 6,461 (89%) | 5,960 (92%) | 4,816 (85%) |
| *Dead* | 2,771 (**12%**) | 870 (24%) | 716 (9.9%) | 421 (6.5%) | 764 (13%) |
| *Referred* | 361 (**1.6%**) | 103 (2.8%) | 72 (1.0%) | 115 (1.8%) | 71 (1.3%) |
| *Absconded* | 19 (<0.1%) | 6 (0.2%) | 0 (0%) | 6 (<0.1%) | 7 (0.1%) |
| *Missing* | 13 (<0.1%) | 1 (<0.1%) | 6 (<0.1%) | 4 (<0.1%) | 2 (<0.1%) |
| **Oxygen need on day 28 of life** | 8 / 72 (11%) | 0 / 32 (0%) | 0 / 15 (0%) | 0 / 6 (0%) | 8 / 19 (42%) |
| *CPAP files available* | 259 | 43 | 87 | 63 | 66 |
| N total admissions per hospital | | | | | |

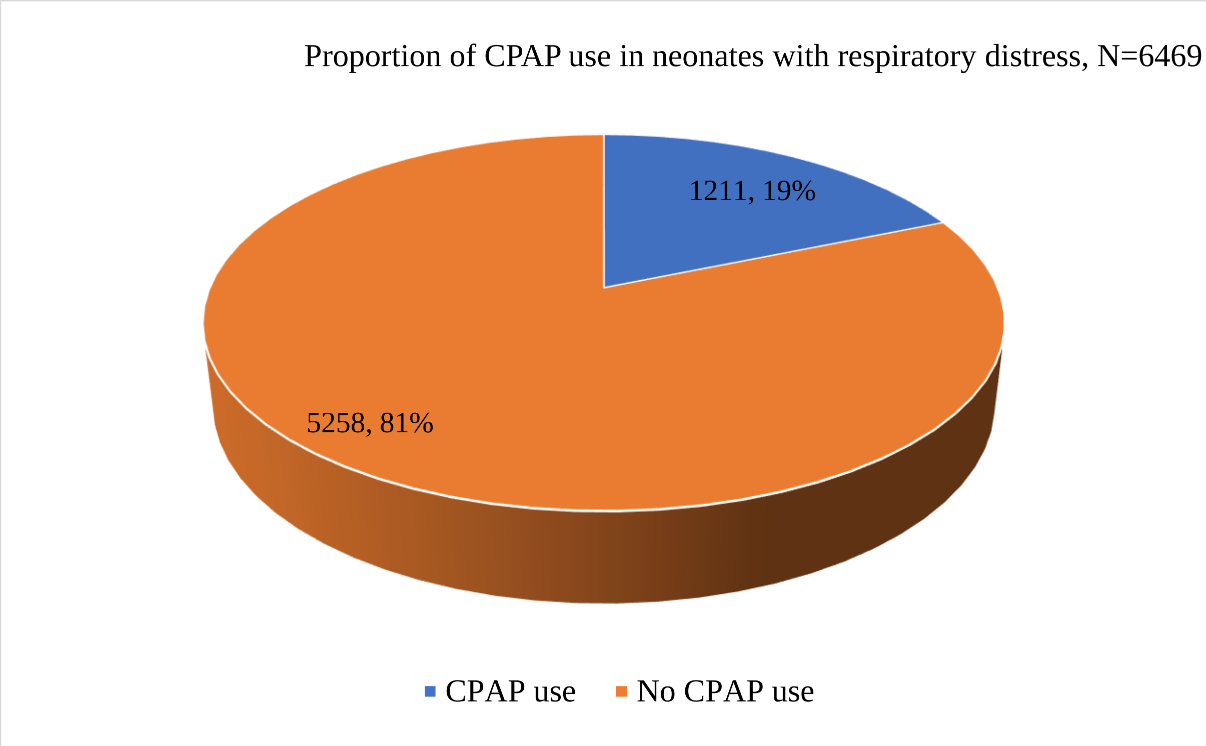


***Figure 5***: CPAP use in neonates with Respiratory distress admitted in the four NBUs from January 2020 to December 2022

#### 4.1.1 Patient demographics and outcomes of 259 neonates managed on CPAP

For neonates who had respiratory distress and managed on CPAP, a total of 259 available patient records were retrieved from the four study sites and data abstracted on CPAP use. The median age at admission was 2 hours (IQR: 0-5 hours) after delivery. 160 (62%) were male, while 99 (38%) were female. Most of the patients 159 (75%) had a low birth weight of between 1000 and 2500 grams, with 69 (27%) having a birth weight of 1500 to 1999 grams, 67(26%) having a birth weight of 1000 to 1499 grams, 59 (23%) having a birth weight of 2000 to 2499 grams and 4(1.5%) having a birth weight >4000 grams. Majority of the neonates were premature with 91(35%) of them born at a gestation of 33 to 36 weeks, and 87 (34%) born at a gestation of 28 to 32 weeks. Over half, 144 (56%) of the neonates were born via spontaneous vertex delivery (SVD), 100 (39%) via emergency caesarean section and 14 (5.4%) via vaginal breech delivery.

The median length of stay was 11 days (IQR: 5-24 days). Of the 259 neonates managed on CPAP, 193 (75%) were discharged alive, 61 (24%) died and 5 (1.9%) were referred for mechanical ventilation. Of the 72 neonates who were in hospital for more than 28 days from birth, 8/72 (11%) required oxygen on day 28 of life, an indicator of chronic lung disease (

Table **4**). The individual hospital data is indicated in Table 5 below.

***Table 5:*** Descriptive statistics of 259 neonates managed on CPAP

| | Characteristic | **Overall**, N = 259[1] | **H1**, N = 43[1] | **H2,** N = 87[1] | **H3**, N = 63[1] | **H4**, N = 66[1] |
|---|---|---|---|---|---|---|
| **Admission age, hours [median (IQR)]** | | 2.0 (0.0, 5.0) | 5.0 (2.5, 11.0) | 0.0 (0.0, 1.0) | 5.0 (2.0, 24.0) | 2.0 (1.0, 2.8) |
| **Gender** | *Female* | 99 (38%) | 13 (30%) | 39 (45%) | 22 (35%) | 25 (38%) |
| | *Male* | 160 **(62%)** | 30 (70%) | 48 (55%) | 41 (65%) | 41 (62%) |
| **Birth weight** | *<1000* | 7 (2.7%) | 5 (12%) | 0 (0%) | 1 (1.6%) | 1 (1.5%) |
| | *1000-1499* | 67 (**26%**) | 11 (26%) | 26 (30%) | 18 (29%) | 12 (18%) |
| | *1500-1999* | 69 (**27%**) | 16 (37%) | 17 (20%) | 18 (29%) | 18 (27%) |
| | *2000-2499* | 59 (**23%**) | 7 (16%) | 22 (25%) | 16 (25%) | 14 (21%) |
| | *2500-4000* | 53 (20%) | 4 (9.3%) | 22 (25%) | 10 (16%) | 17 (26%) |
| | *>4000* | 4 (1.5%) | 0 (0%) | 0 (0%) | 0 (0%) | 4 (6.1%) |
| **Gestation** | *<28* | 19 (7.3%) | 8 (19%) | 1 (1.1%) | 5 (7.9%) | 5 (7.6%) |
| | *28-32* | **87 (34%)** | 18 (42%) | 30 (34%) | 22 (35%) | 17 (26%) |
| | *33-36* | **91 (35%)** | 12 (28%) | 37 (43%) | 19 (30%) | 23 (35%) |
| | *≥37* | **60 (23%)** | 5 (12%) | 19 (22%) | 15 (24%) | 21 (32%) |
| | *Missing* | 2 (0.8%) | 0 (0%) | 0 (0%) | 2 (3.2%) | 0 (0%) |
| **Mode of Delivery** | | | | | | |
| | *Breech* | 14 (5.4%) | 1 (2.3%) | 7 (8.0%) | 5 (7.9%) | 1 (1.5%) |
| | *Elective C/S* | 1 (0.4%) | 0 (0%) | 0 (0%) | 0 (0%) | 1 (1.5%) |
| | *Emergency C/S* | **100 (39%)** | 7 (16%) | 41 (47%) | 23 (37%) | 29 (44%) |
| | *SVD* | **144 (56%)** | 35 (81%) | 39 (45%) | 35 (56%) | 35 (53%) |

| | Characteristic | **Overall**, N = 259[1] | **H1**, N = 43[1] | **H2,** N = 87[1] | **H3**, N = 63[1] | **H4**, N = 66[1] |
|---|---|---|---|---|---|---|
| **Length of Stay, days [median (IQR)]** | | 11.0 (5.0, 24.0) | 6.0 (3.0, 18.5) | 11.0 (6.0, 24.5) | 9.0 (4.5, 17.5) | 13.5 (8.0, 31.0) |
| **Outcome at discharge** | | | | | | |
| | *Alive* | **193 (75%)** | 25 (58%) | 68 (78%) | 43 (68%) | 57 (86%) |
| | *Dead* | **61 (24%)** | 18 (42%) | 19 (22%) | 16 (25%) | 8 (12%) |
| | *Referred* | **5 (1.9%)** | 0 (0%) | 0 (0%) | 4 (6.3%) | 1 (1.5%) |
| **Oxygen need on day 28 of life** | | **8 / 72 (11%)** | 0 / 32 (0%) | 0 / 15 (0%) | 0 / 6 (0%) | 8 / 19 (42%) |

### 4.1.2 Criteria used to initiate CPAP

CPAP was commenced for various indications including respiratory distress syndrome (RDS) in the setting of prematurity, meningitis, birth asphyxia and meconium aspiration syndrome, with some neonates having more than one diagnosis. Figure 6***Figure 6*** below shows, among newborns managed with CPAP, the proportion having each of documented diagnoses.

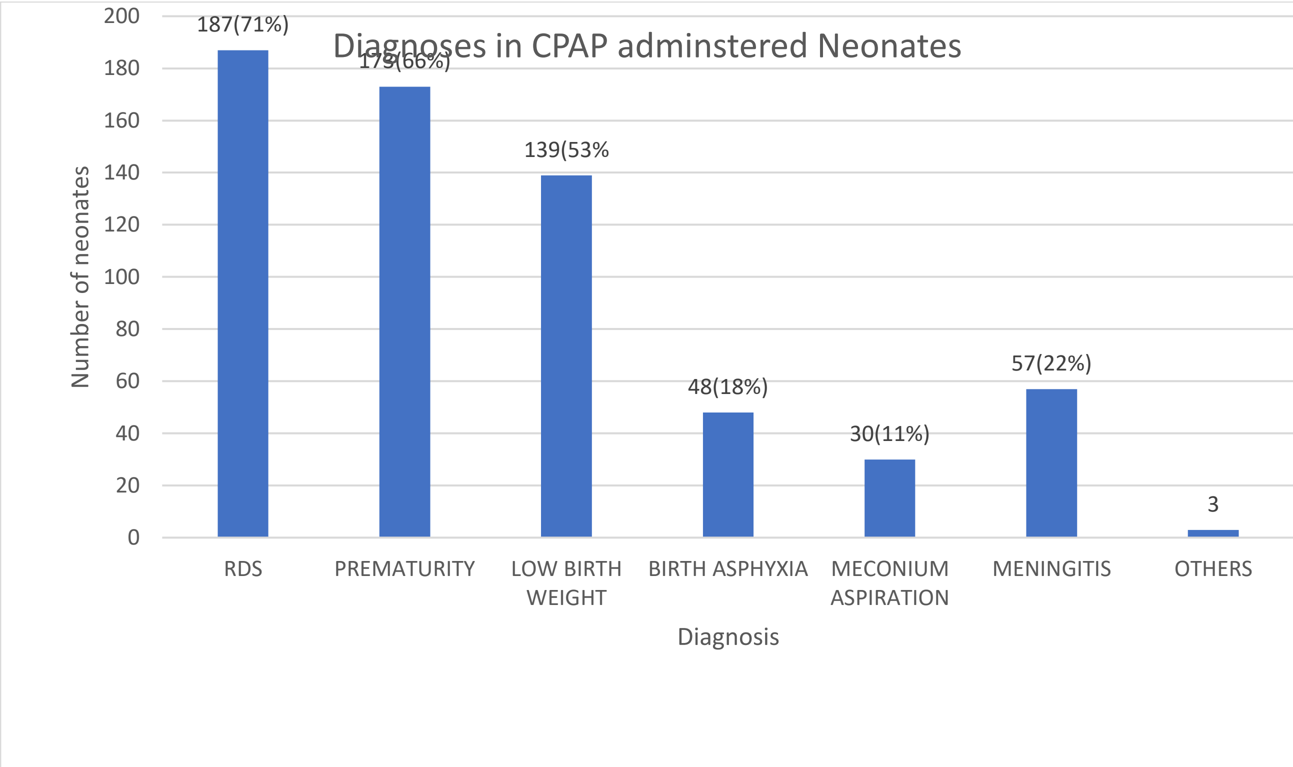


***Figure 6***: Diagnoses in 259 neonates managed on CPAP

Of the 259 records reviewed, 248 (96%) had an Apgar score of ≥5 at the fifth minute, with 11 (4.2%) missing documentation of Apgar scores, as they were born before arrival to the facility. Silverman Anderson Score (SAS), which is used to guide CPAP use, was only indicated in 17/259 (6.6%) of the patient records and as such criteria for CPAP initiation was not clearly documented. CPAP was mostly initiated within the first 24 hours of life, with the median time to initiation from admission of 13.8 hours (IQR: 3.8-35.6 hours). The FiO2 at the start of CPAP was 50% with a CPAP water level (pressure) of 6 cm in 256 of the patients (3 patients had missing documentation). The median duration of CPAP use was 2 days (IQR: 1-3 days) (Table 6)

***Table 6:*** Time of CPAP initiation and duration of use

| **Characteristic** | **Overall** N = 259 | **H1** N = 43 | **H2** N = 87 | **H3** N = 63 | **H4** N = 66 |
|---|---|---|---|---|---|
| **Age at CPAP initiation, hours (median [IQR])** | 24.0 (0.0, 24.0) | 24.0 (0.0, 24.0) | 24.0 (0.0, 48.0) | 0.0 (0.0, 24.0) | 24.0 (24.0, 48.0) |
| *(Missing)* | 39 | 4 | 10 | 7 | 18 |
| **Time to CPAP from Admission (hours)** | **13.8** (3.8, 35.6) | 13.0 (3.2, 27.8) | 11.6 (3.7, 27.8) | 6.3 (2.7, 16.9) | 20.1 (13.0, 38.1) |
| *(Missing)* | 130 | 32 | 37 | 32 | 29 |
| **Duration of CPAP, days (median [IQR])** | **2.0** (1.0, 3.0) | 1.0 (0.0, 1.5) | 2.0 (1.0, 3.0) | 2.0 (1.0, 3.0) | 2.0 (1.0, 3.0) |
| *(Missing)* | 22 | 0 | 7 | 6 | 9 |
| **SAS* Recorded** | 17 / 259 (**6.6%**) | 0 / 43 (0%) | 0 / 87 (0%) | 14 / 63 (22%) | 3 / 66 (4.5%) |
| **APGAR Score 5th min** | | | | | |
| *≥5* | 248 (96%) | 40 (93%) | 86 (99%) | 58 (92%) | 64 (97%) |
| *(Missing)* | 11 (4.2%) | 3 (7.0%) | 1 (1.1%) | 5 (7.9%) | 2 (3.0%) |

SAS* (Silverman Anderson Score)

### 4.1.3 Vital signs monitoring while on CPAP therapy

The median number of observations in the first 24 hours while on CPAP were 4 (IQR: 2-8) respiratory rate observations, 5(IQR: 3-8) heart rate measurements, and 5(IQR: 3-8) oxygen saturation (SpO2) recordings. The median number of FiO2 recordings in the first 24 hours on CPAP were 4 (IQR: 2-7), while CPAP pressure observations were 4(IQR: 3-7). At initiation of CPAP, 105(40%) of the patients had a documented respiratory rate of more than 60. In this subset of neonates, the median time to reduction of respiratory rate to less than 60 breaths per minute was 6 hours (IQR: 3-12 hours). In addition, 48 of the patients had a documented SpO2 of less than 90% at initiation of CPAP, with a median time to increase in SpO2 to ≥90% of 3 hours (IQR: 3-6 hours). Nasal prong position was documented in 86 / 259 (33%) while nasal skin condition was documented in only 2 / 259 (0.8%). The findings are as shown in

Table 7.

### 4.1.4 CPAP weaning and cessation

Only 10/259 (3.9%) of the patient records had documented weaning of FiO2 down by 10% up to 30%, prior to cessation of CPAP. Only 8 / 257 (3.1%) of the patients had documented weaning of CPAP pressure by 1 cm to a minimum of 5 cm of water prior to cessation of CPAP.

***Table 7:*** Vital signs monitoring in the first 24 hours while on CPAP

| Characteristic | Overall, N = 259 | H1 N = 43 | H2, N = 87 | H3, N = 63 | H4, N = 66 |
|---|---|---|---|---|---|
| **Number of RR Observations (1st 24 hours)** | **4.0** (2.0, 8.0) | 4.0 (2.0, 7.0) | 4.0 (3.0, 5.0) | 8.0 (8.0, 8.0) | 2.0 (1.0, 4.8) |
| **Number of HR Observations (1st 24 hours)** | **5.0** (3.0, 8.0) | 4.0 (2.0, 7.0) | 4.0 (3.0, 5.0) | 8.0 (8.0, 8.0) | 4.0 (3.0, 6.0) |
| **Number of SpO2 Observations (1st 24 hours)** | **5.0** (3.0, 8.0) | 4.0 (2.0, 7.0) | 4.0 (3.0, 5.0) | 8.0 (8.0, 8.0) | 4.0 (3.0, 6.0) |
| **Time to decrease in RR to ≤ 60 bpm, hours (median[IQR])** | **6.0** (3.0, 12.0) | 10.5 (3.0, 19.5) | 4.0 (3.0, 6.0) | 12.0 (3.0, 20.2) | 4.0 (1.8, 6.6) |
| *(Missing initial RR)* | 154 | 37 | 37 | 21 | 59 |
| **Time to increase in SpO2 to ≥ 90%, hours (median[IQR])** | **3.0** (3.0, 6.0) | 5.0 (3.0, 9.0) | 3.0 (3.0, 3.8) | 3.0 (2.0, 6.0) | 3.0 (1.5, 12.0) |
| *(Missing initial SpO2)* | 206 | 32 | 75 | 52 | 47 |
| **Number of FiO2 observations in 1st 24 hours** | **4.0** (2.0, 7.0) | 1.0 (1.0, 3.0) | 4.0 (3.0, 5.0) | 8.0 (6.0, 8.0) | 5.0 (4.0, 7.0) |
| **Number of CPAP pressure observations in 1st 24 hours** | **4.0** (3.0, 7.0) | 1.0 (1.0, 5.0) | 4.0 (3.0, 5.0) | 8.0 (6.0, 8.0) | 5.0 (4.0, 7.0) |

**(RR respiratory rate, HR heart rate)**

### 4.2 Secondary Objectives

#### 4.2.1 Secondary objective 1: Outcomes of neonates who received nasal CPAP

Of the 23,119 total neonatal admissions over the study period, 6469 (28%) had features of respiratory distress of various diagnoses including RDS. Among these neonates, 25% (1604/6469) died, accounting for 58% (1604/2771) of all neonatal deaths during the study period. Of the 1,211 neonates managed on CPAP, 420 (35%) died, while 445 (25%) of the 1,810 neonates managed on oxygen alone died. The proportions in the four hospitals are summarized in

Table 8

***Table 8:*** **Outcomes of newborns with Respiratory Distress managed on CPAP or on oxygen**

| **Hospital id & Admissions** | **Mortality** | **Respiratory Distress %** | **Respiratory Distress Mortality %** | **CPAP %** | **Mortality in CPAP %** | **Oxygen %** | **Mortality in Oxygen %** |
|---|---|---|---|---|---|---|---|
| All Hospitals N= 23,119 | 2771 (**12%**) | 6469 (28%) | 1604 (**25%**) | 1211 (19%) | 420 (35%) | 1810 (28%) | 445 (25%) |
| H1 N= 3,698 | 870 (24%) | 1416 (38%) | 487 (34%) | 620 (44%) | 228 (37%) | 518 (37%) | 165 (32%) |
| H2 N= 7,255 | 716 (10%) | 1195 (16%) | 351 (29%) | 231 (19%) | 94 (41%) | 295 (25%) | 89 (30%) |
| H3 N= 6506 | 421 (6%) | 1252 (19%) | 243 (19%) | 152 (12%) | 37 (24%) | 873 (70%) | 157 (18%) |
| H4 | 764 (13%) | 2606 (46%) | 523 (20%) | 208 (8%) | 61 (29%) | 124 (5%) | 34 (27%) |

### 4.2.2 Secondary objective 2: Factors associated with adverse outcome (death) in 259 neonates with respiratory distress managed on CPAP

***The 259 available medical records of patient managed on CPAP were analyzed for factors associated with adverse outcome by univariate (Table 9) and multivariate analysis (Table 10). There were increased odds of death in neonates who were on CPAP of the male gender (OR =1.14, 95% CI [0.57, 2.35]) and those with a birth weight less than 1500 grams (OR =1.82, 95% CI [0.41, 8.09]. Prematurity (OR =1.33, 95% CI [0.37, 5.37]), presence of hypothermia (OR =1.14, 95% CI [0.57, 2.24]) and maternal diabetes (OR =3.43, 95% CI [0.13, 92.5]) also increased the odds of death. However, these were not statistically significant. Birth weight and gestation were highly collinear, and since birthweight is more reliable than gestation based on maternal recall of the last normal menstrual period, birthweight was represented.Neonates with neonatal sepsis had reduced odds of death (OR= 0.33, 95% CI [0.12, 0.79]) as shown in***

Table 8Table 10

***Table 9:*** Factors associated with adverse outcomes in 259 neonates managed on CPAP, univariate analysis

| **Characteristic** | | **N** | **Crude OR**[1] | **95% CI**[1] | **p-value** |
|---|---|---|---|---|---|
| **Gender** | *Female* | 98 | Ref. | Ref. | |
| | *Male* | 156 | 1.26 | 0.70, 2.34 | 0.445 |
| **Age at admission** | | 254 | 1.00 | 1.00, 1.00 | 0.201 |
| **Birth Weight (grams)** | *2500-4000* | 51 | Ref. | Ref. | |
| | *<1000* | 7 | 24.6 | 3.66, 493 | **0.005** |
| | *1000-1499* | 66 | 2.19 | 0.95, 5.35 | 0.072 |
| | *1500-1999* | 69 | 0.86 | 0.34, 2.23 | 0.757 |
| | *2000-2499* | 57 | 0.87 | 0.33, 2.33 | 0.783 |
| | *>4000* | 4 | 0.00 | | 0.984 |
| **Prematurity** | *No* | 72 | Ref. | Ref. | |
| | *Yes* | 182 | 1.44 | 0.75, 2.90 | 0.285 |
| **Perinatal Asphyxia** | *No* | 222 | Ref. | Ref. | |
| | *Yes* | 32 | 0.70 | 0.25, 1.69 | 0.458 |
| **Hypothermia** | *No* | 142 | Ref. | Ref. | |
| | *Yes* | 109 | 1.35 | 0.75, 2.44 | 0.311 |
| **Maternal Diabetes** | *No* | 233 | Ref. | Ref. | |
| | *Yes* | 3 | 1.51 | 0.07, 16.0 | 0.739 |
| **Multiple gestation** | *No* | 214 | Ref. | Ref. | |
| | *Yes* | 40 | 0.51 | 0.18, 1.20 | 0.152 |
| **Neonatal sepsis** | *No* | 188 | Ref. | Ref. | |
| | *Yes* | 66 | 0.29 | 0.12, 0.65 | **0.005** |

[1]OR = Odds Ratio, CI = Confidence Interval, Ref. = Reference

***Table 10***: Factors associated with adverse outcomes in 259 neonates on CPAP, multivariate analysis

| **Characteristic** | | **N = 259** | **AOR[1]** | **95% CI[1]** | **p-value** |
|---|---|---|---|---|---|
| **Gender** | *Female* | 91 | Ref. | Ref. | |
| | *Male* | 142 | 1.14 | 0.57, 2.35 | 0.710 |
| **Age at admission** | | 233 | 1.00 | 1.00, 1.00 | 0.075 |
| **Birth Weight, grams** | *2500-4000* | 47 | Ref. | Ref. | |
| | *<1000* | 5 | 34,806,316 | 0.00, NA | 0.987 |
| | *1000-1499* | 60 | 1.82 | 0.41, 8.09 | 0.424 |
| | *1500-1999* | 64 | 0.72 | 0.16, 3.12 | 0.657 |
| | *2000-2499* | 53 | 0.62 | 0.14, 2.52 | 0.516 |
| | *>4000* | 4 | 0.00 | | 0.989 |
| **Prematurity** | *No* | 66 | Ref. | Ref. | |
| | *Yes* | 167 | 1.33 | 0.37, 5.37 | 0.667 |
| **Perinatal Asphyxia** | *No* | 206 | Ref. | Ref. | |
| | *Yes* | 27 | 0.63 | 0.14, 2.12 | 0.487 |
| **Hypothermia** | *No* | 133 | Ref. | Ref. | |
| | *Yes* | 100 | 1.14 | 0.57, 2.24 | 0.709 |
| **Maternal diabetes** | *No* | 230 | Ref. | Ref. | |
| | *Yes* | 3 | 3.43 | 0.13, 92.5 | 0.400 |
| **Macrosomia** | *No* | 229 | Ref. | Ref. | |
| | *Yes* | 4 | | | |
| **Multiple gestation** | *No* | 194 | Ref. | Ref. | |
| | *Yes* | 39 | 0.42 | 0.14, 1.07 | 0.084 |
| **Neonatal sepsis** | *No* | 172 | Ref. | Ref. | |
| | *Yes* | 61 | 0.33 | 0.12, 0.79 | **0.020** |

[1]AOR = Adjusted Odds Ratio, CI = Confidence Interval, Ref.-Reference

## 4.3 Facility Audit

The hospitals under study are part of the CIN network and had received CPAP machines among other bundles of Technologies. The principal investigator carried out a facility audit confirming the availability and working condition of CPAP machines and monitoring devices. In addition, number of various cadres of staff in the NBU were documented. It was noted that the nurse-to-patient ratio ranged from 1:20 to 1: 60, depending on the shift. It was noted that at times neonates were not started on CPAP in time as the machines were occupied. In addition the pulse oximeters were 2 to 3 per hospital and shared between neonatal and pediatric wards. There was no continuous pulse oximetry monitoring of neonates on CPAP as the monitoring devices were not adequate. The equipment availability and staffing at the time of data collection are as represented in Table 11 below.

***Table 11:*** Staffing, average admissions, equipment availability in January to March 2023

| **Information** | **H1** | **H2** | **H3** | **H4** |
|---|---|---|---|---|
| **Staffing** | | | | |
| **Nurses** | 12 | 16 | 19 | 22 |
| • **Day shift:** | 4 (2 per 6-hour shift) | 3 | 3 | 3 |
| • **Night shift:** | 1 | 2 | 3 | 2 |
| **Clinical Officers:** | 0 | 2 | 0 | 0 |
| **Clinical Officer Interns** | 0 | 1 | 3 | 2 |
| **Medical Officers:** | 2 | 0 | 1 | 2 |
| **Medical Officer interns** | 1 | 3 | 2 | 2 |
| **Paediatricians** | 1 | 2 | 3 | 1 |
| **Neonatologist** | 1 | 0 | 0 | 1 |
| **Average admissions per month** | 108 | 185 | 180 | 165 |
| **Number of functional CPAP machines** | 6 | 4 | 3 | 6 |
| **Number of functional Pulse Oximeters** | 2 | 2 | 2 | 3 |

# CHAPTER FIVE

## 5.0 DISCUSSION

This study was carried out to audit the implementation of CPAP in comparison to the recommended Kenyan guidelines in the NBUs at four secondary level facilities in Kenya. A total of 23,119 neonates aged 0 to 28 days were admitted to the NBUs of the four hospitals under study between January 2020 and December 2022. Of these, 6,469/23,119 (28%) neonates had a diagnosis of RDS. This was higher than that found in a multisite retrospective cohort study on neonatal mortality in Kenyan hospitals over 2 years (from April 2018 to March 2020). In this study involving 40,183 neonates, RDS accounted for 18% of overall admissions(33). The rates of RDS were higher in our study(28%) likely due to the higher volume of admissions at the selected facilities as county referral facilities. The findings of our study are similar to a cross-sectional descriptive study of 625 newborns admitted to a Nigerian Teaching hospital over 2 years from 2012, found that 164 (26.2%) of them had respiratory distress (31)

In our study, use of CPAP was documented in 1,211/6469 (18.7%) neonates with respiratory distress. This is comparable to the results of a quality improvement initiative carried out at the NBU of Nakuru County and Referral Hospital in Kenya, to increase CPAP use in 2018. Use of bubble CPAP increased from 2% in the pre-initiative period to 17.6% bCPAP use in the post-initiative period (19). The comparable results may be due to capacity building in terms of training and equipment delivery to the study sites among other public hospitals in Kenya.

Of the 1,211 neonates managed on CPAP, 259 medical records were available after retrieval and were audited on CPAP use. The rest of the files could not be retrieved due to archiving and loss. Majority 160/259 (62%) were male, consistent with studies that have shown higher CPAP use among male neonates. In a study done in Malawi in 2014 among 62 neonates managed on CPAP, 60.4% were male. Majority 197/259(76%) of the neonates who were managed with CPAP were premature (born before 37 completed weeks) and 202/259 (78%) of the patients had a low birth weight (less than 2500 grams). This is comparative to the 2014 Malawian study in which 77% of CPAP use was very low birth weight preterms less than 1500 grams (14). Only 7(2.7%) of the neonates were less than 1000 grams. This is in accordance with the Kenyan guidelines that make provisions for CPAP use in those under 1000 grams if resources permit.

Of the audited records, 193/259 (75%) were discharged alive, 61/259 (24%) died 5/259 (1.9%) were referred for mechanical ventilation. The neonates were referred due to lack of neonatal intensive care units in these facilities. The findings are similar to the mortality rate of 26.5% in a study done in a regional hospital in Uganda after introduction of bubble CPAP in 2016 (11) . Survival to discharge was congruent with a systematic review of 17 studies on CPAP use and barriers to care in sub-Saharan African health facilities , that showed survival to discharge rates with bubble CPAP from 42 to 85% in rural district level referral hospitals(22). In our study, 72 neonates were in hospital beyond day 28 of life, among whom 8(11%) required oxygen on day 28 of life indicating chronic lung disease (bronchopulmonary dysplasia).

Of the 1,211 neonates managed on CPAP in our study, a total of 259 available patient records were retrieved and audited. The Silverman Anderson Score (SAS), which is used to guide CPAP use, was only indicated in 17(6.6%) of the patient records. CPAP was mostly initiated within the first 24 hours of life, with the median time to initiation from admission of 13.8 hours (IQR: 3.8-35.6 hours), representing a delay. The FiO2 and CPAP pressure at the start was appropriate in majority of the cases. However, monitoring was found to be inadequate, as well as lack of titration and weaning of CPAP prior to cessation.

A few studies have been carried out in NEST 360 implementing countries such as Malawi, Tanzania, Kenya, and Nigeria. Most of these studies have been in tertiary level facilities where CPAP was piloted. In Kenya, a similar audit of 72 neonates managed on CPAP was carried out in Kenyatta National Hospital(KNH), a tertiary referral hospital in 2021(42). In the KNH study, complete documentation of examination findings was not done in all the 72 neonates who were managed on CPAP. In addition, SAS score , indications for CPAP use and CPAP equipment monitoring were also poorly documented in the KNH study (42), similar to what we observed in our study.

CPAP was commenced for various indications including respiratory distress syndrome (RDS) in the setting of prematurity and respiratory distress in neonates with meningitis, birth asphyxia and meconium aspiration syndrome. Majority 248/259 (96%) of the patient in our study had an Apgar score of ≥5 at the fifth minute, with 11 (4.2%) having missing documentation of Apgar scores. This is in-keeping with the local guidelines that contraindicate the use of CPAP in neonates with Apgar scores less than 5.

In our study CPAP was mostly initiated within the first 24 hours of life, with the median time to initiation from admission of 13.8 hours (IQR: 3.8 - 35.6 hours) with a median duration of CPAP use of 2 days (IQR: 1-3 days). This represents a delay in initiation of CPAP as the guidelines stipulate initiation of prophylactic CPAP in preterms 1001 to 1300 grams immediately after delivery in the delivery room or immediately after transfer to the NBU. It further stipulates that rescue CPAP should be commenced in those more than 1300 grams, who after 15 minutes of oxygen via nasal prongs, have and SpO2 less than 90% and have signs of increased work of breathing.

According to the comprehensive newborn protocol, CPAP should be initiated at the following initial settings: FiO2 50%, total flow 6L/min, Oxygen 3L/min, CPAP Water level 6 centimeters(cm). In this study the FiO2 at the start of CPAP was 50% with a CPAP water level (pressure) of 6 cm in 256 of the patients. Three patients had missing documentation of the same. The initial settings in this study were consistent with the current guidelines.

The Kenyan guideline further stipulates that once initiated FiO2 must be adjusted against the SpO2 by 20% every 60 seconds until SpO2 of 90-95% is achieved and the oxygen flow up or down by 0.5L/min every 60 seconds. This was however not documented in any of the patient records audited. The patient should then be reassessed (heart rate, respiratory rate, (SpO2) signs of respiratory distress) after 15 minutes, 1 hour, then 3 hourly and whenever the CPAP settings are changed. In this study, patient monitoring was inadequate with the median number of observations in the first 24 hours while on CPAP being 4 (2-8) respiratory rate, 5(3-8) heart rate and 5(3-8) oxygen saturation (SPO2) observations. This is contrast to the recommended minimal 3 hourly observations in the Kenya newborn monitoring chart, amounting to at least 8 observations in 24 hours. These findings may be due to understaffing and lack of adequate monitoring equipment as documented in section 4.3 above. Over 40% (105/259) of the patients managed on CPAP had a documented respiratory rate of more than 60 at initiation. In this subset of neonates, the median time to reduction of respiratory rate to less than 60 breaths per minute was 6 hours (IQR: 3-12 hours). 48/259 (18.5%) of the patients had a documented SPO2 of less than 90% at initiation of CPAP, with a median time to increase in SPO2 to ≥90% of 3 hours (IQR: 3-6 hours). None of these patients had a documented titrated increase in SPO2 or CPAP water level in response to the tachypnea and hypoxia (SPO2 < 90%), contrary to the recommendations. Nasal prong position was documented in 86 / 259 (33%) while nasal skin condition was documented in only 2 / 259 (0.8 %). This implies that there was poor monitoring of nasal injuries and complications of CPAP malposition.

Only 10/259 (3.9%) of patients started on CPAP had documented weaning of FiO2 by 10% up to 30% prior to cessation of CPAP, and only 8 / 257 (3.1%) of the patients had documented weaning of CPAP pressure by 1 cm to a minimum of 5 cm of water prior to cessation of CPAP. The findings are contradictory to the recommended weaning criteria in our local guidelines. In the KNH audit, weaning from CPAP was gradual in 23.6% of cases compared to 3.9% in our study. This indicates a gap in guideline implementation in these secondary level facilities.

Male gender, birth weight less than 1500 grams, prematurity, hypothermia and maternal diabetes increased odds of death but these were not statistically significant at multivariate analysis after adjusting for confounders.

Neonates with neonatal sepsis had significantly increased odds of survival (OR= 0.33, 95% CI [0.12, 0.79]). This is probably due to antibiotic use to treat sepsis. There is possibility of missed sepsis in other neonates with respiratory distress in whom a diagnosis of neonatal sepsis was not made.

**5.1 Study Strengths**

The study had several strengths. It was carried out across 4 secondary level facilities in our setup, hence allowing and audit of CPAP use in lower-level facilities in Kenya. The findings provide valuable information on the implementation of CPAP in secondary level facilities that had received CPAP machines as well as other newborn technologies through various donations. The audit has determined the uptake and implementation of local guidelines in the management of respiratory distress in neonates in these facilities. It has revealed the gaps in guideline implementation in terms of indication for CPAP use, initiation, monitoring, weaning and cessation of CPAP. The study findings will guide on strategies to improve the efficient use of CPAP for the management of respiratory distress in neonates in lower-level facilities. This will be by dissemination of the same to the relevant county and health facility with an aim to stimulate discussion on improving quality of CPAP care.

## 5.2 Study Limitations

There were several limitations to this study. The four study hospitals are not a representative sample of Kenyan public hospitals and therefore the findings of this study may not be generalizable. In addition, we used retrospective data from patient medical records and facility CPAP books to audit CPAP use in these hospitals. There were challenges in obtaining medical records for prior years of study and especially mortality files due to archiving and record storage issues at the facilities. There were missing data due to poor documentation in monitoring charts and patient files, a weakness of the retrospective study design. The missing data reduces the sample size and hence the power of the study to detect true effect. There may also be a measurement bias in parameters such as respiratory rate that require one to count for one minute.

Some of these limitations were overcome by abstracting data from the CIN- Neonatal database, which is more reliable due to stringent data quality assurance systems, and prior work put in to improve documentation practices. This allowed access to quality data that was otherwise not available to us from the manual data registries in the facilities.

We used birth weight in our analysis instead of gestation at birth. This is because the documented gestation at birth is highly variable and dependent on mother's memory of last menstrual period. In addition, more objective ways of assessing gestation such as Ballard's score early pregnancy scans are not commonly done in these set-ups.

In addition, there were logistical limitations such as delay in obtaining ethical approval from the KNH/UON ethics committee as well as county and hospital approvals to collect data. There were also the attendant costs of research permits and approvals at the various county offices and at individual hospitals and logistical challenges of studying four different sites. These challenges were partly overcome by coordination with the relevant authorities including county directors of health, hospital medical superintendents as well as the staff in the facilities. Having research assistants who were based in the facility and had been trained beforehand by KEMRI, helped to collect data in a more accurate and efficient way. In addition, ethical considerations were strictly followed in obtaining data from the facilities.

## 5.3 Conclusion

Use of CPAP was low with only 18.7% (95% CI [17.8, 19.7]) of neonates with respiratory distress managed on CPAP. There was delayed initiation of CPAP and inadequate monitoring while on CPAP therapy. There was also lack of proper titration, weaning and cessation of CPAP therapy. The local guidelines were not followed in most of the patients.

Concerted efforts need to be put in training health workers, guideline sensitization and implementation. Adequate monitoring equipment and staffing challenges also require to be addressed.

## 5.4 Recommendations and implications for policy and practice

In view of delayed initiation of CPAP as well as inadequate titration and monitoring found in this study, we recommend staff sensitization with emphasis on the timing of commencing CPAP (early or prophylactic and rescue) as per the Kenyan guidelines. We also recommend equipping of facilities with cardiorespiratory monitors and pulse oximeters for all neonates on CPAP to facilitate adequate monitoring and titration of care. Investment into adequate staff-patient ratios is required to improve patient monitoring and quality of care. We recommend the recording of the required monitoring data in the standardized newborn monitoring chart. In addition, a CPAP initiation recording tool should be developed to ensure that the health care worker doing the initial set up and titration is prompted to follow and record the required steps upon connecting the neonate to CPAP. We also recommend that county governments and hospital management teams ensure availability of adequate number of CPAP machines to manage these neonates and hence reduce morbidity and mortality.

### 5.5 Conflict of Interest

There was no conflict of interest.

### 5.6 Study dissemination plan

The study findings were presented to the UON department of Paediatrics and Child Health as part of the requirements of the Master of Medicine Program in both soft and hard copies. Additionally, soft copies of the dissertation shall be sent to the University of Nairobi repository for printing and storage. The individual hospital findings will be shared with the hospitals. We shall also organize training in the form of Continuous Medical Education (CMEs) on management of neonatal respiratory distress. The findings will also be shared with the relevant County health committees, with an aim of stimulating engagement for improvement of care, including training and staffing. The study shall also be submitted for publication in peer reviewed scientific journals.

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# APPENDICES

## *Appendix 1: Authorization to conduct research study*

My name is Dr. Jane Nyawira Magondu. I am a postgraduate student in the Department of Paediatrics and Child Health at the University of Nairobi (UON), School of Medicine. As part of my post-graduate studies, I am required to carry out a research project. My research study is to audit the use of nasal continuous positive airway pressure (NCPAP) in neonates with respiratory distress admitted to the newborn units of CIN- Neonatal participating hospitals. I would like to include your hospital as part of the study. I hereby request authorization to conduct my study in your facility's New Born Unit. I will require to access selected patient files as well as physical access to the NBU.

**Purpose of the Study**

Respiratory distress is one of the most common conditions in term and preterm neonates admitted to the NBU. Respiratory distress occurs in premature babies because the baby has been born before their lungs have matured adequately to allow them to be able to breathe effectively on their own. The baby does not have the necessary lung protein that is important in keeping the airways open or it may be present in very small amounts. Other conditions such as infection can also cause difficulty in breathing in newborns. As a result, these neonates require to be assisted in breathing in form of oxygen support and the use of CPAP. I am conducting a study on the use of nasal continuous positive airway pressure in neonates with respiratory distress admitted to the newborn unit.

**Procedures**

The study will obtain data from CIN-Neonatal database as well as patient medical records and facility CPAP records.

**Benefits of the Study**

The results of the study will inform implementation of guidelines to help improve care of newborns with respiratory distress.

**Rights and confidentiality**

The information collected from patient files and from the CIN- database, which your hospital participates in, will be strictly confidential.

There will be no financial rewards or tokens for participating in the study.

**Contacts**

If you have any questions regarding the study, you may contact the principal researcher Dr. Jane Nyawira Magondu on 0721886445 and the Co-Investigator Dr. Michuki Maina, KEMRI Wellcome Trust Research Programme, P.O. Box 43640, Nairobi 00100. Telephone: 0722248890

In case of further queries regarding the study you may contact The Secretary, KNH/UON – ERC on P.O. Box 20723, Nairobi; Telephone 020 2726300 extensions 44355; 726300-9

**Declaration of the Hospital Management**

I/We have understood that the purpose of the study is to audit the use of nasal continuous positive airway pressure (NCPAP) in neonates with respiratory distress admitted to the newborn unit. I/We authorize/ do not authorize (circle as appropriate) for hospital records to be used in this study as well as access to the New Born Unit (NBU)

Signature…………………………………….. Date ….............................................

*Appendix 2: Facility Study Instrument*

**(Filled by Principal Investigator upon physical auditing)**

| **Question** | | **Answers/Choices** |
|---|---|---|
| 1 | Which CPAP system is existing in the facility? | a. Improvised bubble CPAP system |
| | | b. Commercial bubble CPAP system |
| | | c. Infant flow driver CPAP system |
| | | d. Mechanical ventilator (set in the CPAP mode) |
| | | e. High flow nasal cannula |
| | | f. Other…………………………… |
| 2 | How many CPAP machines are available | |
| 3 | How many of the CPAP machines are working/functional | |
| 4 | Are CPAP-specific breathing circuits used? | a. Always |
| | | b. Sometimes |
| | | c. Never |
| 5 | Which gas/gases is/are used to generate pressure? | a. Air and oxygen |
| | | b. Air only |
| | | c. Oxygen only |
| 6 | Is the system equipped with a humidifier? | a. Always |
| | | b. Sometimes |

| | | |
|---|---|---|
| | | c. Never |
| 7 | Is there a clinical guideline for the use of CPAP available in the immediate area of care? If present, specify which guidelines they use | a. Yes |
| | | b. No |
| 8 | Is there pulse oximeters for every CPAP machine | a. Yes |
| | | b. No |
| 9 | Is there a cardiorespiratory monitor for every CPAP machine? | a. Yes |
| | | b. No |

*Appendix 3: Patient records data collection tool*

**a. Eligibility Criteria**

Instructions: Tick box as appropriate

| | |
|---|---|
| Neonate less than 28 days old admitted in the new-born unit with respiratory distress | a. Yes |
| | b. No |
| Neonate with respiratory distress who are managed with nasal CPAP | a. Yes |
| | b. No |
| Birth weight more than 1000 grams | a. Yes |
| | b. No |
| Neonates without severe congenital malformations | a. Yes |
| | b. No |
| Neonate without severe birth asphyxia with an Apgar score more than 4 at 5 minutes after delivery | a. Yes |
| | b. No |
| Neonate without uncontrolled seizures, prolonged apnea or gasping respirations at the time of CPAP start | a. Yes |
| | b. No |
| Multiple gestation | a. Yes |
| | b. No |

**Patient records data collection tool**

| | | |
|---|---|---|
| | On the clinical observation chart, are the following measurement recorded? (**If yes, indicate number of measurements per shift**) | |
| 1. | Oxygen saturation | a. Yes |
| | | b. No |
| 2. | Hearth rate | a. Yes |
| | | b. No |
| 3. | Respiratory rate | a. Yes |
| | | b. No |
| 4. | Respiratory distress status as per the Silverman Anderson Score ( Appendix 4) | a. Yes |
| | | b. No |
| 5. | Correct position and fixation of the nasal interface | a. Yes |
| | | b. No |
| 6. | Nasal skin condition | a. Yes |
| | | b. No |
| 7. | CPAP pressure | a. Yes |
| | | b. No |
| 8. | Gas flow | a. Yes |
| | | b. No |
| 9. | Humidification of gas reaching the baby | a. Yes |
| | | b. No |

<table>
<tr><td rowspan="2">10.</td><td rowspan="2">The temperature of gas reaching the baby</td><td colspan="2">a. Yes</td></tr>
<tr><td colspan="2">b. No</td></tr>
<tr><td rowspan="4">11.</td><td rowspan="4">Is there a standardized weaning process of CPAP?<br>i. Is FiO2 weaned once SPO2, is consistently >95% to a FiO2 of 30% before pressure is weaned?<br>ii. Is pressure weaned by 1 cm every 3 hours until a minimum of 5 cm water/PEEP of 5</td><td rowspan="2">i.</td><td>a. Yes</td></tr>
<tr><td>b. No</td></tr>
<tr><td rowspan="2">ii.</td><td>a. Yes</td></tr>
<tr><td>b. No</td></tr>
<tr><td rowspan="5">iii.</td><td rowspan="5">Indicate the start date, stop date, level of FiO2, SPO2, etc. for weaning off</td><td colspan="2">CPAP start (date………………)</td></tr>
<tr><td colspan="2">CPAP level (cm)/PEEP ………………………………</td></tr>
<tr><td colspan="2">CPAP stop (date…………….)</td></tr>
<tr><td colspan="2">FIO2 at time of stopping CPAP ……………………………..</td></tr>
<tr><td colspan="2">SPO2 at time of stopping CPAP ………………………..</td></tr>
</table>

*Appendix 4: Silverman Anderson Score*

| Silverman- Anderson Score | | | |
|---|---|---|---|
| **Feature** | **Score 0** | **Score 1** | **Score 2** |
| Chest Movement | Equal | Respiratory Lag | Seesaw Respiration |
| Intercostal Retraction | None | Minimal | Marked |
| Xiphoid Retraction | None | Minimal | Marked |
| Nasal Flaring | None | Minimal | Marked |
| Expiratory Grunt | None | Audible with Stethoscope | Audible |

**Ministry of Health-Kenya (MoH), Basic Paediatric Protocols, 2016**

Score of 0- no respiratory distress

Score 1-3 –mild respiratory distress

Score 4-6 moderate respiratory distress

Score ≥7: impending respiratory failure

Score of 10: severe respiratory distress.

*Appendix 5: KNH/UON ethics approval*

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/403

12th October, 2022

Dr. Jane Nyawira Magondu
Reg No. H58/37527/2020
Dept of Paediatrics & Child Health
Faculty of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 12 OCT 2022 KNH/UoN-ERC P.O. Box 20723 - 00202, NAIROBI

Dear Dr. Magondu,

**RESEARCH PROPOSAL: CROSS-SECTIONAL OBSERVATIONAL STUDY TO AUDIT THE USE OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (NCPAP) IN NEONATES WITH RESPIRATORY DISTRESS, ADMITTED TO THE NEWBORN UNITS OF FOUR COUNTY AND SUB-COUNTY HOSPITALS IN KENYA (P202/03/2022)**

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P202/03/2022.** The approval period is 12th October 2022 – 11th October 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.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

**DR. BEATRICE K.M. AMUGUNE**
**SECRETARY, KNH-UoN ERC**

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Assistant Director, Health Information Dept., KNH
The Chairperson, KNH- UoN ERC
The Chair, Dept, of Paediatrics & Child Health, UoN
Supervisors: Dr. Jacqueline Oliwa, Dept, of Paediatrics & Child Health, UoN
Dr. Brian Maugo, Dept. of Paediatrics & Child Health, UoN
Dr. Michuki Maina KEMRI Wellcome Trust Research Programme

## *Appendix 6: NACOSTI licence*

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION



Ref No: **778841**

Date of Issue: **08/December/2022**

# RESEARCH LICENSE

**This is to Certify that Dr.. Jane Nyawira Magondu of University of Nairobi, has been licensed to conduct research as per the provision of the Science, Technology and Innovation Act, 2013 (Rev.2014) in Bungoma, Kiambu, Machakos, Nairobi on the topic: CROSS-SECTIONAL OBSERVATIONAL STUDY:TO AUDIT THE USE OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (NCPAP) IN NEONATES WITH RESPIRATORY DISTRESS, ADMITTED TO THE NEWBORN UNITS OF FOUR COUNTY AND SUB-COUNTY HOSPITALS IN KENYA for the period ending : 08/December/2023.**

License No: **NACOSTI/P/22/21989**

**778841**

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

**See overleaf for conditions**

*Appendix 7: KEMRI/SERU approval*

# KENYA MEDICAL RESEARCH INSTITUTE

P.O. Box 54840-00200, NAIROBI, Kenya
Tel: (254) 2722541, 2713349, 0722-205901, 0733-400003, Fax: (254) (020) 2720030
Email: director@kemri.org, info@kemri.org, Website. www.kemri.org

**KEMRI/RES/7/3/1** **May 13, 2022**

**TO:** **DR. JACKSON MICHUKI MAINA**
**PRINCIPAL INVESTIGATOR**

**THROUGH:** **THE DEPUTY DIRECTOR, CGMR-C**
**NAIROBI.**

Dear Sir,

**RE:** **KEMRI/SERU/CGMR-C/229/4203 (*REQUEST FOR ANNUAL RENEWAL*): EVALUATING THE EFFECTS OF TECHNOLOGY AND WORKFORCE ENHANCEMENT TO SUPPORT NEONATAL HOSPITAL CARE IN KENYA**

Thank you for the continuing review report for the period **May 27, 2021** to **April 12, 2022.**The Expedited Review Team of the KEMRI Scientific and Ethics Review Unit (SERU) acknowledges receipt of the following documents:

1. Continuing Review Report
2. The last KEMRI SERU CGMR-C approval letter
3. The currently approved protocol, version 3.0.
4. Two manuscripts submitted for publication.

This is to inform you that the Expedited Review Team of the KEMRI SERU was of the informed opinion that the progress made during the reported period is satisfactory. The study has therefore been granted **approval** for continuation.

This approval is valid from **May 27, 2022** through to **May 26, 2023.** Please note that authorization to conduct this study will automatically expire on **May 26, 2023.** If you plan to continue with data collection or analysis beyond this date, please submit an application for continuing approval to SERU by **April 14, 2023.**

You are required to submit any amendments to this protocol and any other information pertinent to human participation in this study to SERU for review prior to initiation. You may continue with the study.

Yours faithfully,

**PROF. CHARLES OBONYO,**
**THE ACTING HEAD,**
**KEMRI SCIENTIFIC AND ETHICS REVIEW UNIT.**

In Search of Better Health

*Appendix 8: NACOSTI license (KEMRI study)*

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **331535**

Date of Issue: **21/July/2022**

**RESEARCH LICENSE**

**This is to Certify that Dr.. Jackson Maina of CENTRE FOR GEOGRAPHIC MEDICINE RESEARCH-COAST (CGMRC), has been licensed to conduct research in Bungoma, Embu, Kakamega, Kiambu, Kirinyaga, Kisumu, Machakos, Nairobi, Nakuru, Nyeri on the topic: Evaluating the effects of technology and workforce enhancement to support neonatal hospital care in Kenya for the period ending : 21/July/2023.**

License No: **NACOSTI/P/22/18906**

**331535**

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

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*Appendix 9: Letter of support from KEMRI*

KEMRI/ WELLCOME TRUST
RESEARCH PROGRAMME
(Centre for Geographic Medicine Research – Coast)

wellcometrust

P.O. Box 230, 80108, Kilifi, Kenya
Tel: (+254) 709 983 000/ 709 983 677/ 709 983 676
Email: info@kemri-wellcome.org

P.O. Box 43640, 00100, Nairobi, Kenya
Tel: (+254) 709 203000

29th July, 2022

Ethics Review Board
UON/KNH

Dear Sir/Madam

RE: Letter of Support for Dr Jane Nyawira Magondu

Dr Jane Nyawira, is a post graduate student at the University of Nairobi's, Department of Paediatrics and Child Health. As part of her dissertation, and in keeping with our continued collaboration with the University of Nairobi, she will be working alongside researchers at the KEMRI Wellcome Trust programme under a project Harnessing Innovation in Global Health for Quality Care (HIGH-Q).
This is a project that aims to understand how technological and human resource interventions can be designed and implemented successfully to enhance the quality of inpatient and post-discharge neonatal care. Dr Nyawira will be specifically examining the use of nasal continuous positive airway pressure (CPAP) in four of the neonatal units in the study.
We are happy to provide Dr Nyawira with any necessary support she needs to independently undertake her dissertation work.
Attached is the KEMRI Scientific and Ethics Review Unit (SERU) approval for the project
In case of any clarifications, please feel free to get in touch

Yours Faithfully

Dr Michuki Maina MBChB, MMed (Paed), MPH, PhD
Principal Investigator
HIGH-Q Programme KEMRI Wellcome TrustProgramme
mmaina@kemri-wellcome.org

Harnessing Innovation in Global Health for Quality Care (HIGH-Q)
KEMRI Wellcome Trust
University of Oxford
Keprecon

*Appendix 10: Kiambu County Approval Letter*

COUNTY GOVERNMENT OF KIAMBU
DEPARTMENT OF HEALTH SERVICES

All correspondence should be addressed to HEAD
HRDU – HEALTH DEPARTMENT
Email address: mndiritu@gmail.com
mkwasa@live.com
Tel. Nos: 0721641516
0721974633

HEALTH RESEARCH AND DEVELOPMENT UNIT
P. O. BOX 2344 – 00900
KIAMBU

Ref. No.: KIAMBU/HRDU/22/12/19/RA_MAGONDU     Date: 19th Dec 2022

TO WHOM IT MAY CONCERN

RE: CLEARANCE TO CONDUCT RESEARCH IN KIAMBU COUNTY

Kindly note that we have received a request from Dr. Jane Nyawira Magondu of University of Nairobi to carry out her study in Kiambu County, the research topic being on "Cross-Sectional Observational Study To Audit The Use Of Nasal Continuous Positive Airway Pressure (NCPAP) In Neonates With Respiratory Distress, Admitted To The Newborn Units Of Four County And Sub-County Hospitals In Kenya"

We have duly inspected her documents and found that she has been cleared by NACOSTI to carry out the research for a period ending 8th December 2023. She thus does not need any further clearance with another regulatory body in order to conduct research within the county of Kiambu.

However, it is incumbent upon the institution where she is carrying out research to ensure that she receives adequate supervision during the process of conducting the research. This note also accords her the duty to provide a feedback on her research to the county at the conclusion of her research.

DR. MWANCHA KWASA
COUNTY CLINICAL RESEARCH OFFICER
KIAMBU COUNTY

*Appendix 11: Kiambu County Referral Hospital Approval*

# COUNTY GOVERNMENT OF KIAMBU

## DEPARTMENT OF HEALTH SERVICES

Telephone: (066) 2022191
Email address:
kiambudistricthospital@yahoo.com

When replying please quote:

KIAMBU COUNTY REFERRAL
LEVEL 5 HOSPITAL
P. O. BOX 39 – 00900,
KIAMBU

---

Ref No: KBU/STAFF.14/XL IV/ANNEX/48

Dates: 30th January 2023

DR JANE NYAWIRA MAGONDU

UNIVERSITY OF NAIROBI

**RE: REQUEST FOR APPROVAL TO CONDUCT RESEARCH IN KIAMBU REFERRAL HOSPITAL**

In reference to your request letter dated 14th December 2022 on conducting research in this facility titled: the use of Nasal Continuous Positive Airway Pressure (NCPAP) in neonates with respiratory distress admitted to the newborn units of clinical Information Network (CIN) – Neonatal participating hospitals, we hereby inform you that your request has been approved.

MEDICAL SUPERINTENDENT
KIAMBU SUB COUNTY LEVEL 4
HOSPITAL
P.o. Box 39-00900
KIAMBU
TEL: 0662022191

DR WATURI KIBUTI

DEPUTY MEDICAL SUPERINTENDENT

KIAMBU COUNTY REFERRAL HOSPITAL

*Appendix 12: Nairobi City County Research Authorization*

# NAIROBI CITY COUNTY

Telephone 020 344194

Web: www.nairobi.go.ke

City Hall,
P. O. Box 30075-00100,
Nairobi,
KENYA.

## COUNTY HEALTH SERVICES

**REF: NCCG/DHS/REC/272**

**DATE: 13th January 2023**

JANE MAGONDU
UNIVERSITY OF NAIROBI
NAIROBI.

Dear Ms. Jane,

**RE: RESEARCH AUTHORIZATION**

This is to inform you that the Nairobi City County – County Health Services Research Ethics Committee (REC) reviewed the documents on the study titled "CROSS-SECTIONAL OBSERVATIONAL STUDY TO AUDIT THE USE OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (NCPAP) IN NEONATES WITH RESPIRATORY DISTRESS, ADMITTED TO THE NEWBORN UNITS OF FOUR COUNTY AND SUB-COUNTY HOSPITALS IN KENYA "

I am pleased to inform you that you have been authorized to carry out the study at Mama Lucy Kibaki Hospital in Nairobi County. The researcher will be required to adhere to the ethical code of conduct for health research in accordance with the Science Technology and Innovation Act, 2013 and the approval procedure and protocol for research for Nairobi.

On completion of the study, you will submit one hard copy and one copy in PDF of the research findings to the REC. In addition, you will disseminate recommendations of the research at a virtual meeting organized by the REC. By copy of this letter, Medical Superintendent – Mama Lucy Kibaki hospital is to accord you the necessary assistance to carry out this research study.

Yours sincerely,

**DR. ANDREW TORO**
**CHAIR - RESEARCH ETHICS COMMITTEE**

Cc: Chief Officer - Medical Services
Medical Superintendent – Mama Lucy Kibaki Hospital

*Appendix 13: County Government of Bungoma Research Authorization*

**REPUBLIC OF KENYA**

**COUNTY GOVERNMENT OF BUNGOMA**
**MINISTRY OF HEALTH**
**OFFICE OF THE COUNTY DIRECTOR HEALTH**

Telephone: 0725393939
E-mail: heallth@bungoma.go.ke
When replaying please quote

COUNTY DIRECTOR OF HEALTH
BUNGOMA COUNTY
P. O. BOX 18-50200
**BUNGOMA**

**OUR REF:** CG/BGM/CDH/RESRC/VOL.1

**DATE:** 22nd December, 2022

Dr. Jane Nyawira Magondu
P.O. Box 917-00100
**NAIROBI**

**RE: RESEARCH AUTHORIZATION.**

Following your request for authority to carry out research on **"Cross-sectional observational study to audit the use of nasal continuous poditive airway pressure (NCPAP) in neoates with respiratory distress, admitted to the newborn units in Bungoma ."** I am pleased to inform you that you have been authorized to undertake the research for the period ending 8th December, 2023.

Kindly note that you shall deposit **a copy** of the final research report to the County Director of Health. The soft copy of the same should be submitted through the online Research Information System.

Thank you.

Dr. Caleb Wanambisi Watta
County Director of Health
**Bungoma**

*Appendix 14: Bungoma County Referral Hospital Research Authorization*

REPUBLIC OF KENYA

COUNTY GOVERNMENT OF BUNGOMA

OFFICE OF MEDICAL SUPERINTENDENT

MINISTRY OF HEALTH

Telephone: 0921517633
website : www.bungoma referral.go.ke
E-mail: dwanix@yahoo.co.uk

Medical Superintendent
Bungoma County Referral Hospital,
P.O Box 14,
BUNGOMA.

REF NO.BDH/TP/8/VOL 2

DATE: 22nd December, 2022.

Dr. Jane Nyawira Magondu
Reg. No. H58/37527/2020
Dept of Paediatrics & Child Health
Faculty of Health Sciences
UNIVERSITY OF NAIROBI

Dear Sir/Madam,

RE: APPROVAL TO CONDUCT RESEARCH

Following your request for authority to carry out research on "*Cross-Sectional Observation Study to Audit the use of use of Nasal Continuous Positive Airway Pressure (NCPAP) in Neonates with Respiratory Distress, Admitted to the Newborn Units of Four County and Sub-County Hospitals in Kenya (P202/03/2022)*". I am pleased to inform you that you have been authorized to undertake the research for the period ending *11th Oct 2023*. You will equally utilize the Bungoma County Referral Hospital clinical information network data.

Kindly note that you shall deposit a copy of the final research report to the Medical Superintendent.

The soft copy of the same should be submitted to through the online Research Information System.

Thank you.

BUNGOMA COUNTY REFERRAL HOSPITAL
MEDICAL SUPERINTENDENT
GLAD TO SERVE
P.O. BOX 14-50200, BUNGOMA

Dan Oswana
For:Medical Superintendent
BUNGOMA COUNTY REFERRAL HOSPITAL

*Appendix 15: Machakos County Approval*

**REPUBLIC OF KENYA**

**GOVERNMENT OF MACHAKOS COUNTY**
**DEPARTMENT OF HEALTH AND EMERGENCY SERVICES**
***Office of the County Director of Medical Services***

Telephone: +254-44-20575
Fax: 254-44-20655

Machakos Highway
P.O. Box 2574-90100
**Machakos, Kenya**
**22/12/2022**

**Ref No. MKS/DHES/RSCH/VOLI/278**

Dear Dr. Jane Magondu,

**RE: LETTER OF AUTHORIZATION FOR CONDUCTING PROPOSED RESEARCH**

The Department of Health and Emergency Services, Machakos County is keen to collaborate in your study titled, **"Cross-Sectional Observational study to audit the use of nasal continuous positive airway pressure (NCPAP) in neonates with respiratory distress, admitted to the newborn units of four county and sub-county hospitals in kenya."**

Note is taken of the letter of Ethical clearance from KNH-UoN ERC, **REF: P202/03/2022**, for the approval period **12th October 2022 to 11th October 2023** as well as the Research License from the National Commission for Science, Technology & Innovation number **NACOSTI/P/22/21989** for the period ending **8th December 2023**.

You are hereby authorized to proceed with the research in Machakos County and urged to share the findings with the Department of Health and Emergency Services; Machakos County, through this Email: research.dhes@gmail.com

Sincerely,

Dr. Sharon Mweni
County Director Medical Services & Research
**Machakos County**

CC:
County Executive Committee Member – Health
County Research Committee

*Appendix 16: Study Budget*

| **Activity** | **Amount (Kshs.)** |
|---|---|
| Typing, printing, and internet costs | 20,000 |
| Travel and accommodation | 30,000 |
| Training costs | 10,000 |
| Data analysis and dissemination | 50,000 |
| Data collection personnel | 60,000 |
| Two publications | 20,000 |
| Miscellaneous | 15,000 |
| **Total** | **205,000** |

*Appendix 17: Similarity index*

AN AUDIT OF THE USE OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE IN NEONATES WITH RESPIRATORY DISTRESS, ADMITTED TO THE NEWBORN UNITS OF FOUR COUNTY AND SUB-COUNTY HOSPITALS IN KENYA

ORIGINALITY REPORT

| 15% | 14% | 8% | 3% |
| --- | --- | --- | --- |
| SIMILARITY INDEX | INTERNET SOURCES | PUBLICATIONS | STUDENT PAPERS |

PRIMARY SOURCES

| | | |
| --- | --- | --- |
| 1 | erepository.uonbi.ac.ke<br>Internet Source | 3% |
| 2 | www.researchgate.net<br>Internet Source | 1% |
| 3 | erepository.uonbi.ac.ke:8080<br>Internet Source | 1% |
| 4 | www.science.gov<br>Internet Source | 1% |
| 5 | researchonline.lshtm.ac.uk<br>Internet Source | 1% |
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