A SHORT LONGITUDINAL SURVEY DESCRIBING THE USE OF BUBBLE CONTINOUS POSITIVE AIRWAY PRESSURE IN PREMATURE NEONATES WITH RESPIRATORY DISTRESS SYNDROME AT THE AIC KIJABE HOSPITAL.

A PROPOSAL FOR A DISERTATION TO BE SUBMITED IN PART FULFILMENT FOR THE DEGREE OF MASTER OF MEDICINE IN PAEDIATRICS AND CHILD HEALTH OF THE UNIVERSITY OF NAIROBI

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DECLARATION

This dissertation is my original work and has not been presented for a degree in any other university.

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This dissertation has been submitted in part fulfillment for the degree of masters of Medicine (pediatrics and Child health) at the University of Nairobi with our approval as supervisors.

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DEDICATION

This book is dedicated to my husband Peter and our two lovely angels Abigail and Audrey whose presence has made it all worthwhile.

My parents Mr. and Mrs. William Omoding for their persistent love, encouragement and support- Asanteni sana

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LIST OF ABBREVIATIONS

RDS	Respiratory Distress Syndrome.
CLD	Chronic Lung Disease.
BPD	Bronchopulmonary Dysplasia.
CPAP	Continuous Positive Airway Pressure.
NBU	New Born Unit.
SPSS	Statistical Package for Social Sciences.
ELBW	Extremely Low Birth Weight.
IVF	Intravenous Fluid.
FIO_2	Fraction of inspired oxygen.
PEEP	Positive End Expiratory Pressure.
GA	Gestational Age.
NEC	Necrotising Enterocolitis.
NICU	Neonatal Intensive Care Unit.
IFD	Infant Flow Driver.
IT ratio	Imature to total Neutrophil Ratio.
NNS	Neonatal sepsis.
CHD	Congenital Heart Disease.
PDA	Patent Ductus Arteriosus.

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ABSTRACT

BACKGROUND: The premature neonate is particularly susceptible to Respiratory distress Syndrome. This is due to the inherent lack of pulmonary surfactant. Mechanical ventilation has been used as the conventional therapy and is associated with a high cost of maintenance and establishment. It is labour intensive, requires high level of expertise as well as the man hours that are employed. Significantly is the associated increased incidence of Chronic Lung Disease (CLD). Newer strategies in the management of RDS that are associated with gentler ventilation are being employed and these include the use of Bubble Continuous Positive Airway Pressure (BCPAP).

OBJECTIVES: The purpose of this study was to describe the experience of the use of BCPAP for preterm neonates with Respiratory Distress Syndrome (RDS) at the AIC Kijabe Hospital.

METHODOLOGY: This was a short longitudinal survey. The study included 61 preterm neonates with RDS admitted at the AIC Kijabe Hospital new born unit who satisfied the inclusion criteria. The study period was 7 months. The outcomes of interest included duration of BCPAP support in days, duration of oxygen therapy and oxygen requirements at 36 weeks Gestational Age (GA). Other outcomes evaluated were: gestational age of the infants when full enteral feeds were tolerated, and the complications of BCPAP.

ANALYSIS: The normally distributed variables were represented as medians (range). The maternal, infant and clinical data were compared between infants who succeed CPAP. P value of < 0.05 was considered to be significant.

RESULTS: 61 preterm neonates were recruited in the study, 54.1% male and 45.9% female. 91% of the neonates started BCPAP on day one of life. The neonates were classified based on Birth weight as LBW<2500 gms (23), VLBW<1500gms (26) and ELBW<1000gms (12). The median duration of BCPAP treatment was 5 days (IQR 3 to 7 days), and this was significantly associated with Birth Weight (p=0.044). The median duration of Oxygen therapy was 6 days (IQR 4-17 days), and this was significantly associated with GA (p=0.003). 20% of the neonates had CLD requiring Oxygen administration at 36 weeks for 82% of the sample. The median age of full enteral feeds was 18 days (IQR 12- 25 days). There was no report of the major complications of

BCPAP in the study i.e. pneumothorax. CPAP belly or nasal trauma. The mortality rate of preterms treated with BCPAP was 13.1%.

CONCLUSION: Bubble CPAP is a safe mode of respiratory support for preterm neonates with RDS at the AIC Kijabe hospital and was associated with a mortality rate of 13.1%. The duration of respiratory support i.e. duration of BCPAP therapy and oxygen therapy was 5 and 6 days respectively. Ten (20%) neonates required continued oxygen use beyond 36 weeks GA.The use of Bubble CPAP was associated with achievement of full enteral feeding at a median age of 18 days. No complications were reported among the premature neonates who were treated with Bubble CPAP.

1.0 BACKGROUND

1.1 Introduction

Premature birth is defined as birth occurring at less than 37 completed weeks or 259 days of gestation[1]. It is a major determinant of neonatal mortality and morbidity and has long term adverse consequences on health[2, 3]. No data has been published on the global incidence of prematurity[4]. However, with regard to the early neonatal deaths (deaths occurring within the first 7 days of life) that are not related to congenital malformations, 28% are due to prematurity[5]. Preterm birth rates have been reported to range from 5%-7% in the developed countries. These figures are thought to be significantly higher in the developing countries[5]. The premature neonate is particularly vulnerable to Respiratory Distress Syndrome (RDS). This is the most common respiratory disorder in the preterm. This study aims at evaluating the use of bubble Continuous Positive Airway Pressure (CPAP) as a treatment modality in a resource limited setting.

1.2 Respiratory distress syndrome in the premature neonate

RDS typically affects preterm infants below 35 weeks of gestation, however, term infants may present with RDS due to certain associated conditions. Its incidence is inversely related to gestational age and birth weight. It occurs in 60-80% of infants less than 28weeks of gestational age, in 15-30% of those between 32 and 36 weeks, in about 5% beyond 37weeks, and rarely at term[6]. The risk of developing RDS increases with maternal diabetes, multiple births, cesarean section delivery, precipitous delivery, asphyxia, cold stress and a history of previously affected infants[5, 6].

The primary cause of RDS is a deficiency of pulmonary surfactant which is developmentally regulated. The fetal lung is filled with fluid and provides no respiratory function until birth. In preparation for air breathing during the third trimester of pregnancy, surfactant is expressed in the lungs and antioxidants are induced[7]. Pulmonary surfactant is a complex mixture of lipids and proteins that lowers alveolar surface tension. It comprises 80% phospholipids which include phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol and phosohatidylethanolamine;

10% protein -the proteins are the hydrophobic surfactant protein SP-B and SP-C and the hydrophilic surfactant protein SP-A and SP-D; 10% neutral lipids-mainly cholesterol[8, 9].

The Pathophysiology of RDS is explained by a morphological and biochemical immaturity. The lack of pulmonary surfactant leads to an increase in the alveolar surface tension and a tendency for alveolar collapse, progressive atelectasis and reduced compliance. There is resultant ventilation perfusion mismatch, severe hypoxemia and lung injury with spontaneous or mechanical ventilation. In addition, the premature infant has increased chest wall compliance which further complicates the lung mechanics[10].

RDS presents at birth or shortly thereafter (within 6 hours) with grunting respirations, chest wall in drawing, nasal flaring and increased work of breathing. The neonate will often have progression of symptoms and requires supplemental oxygen[11]. The typical Blood Gas Analysis will characteristically show hypoxemia and hypercarbia with variable degrees of metabolic and respiratory acidosis[11]. The pathognomic changes in the chest radiograph include reduced lung volumes and diffuse reticulonodular ground glass pattern with air bronchograms. In the severe case, one may also appreciate a pneumothorax or other air leaks as well as a complete 'white out' on the radiograph[11].

The management of RDS in preterm infants is based on various modalities of respiratory support and the application of fundamental principles of neonatal care. For best results a multidisciplinary approach is best instituted.[11] Survival and outcomes for infants with RDS have improved in the past 30 years as a result of development of exogenous surfactant, CPAP and better mechanical vent lation[12].

Exogenous surfactant has been shown to significantly reduce the mortality and morbidity associated with RDS, as early back as 1980 when Fujiwara et al studied the first 10 neonates. In their uncontrolled trial, the neonates were successfully treated with a modified bovine extract[13]. Exogenous surfactant reduces the mortality and short term respiratory morbidity in preterms with RDS[14] but requires intubation and mechanical ventilation to administer. Mechanical ventilation increases the risk of subsequent chronic lung disease(CLD) associated with adverse pulmonary

and neurodevelopmental outcomes[15, 16]. The use of surfactant in our setting is not very common mainly because of its prohibitive cost.

All forms of mechanical ventilation for the immature lung probably promote some form of ventilator induced lung injury. Techniques that favor spontaneous breathing with early lung recruitment may be required to decrease BPD. Early lung recruitment is crucial and imperative to reduce the deleterious effects of atelectotrauma (damage that can occur when lungs are allowed to collapse absolutely and then are re expanded) and should probably begin in the delivery room.[17] This is why there has been renewed interest in pursuing respiratory management strategies for RDS that minimize mechanical ventilation in an effort to reduce the incidence of BPD which include CPAP in the delivery room[18, 19, 20] and early extubation from mechanical ventilation to CPAP[21].

CPAP as a modality of care for the preterm with RDS was first used in the 1970s after its introduction by Gregory and others[22]. It supports breathing of preterm infants in several ways. The upper airway of the preterm is very compliant and is therefore prone to collapse. CPAP splints the upper airway and decreases obstruction and apnea[23] The preterm with RDS struggles to establish and maintain lung volume due to surfactant deficiency, muscle hypotonia, slow clearance of lung fluid and a compliant chest wall. CPAP assists in expansion of the lungs and prevents alveolar collapse. In so doing, it reduces protein leak and conserves surfactant. In other words, it maintains positive pressure in the airways during spontaneous breathing hence increasing functional residual capacity and improving oxygenation in infants with RDS.

The CPAP system has three main components. The gas source, which provides a continuous flow of warm humidified air and or oxygen. The patient interphase, which connects the CPAP circuit to the infant's airway using an endotracheal tube, nasopharyngeal tube, nasal tube, nasal prongs (mono/ bi –nasal), a face mask or a head box. The third component is the pressure generator which creates positive pressure in the circuit[24] The devices that generate positive airway pressure are either of variable flow or continuous flow, based on their gas flow characteristics. The bubble CPAP (Fischer and Payne Healthcare, Auckland New Zealand) is a continuous flow device[25] while the Infant Flow Driver (IFD) CPAP (Electro Medical Equipment, Sussex, UK) is a variable flow device[26]. IFD CPAP uses a dedicated flow driver and generator

with a unique fluidic flip mechanism to adjust the gas flow throughout the respiratory cycle. The fluidic flip action of the IFD aids spontaneous breathing and provides more stable pressure delivery and better functional residual capacity. It also causes less thoracoabdominal asynchrony and is associated with reduced work of breathing[27].

With regard to Bubble CPAP, gas flows past the nasal device and the pressure is generated in the circuit by placing the distal limb of the CPAP circuit under a known depth of water. Gas flow is increased until continuous bubbling is achieved. This is a simple effective technique which can be applied by inexpensive equipment. A unique feature is that loss of CPAP pressure for example due to a large leak around the prongs or prong dislodgement is detectable by disappearance of bubbling[28]. Bubble CPAP is characterized by noisy variations in the pressure generated by gas bubb'ing quickly under water. It produces pressure oscillations of up to 4cm of water measured in the circuit. It has been suggested that Bubble CPAP is more effective than ventilator CPAP due to these oscillations[29]. Bubble CPAP improves gas exchange and protects against lung injury by promoting airway patency.

2.0 LITERATURE REVIEW

Clinical benefits have been associated with the use of CPAP in the premature infant. This was noted as far back as in the pre-surfactant era when no antenatal steroid use was available. Evidence then showed that early application of CPAP was associated with reduced need for mechanical ventilation and the associated adverse effects[30]. Further, infants who were extubated to nasal CPAP experienced a reduction in respiratory failure necessitating assisted ventilation[31]. Specifically, Bubble CPAP was developed in the seventies by Dr. Jen-Tien Wung at the Columbia Presbyterian Medical Centre New York using short nasal prongs. Nasal CPAP was used as the predominant mode of respiratory support in this centre and was associated with a relatively low incidence of chronic lung disease.

Avery et al[32] in their retrospective analytical study surveyed 1625 infants with birth weights of 700-1500gms in eight different intensive care nurseries. The study aimed at establishing why CLD was more common in some hospitals than in others taking into account established risk factors such as birth weight, gender and ethnicity. Experiences in the eight centers were surveyed and results showed that there was not much variation in the overall survival among the centers ranging from 78% to 84%. There were significant differences in the number of infants requiring oxygen at 28 days with a range of 58% to 79%, $p<0.01$ even when birth weight, race and sex were taken into consideration. Columbia had one of the best outcomes for LBW infants and the lowest incidence of CLD. The lower rate of CLD could be attributed to early application of 5cm of water CPAP via nasal prongs after birth in all age groups. The two units with the highest rates of CLD used nasal CPAP infrequently or never used them.

De Klerk and De Klerk[33] in their study in 2000 which was an analytical study with historic cohorts, looked at the outcomes in two groups of preterms with birth weights of 1000-1499 grams and compared them retrospectively over a 5 year period before period 1; n=57 and after period 2; n=59 the initiation of a primarily nasal CPAP approach. In the two time periods there was a decline in the number of infants ventilated (65% vs.14% respectively)and receiving surfactant (40% vs. 12% respectively) and in the mean days of ventilation (6 vs. 2 respectively) and oxygen(4 vs. 2 respectively). There was also a decrease in CLD at 28 days (11% vs. 0% respectively), death or CLD at 28 days (16% vs. 3% respectively) use of pressure support (34%

vs. 7% respectively), the incidence of NEC (11% vs. 0% respectively), time to reach full oral feeds (17.3 vs. 13.2 days respectively), discharge weight (2569 vs. 2314 gms respectively) and average length of stay in hospital (61 vs. 52.9 days respectively). No differences in neurosonographic or other morbidity outcomes were noted. This historical cohort study provided information on the impact of changing the respiratory support system to mainly a bubble CPAP system. The data collectively suggests that in the VLBW infants use of the bubble CPAP system, may reduce the need for and duration of mechanical ventilation ,the duration of oxygen exposure and the total duration of respiratory support.

Chan and Chan[34] in their study in 2007 further evaluated the short term outcomes of premature infants delivered at the United Christian Hospital with birth weights of less than 1499grams. This was an analytical survey with historic cohorts. 45 infants in the VLBW category were evaluated and 35 in the ELBW category in a two time period. During both study periods there was no major change in technology and medical management of the premature infant in the unit. The only difference was the use of Bubble CPAP in period 2 which substituted the use of mechanical ventilation. The results were such that in the VLBW category, no difference in the duration of mechanical ventilation support or extubation failure in both study periods was noted. Though the duration of Bubble CPAP was significantly shorter in babies in period 1, the no of days of patients with significant Apnea during Bubble CPAP was significantly less. No difference in the duration of oxygen support in both study periods was noted and the infants were weaned off oxygen at mean Gestational Age (GA) of 35 weeks. Around 10% of VLBW infants required Oxygen supply greater than 30% at GA of 36 weeks. However all of them survived and could be soon weaned off oxygen before GA of 40 weeks. Similar results were replicated in the ELBW infants. There was no significant difference in failed extubation and duration for Mechanical Ventilation. In addition, there was a significantly longer duration of CPAP support in period 2. The number of days with significant apnea during Bubble CPAP was significantly less. There was no difference in the duration of oxygen support in both study periods and neonates were weaned off oxygen at the mean GA of 39 weeks. Thirty percent of the ELBW infants in both study groups required oxygen support greater than 30% at mean GA of 36weeks but majority could be weaned off oxygen successfully at 44 weeks. The non respiratory outcome of both study periods was similar with enteral feeding being tolerated sooner; importantly there

was no increase in the incidence of Intraventricular hemorrhage and no baby on BCPAP suffered from NEC.

Prashanth Urs et al[35] in 2006 conducted a prospective observational study in Bangalore India. They evaluated the effectiveness of bubble CPAP as a simple and non invasive option in a developing country. Theirs was a population of fifty babies requiring respiratory support for RDS with birth weights of 1000-1500grams. They found that bubble CPAP was effective in eighty percent (80%) of the neonates. The mean duration of treatment in this success group was found to be 30.8+/- 8.6 hrs (range 18 -70 hours). The effectiveness of Bubble CPAP was judged using the Downe's score and there was a marked improvement in the score following Bubble CPAP treatment in newborns with RDS. FiO_2 requirements were significantly reduced and there was an increase in PaO_2 levels in babies who responded to Bubble CPAP treatment. None of the babies developed pneumothorax. The success rate of Bubble CPAP in mild (n=6, 12%) moderate (n=29, 59%) severe (n=15, 30%) RDS was 100%, 93.1% and 46.6% respectively.

In Suva Fiji, in 2003 Lanieta K et al[36] conducted a retrospective study using prospectively collected data. This was an evaluation of Bubble CPAP in a Neonatal unit in a developing Country, as an effective respiratory support that can be applied by nurses. They studied all neonates admitted to Neonatal Intensive Care Unit(NICU), 18 months before and 18 months after the introduction of bubble CPAP. They found that the introduction of bubble CPAP was associated with a 50% reduction in the need for mechanical ventilation. This was from 113 of 1106 (10.2%) prior to Bubble CPAP to 70 of 1382(5.1%) after the introduction of Bubble CPAP(x^2, $p< 0.001$). There was no difference in mortality between the two time periods. Among the 1106 neonates in period 1, there were 79 deaths (case fatality of 7.1%). Among 1302 neonates in period 2 there were 74 deaths (case fatality 5.4%).

Prakash Jeena et al[37] in 2000 in South Africa looked at the outcomes in neonates with acute respiratory failure supported initially either by rescue mechanical ventilation or by nasal CPAP. This was a retrospective review of cases and 89 and 85 neonates were examined in the two time periods respectively. The median weights (1900 vs. 1650 gms, male to female ratio (1.74:1 vs. 1.34:1), median gestation age of 32 vs. 34 wks was similar in the two groups. Of the 89 neonates who required IPPV, 17 failed initial Nasal CPAP and 7 required ventilator support for secondary

reasons after nasal CPAP was initially successful. In the remainder n=65 who initially received IPPV the mortality rate was 39% n=25 compared with 25% n=21 in the group who received Nasal CPAP initially. Sixty three neonates (74%) were initially successfully supported with Nasal CPAP alone. In this unit, nasal CPAP was found to be a useful adjunct to mechanical ventilation in the treatment of newborns with a variety of respiratory conditions especially RDS. The delay in instituting Mechanical ventilation by initial use of Nasal CPAP did not adversely affect outcome.

Samir Gupta et al[38] in 2009 in Middleburgh UK conducted a randomized controlled trial of post extubation Bubble CPAP versus IFD CPAP in preterm infants with RDS. They randomized preterms at birth between 24 and 29 weeks of gestation to receive either IFD CPAP (71 infants) or Bubble CPAP (69 infants). The mean gestational age and birth weights were similar in the two groups as were the proportion of infants who achieved successful extubation after 72 hours and for 7 days thereafter. They found that the median duration of CPAP support was 50% shorter in infants on Bubble CPAP. Moreover, of the subset of infants who were ventilated for less than 14 days, those on Bubble CPAP had a significantly lower extubation failure rate. There was no difference in the incidence of CLD or other complications in the two groups. Bubble CPAP was found to be associated with a significantly higher rate of successful extubation as well as a significantly reduced duration of CPAP support among the infants who had been ventilated for less than 14 days.

The use of Bubble CPAP is not without complications. These have been noted to arise during the delivery of nasal CPAP. Pneumothorax is more likely to occur in the acute phase of respiratory distress. It however is not a contraindication to continuing nasal CPAP therapy. Nasal obstruction tends to occur due to secretions and improper positioning of the Nasal CPAP prongs. To avoid obstruction the position of the prongs should be checked and the nares suctioned frequently. Nasal septum erosion or necrosis occurs due to pressure or friction to the nasal septum. This is avoided by having a small cushion of air between the bridge of the prongs and the septum. Gastric distention occurs from swallowing air. Gastric distention is a benign finding and does not predispose the infant to necrotizing Enterocolitis or bowel perforation. It occurs in

the chronic phase of respiratory distress and is often managed by intermittent aspiration of gastric contents.

, TABLE 1. SUMMARY OF STUDIES AND OUTCOMES OF USE OF BUBBLE CPAP TO TREAT RDS IN PRETERMS

Study	Study design	Country and sample size.	Outcome measures.	Results
Vivek Narenderan et al; 2001. Early Bubble CPAP and outcomes in ELBW preterm infants.	Retrospective analytical study with historic cohorts.	India- Bangalore. 84 neonates.	**Primary outcome;** to determine whether early Bubble CPAP in the delivery room was safe and resulted in improved respiratory outcomes in ELBW infants.	Early Bubble CPAP reduced delivery room intubations; days spent on mechanical ventilation, post natal steroid use and were associated with increased post natal weight gain with no increased complications.
Jagdish Koti et al;2009.Bubble CPAP for RDS in preterm infants	Prospective analytical study.	India –Hydrabad. 54 neonates.	**Primary outcome;** CPAP failures- infants requiring ventilation in the first week.	Bubble CPAP is safe in preterms with RDS. Those with white out CXR, PDA, partial or no exposure to antenatal steroids, sepsis or pneumonia and those with higher FIO2 requirement after initial stabilization are at high risk for failure.

Morley et al.NEJM 2008.COIN trial, early bubble CPAP vs. mechanical ventilation	Multicentre randomized control trial.	USA 610 preterm infants	**Primary outcome;** death or BPD at 36 weeks GA. Death or oxygen needed at 28 weeks GA.	CPAP group had reduced rates of intubation 46% vs. 53% in the 25-26wks GA during the first 5 days. The use of surfactant was halved 38%vs77%; p<0.001.
Thompson et al. Biol Neonate 2002. Early surfactant administration with rapid extubation IFDAS-Trial.	Multicentre randomized control trial.	USA. 241 preterms.	**Primary outcome;** Mortality, requirement for mechanical ventilation.	NCPAP reduced the need for mechanical ventilation through day 5 of life. No reduction in the total duration of respiratory support or oxygen dependency.
Adam G Buckmaster et al.2007.CPAP therapy for infants with RDS in non tertiary care centers	Randomized control trial	Sydney-Australia. 300 preterms.	**Primary outcome;** to evaluate the need for mechanical ventilation in preterm neonates managed with BCPAP.	Bubble CPAP reduced the need for up transfer of infants with RDS to tertiary centers
Avery ME et al.1987. Is chronic lung disease in	Multicentre review of	Columbia, Vanderbilt,Dallas,Seattle, Sanfransisco,Boxton,Houston,	**Primary outcome;** to establish why CLD was more common in	Columbia had the lowest rate of CLD of prematurity attributed to the early application of 5cm of

LBW preventable? A survey of 8 centers.	cases.	Toronto.	some centers.	water CPAP after birth in all age groups.
De Klerk and De Klerk.2001. Nasal CPAP and outcomes of preterm infants.	Historical cohort study.	Middlemore hospital. New Zealand.161 premature neonates	**Primary outcomes;** respiratory and non respiratory outcomes in preterm infants treated with BCPAP.	In the VLBW category of preterm infants, the system decreased the need for and duration of mechanical ventilation, the duration of oxygen exposure and the total duration of respiratory support.
Chan and Chan 2007. The use of Bubble CPAP in premature infants; a local experience.	Retrospective survey with historic control.	United Christian hospital Hong Kong. 80 preterms.	**Primary outcomes.** Evaluate the effects of BCPAP on the respiratory and non respiratory outcomes in premature infants in the unit.	There was no increase in the adverse respiratory outcomes. BCPAP was found to be safe, associated with less apnea and more favorable non respiratory outcomes.
Prashanth Urs et al 2006.BCPAP a primary respiratory	Prospective observational	MS Ramaiah Medical teaching college. India. 50	**Primary outcome.** To evaluate the effectiveness of	BCPAP was found to be safe and effective in treating mild and moderate grade RDS. It was also

,support for RDS in newborns.	study.	neonates.	BCPAP as an effective mode of primary respiratory support.	observed to be more effective in mothers who had received a course of antenatal steroids.
Lanieta K. et al. 2003. An evaluation of BCPAP in a neonatal unit in a developing country as an effective respiratory support that can be applied by nurses.	Retrospective analytical survey with historic controls.	Suva Fiji. 2400 neonates in the two time periods.	**Primary outcome.** To investigate the effect of BCPAP on need for mechanical ventilation and mortality. **Secondary outcome.** to investigate the feasibility of nurses implementing BCPAP.	BCPAP was associated with a 50% reduction in the need for mechanical ventilation with no difference in mortality. Nurses could safely apply BCPAP after 1 to 2 months of on the job training.
Samir Gupta et al. 2009. A randomized controlled trial of post extubation BCPAP vs IFDCPAP in preterms with RDS.	Randomized control trial.	Middleburgh U.K. 140 preterms.	**Primary outcome;** To compare the efficacy and safety of BCPAP and IFD CPAP in preterms.	BCPAP was as effective as IFD CPAP, however in infants ventilated for less than 14 days BCPAP was associated with a higher rate of successful extubation. BCPAP was also associated with a significantly reduced duration of CPAP support.

3.0 STUDY JUSTIFICATION/ UTILITY

Respiratory Distress Syndrome is the single most important cause of mortality and morbidity in the premature neonate. The management involves the timely institution of respiratory support as well as surfactant. The conventional therapy of mechanical ventilation is associated with a high incidence of chronic lung disease (CLD) high cost, labour intensive and out of reach in most resource limited settings. Establishing a NICU with mechanical ventilation would require high level of expertise and trained personnel, which is far from reality in many of the peripheral and district hospitals in Kenya. Bubble CPAP is a simple innovative modality of respiratory support that has been shown to have less incidence of Chronic Lung Disease (CLD). Lanieta, *et al.*[36] successfully demonstrated the usefulness of Bubble CPAP in a developing country, and its cost effectiveness. Pieper *et al.* have shown the importance of CPAP in the absence of neonatal intensive care and also the improved outcome in neonates treated with CPAP prior to transfer to a tertiary facility.[48]

Bubble CPAP in Kenya is available only at two centers, the AIC Kijabe Hospital and Tenwek Mission Hospitals. This study will allow the evaluation of this practiced experience at the Kijabe AIC hospital as well as review and draw lessons learnt and more importantly, evaluate how this can be applied to other levels of hospital management with regard to care of the premature neonate.

4.0 OBJECTIVES OF THE STUDY

To describe the experience of the use of Bubble CPAP in preterm neonates with Respiratory Distress Syndrome at the AIC Kijabe hospital.

5.0 METHODOLOGY

5.1 STUDY DESIGN

This was a short longi udinal survey.

5.2 STUDY AREA

The study was carried out at the AIC KIJABE MISSION HOSPITAL new born unit.

5.3 STUDY POPULATION

The study population was all consecutively admitted preterms with RDS treated with bubble CPAP at the New Born Unit (NBU) during the study period.

5.3.1 Inclusion criteria

1. All preterms admitted with a diagnosis of RDS and put on bubble CPAP.
2. Patients whose parent(s) gave consent.

5.3.2 Exclusion criteria

1. Patients whose parent(s) declined to give consent.

5.4 SAMPLE SIZE DETERMINATION

Sample size was calculated using Fischer's formula;

$$n = \frac{Z^2_{\alpha/2} \times P(1-P)}{d^2}$$

Where

n = sample size

$Z^2_{\alpha/2}$ = the corresponding value to the 95% confidence level (1.96)

d = absolute precision (10%)

p = known prevalence from other studies

The prevalence (P) of the study outcome was based on an Indian study by Jagdish Koti et al.[40] In that study, approximately 20% of neonates were not weaned off bubble CPAP in the first week of life. The sample size calculation in the present study aimed at providing a precision (d) of 10% around the estimated proportion for prevalence of short term outcomes for premature infants treated with bubble CPAP at Kijabe AIC hospital.

Therefore $n = \frac{1.96^2 (0.2)(0.8)}{0.01}$

n = 61 preterms.

5.5 SAMPLING METHODS

All consecutively admitted preterms that satisfied the inclusion criteria were recruited during the study period.

5.6 CASE DEFINITION

1. RDS was diagnosed by;

- Clinical findings of a preterm with progressive respiratory distress that was indicated by increased work of breathing and increased oxygen requirements. The clinical signs of respiratory distress that were examined for by the principal investigator and or the assistant included: Tachypnea, nasal flaring, grunting, cyanosis and intercostal and subcostal retractions.

2. Preterm neonate;

- An infant born at a gestation less than 37 completed weeks or 259 days of gestation as was evaluated using the New Ballard score (Appendix 6).

5.7 STUDY PROCEDURE

In order to achieve the main objective of the study, informed consent for study participation was sought from women admitted consecutively to the labour ward for possible preterm delivery. Preterm babies of consenting women delivered at the AIC Kijabe mission hospital were examined using a standardized tool to determine the gestational age i.e. the New Ballard Score and the weight and head circumference taken and recorded. The babies were further examined for signs of respiratory distress (Tachypnea, nasal flaring, grunting, cyanosis and intercoastal and subcoastal retractions). The mothers clinical notes were reviewed to collect information on mothers health during pregnancy(UTI in late pregnancy ,hypertension, gestational diabetes, use of antenatal steroids) : nd delivery (location of birth, mode of delivery, PROM, duration of 1st and 2nd stage of labour) as well as immediate infant outcomes (APGAR score at 1 and 5

minutes). All preterms with Tachypnea >60 per minute were admitted to the new born unit (NBU) and started on oxygen.

Babies were eligible for Bubble CPAP if they had persistent respiratory distress and were able to breathe spontaneously. Eligible babies were started on Bubble CPAP with binasal Hudson prongs. Positive End Expiratory Pressure (PEEP) was started at 5cm of water and adjusted to maintain SPO_2 between 87% and 95%. Flow was titrated to the minimum to produce continuous bubbling in the bubble chamber. Babies were nursed in a thermal neutral environment, checked for hypoglycemia and baseline investigations done- full hemogram and Immature to Total Neutrophil ratio (IT ratio), blood culture, Urea Electrolyte and Creatinine levels.

Follow up of babies when on Bubble CPAP.

The AIC Kijabe hospital management protocol was followed in the care of the premature neonates. During the study period, all the infants were reviewed twice daily and the FIO_2, SPO_2, were reviewed and adjusted accordingly; feeding requirements, and PEEP. Weighing of the neonates was done on alternate days and a discharge weight was recorded as well as the weight at 36 weeks gestation.

The following variables were evaluated and reviewed by the principal investigator: Apgar scores, chest radiograph findings where a chest radiograph had been done and FIO_2 requirements. Other clinical data recorded was incidence of pneumothorax, pneumonia, Necrotising Enterocolitis (NEC -modified Bells criteria), culture proven sepsis, duration of hospital stay among survivors and mortality. This was abstracted from the patients' records at the end of shift in the evening from the second data collection tool (Appendix 3).

The study assessed the following primary outcome indicators: death or discharge alive. The second level indicators assessed were: respiratory outcomes (duration of CPAP support, duration of oxygen therapy, the gestational age of the infant when oxygen therapy was terminated, and number of infants requiring $FIO_2 > 30\%$ at gestational age of 36 weeks). The following non respiratory outcomes were also assessed: post natal age of the infants when full enteral feeds were tolerated, and complications of Bubble CPAP (CPAP belly, nasal trauma, and pneumothorax).

Bubble CPAP was considered successful if the respiratory distress improved and the neonate could be successfully weaned off from Bubble CPAP. The criteria for weaning were;

- Absence of respiratory distress clinically i.e. minimal or no chest retractions and RR between 30 and 60 breaths per minute.
- $SPO_2 > 90\%$ on $FIO_2 < 30\%$ and PEEP < 5cm of water.
- Free from apnea for 24 hours.
- Tolerating gentle nasopharyngeal suctioning without increasing FIO_2 requirements with CPAP removed.

Those who did not satisfy the above criteria i.e. had persistent Tachypnea, apnoiec attacks and required more respiratory support in terms of PEEP and FIO2 were considered to have failed and hence transferred cn to mechanical ventilation where this was available.

5.8 DATA MANAGEMENT.

Variables distributed normally were represented as medians with interquartile ranges. Maternal, neonatal and clinical data was compared among neonates who had successful Bubble CPAP .Data was entered into an MS Access database. Each field in the database had range and consistency checks tc minimize errors during data entry. Verification and cleaning of all variables was done in MS Access before commencing the analysis.

5.9 STATISTICAL ANALYSIS

Data was analyzed in the statistical package for social sciences SPSS (SPSS version 17.0).

Descriptive statistics of sample characteristics was obtained by calculating means (SD) or medians (ranges) for continuous variables. Categorical variables were summarized using frequency tables. and graphs. Birth weight was categorized into Extremely Low Birth Weight. Very Low Birth weight and Low Birth Weight. These factors were compared with outcome of patients treated with bubble CPAP using chi square tests and the appropriate *p*-values reported at the 5% level of significance. Multivariate logistic regression was used to obtain adjusted estimates of the effect of birth weight. age. morbidity and other independent variables on the outcome of patients receiving bubble CPAP treatment.

5.10 ETHICAL CONSIDERATIONS

1. The study was conducted after approval from the Department of Pediatrics and Child Health. University of Nairobi and The Kenyatta National Hospital Scientific and Research Ethical Review Committee.
2. Approval from the Research and Ethical Committee of the AIC KIJABE HOSPITAL was also sought.
3. The purpose of the study was carefully explained to the children's parents or guardians and a written consent was obtained prior to enrolling any child in the study.
4. Strict confidentiality was maintained throughout the study period.
5. The study findings were presented to the University of Nairobi (UON) Department of Pediatrics and Child Health Academic Staff and Students in fulfillment of the requirements of the Masters in Medicine Program.

6.0 RESULTS

The study enrolled a total of 61 premature neonates with RDS treated using bubble CPAP at AIC Kijabe hospital between July 2011 and January 2012. The main demographic characteristics of the premature infants are summarized in Table 1.

Males accounted for 33 (54.1%) of the newborns participating in this study and the remaining 28 (45.9%) participants were females. The median age of participating preterms was 1 day (range 1 to 14 days). As shown in table 1, bubble CPAP was initiated during the first day of life for 91.8% of the preterms. The average birth weight of the participating newborns was 1425 gms (SD ±461) and the average admission weight was 1422 gms (SD ±460). The average gestational age of the newborns was 30.8 weeks (SD ± 2.7) all the neonates were less than 36 weeks GA. The median APGAR score at birth (1 minute) was 8 and this score increased to 9 at 5 minutes and 10 at 10 minutes.). The length of hospital stay ranged from 26 to 36 days for the premature newborns with a median length of stay of 28 days.

Table 1: Demographic characteristics of preterm infants admitted with RDS at Kijabe Hospital

Characteristic	**Frequency (%)**
Number of participants	61 (100.0)
Males N (%)	33 (54.1)
Females N (%)	28 (45.9)
Age at initiation of BCPAP	
First day of life N (%)	56 (91.8)
First week (2-6 days) N (%)	2 (3.3)
7-14 days N (%)	3 (4.9)
Very low birth weight N (%)	
LBW < 2500 gms	23 (37.7)
VLBW < 1500 gms	26 (42.6)
ELBW < 1000 gms	12 (19.7)
APGAR SCORE	**Median (IQR)**
1 minute	8(4–9)
5 minutes	9 (5-10)
10 minutes	10 (6 – 10)

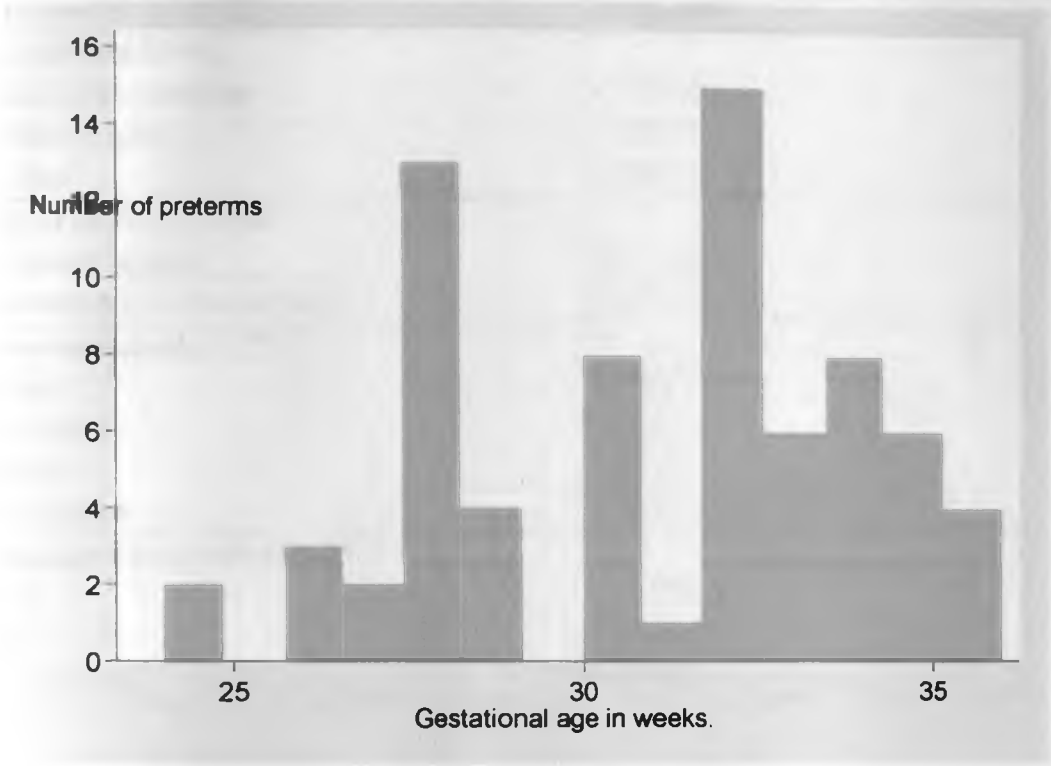

Figure 1: Histogram showing the Gestational Age distribution of the study participants

Clinical characteristics of preterm babies with RDS

Birth details

Table 2 shows that 77% of all deliveries in this study were conducted at Kijabe AIC hospital. Nine (14.8%) newborns were delivered in other hospitals and 5(8.2%) were born at home. Most (53.3%) of the deliveries were spontaneous vertex deliveries and antenatal steroids were administered in 13 (21.3) out of the 61 cases. Surfactant administration was reported in 10 (14.8%) cases.

Table 2: Perinatal information of children with RDS managed with BCPAP at Kijabe hospital

Birth details	Frequency
Place of birth N (%)	
AIC Kijabe Hospital	47 (77.0)
Other hospital	9 (14.8)
Home	5 (8.2)
Mode of delivery N (%)	
Cesarean section	28 (46.6)
Spontaneous vertex delivery	32 (53.3)
Antenatal steroids N (%)	
None	34 (55.7)
Complete	13 (21.3)
Partial	2 (3.3)
Not known	12 (19.7)
Surfactant administered N (%)	
Yes	10 (16.4)
No	42 (68.9)
Not known	9 (14.8)

Diagnosis

RDS was the primary diagnosis in all the 61 infants recruited in the study. However, 22 (36.1%) newborns were diagnosed with at least one comorbid neonatal illness. Figure 1 below shows the neonatal illnesses that were commonly diagnosed among newborns with RDS. Neonatal jaundice and neonatal sepsis were the most common comorbid illnesses occurring in 23% and 16.4% of newborn, respectively.

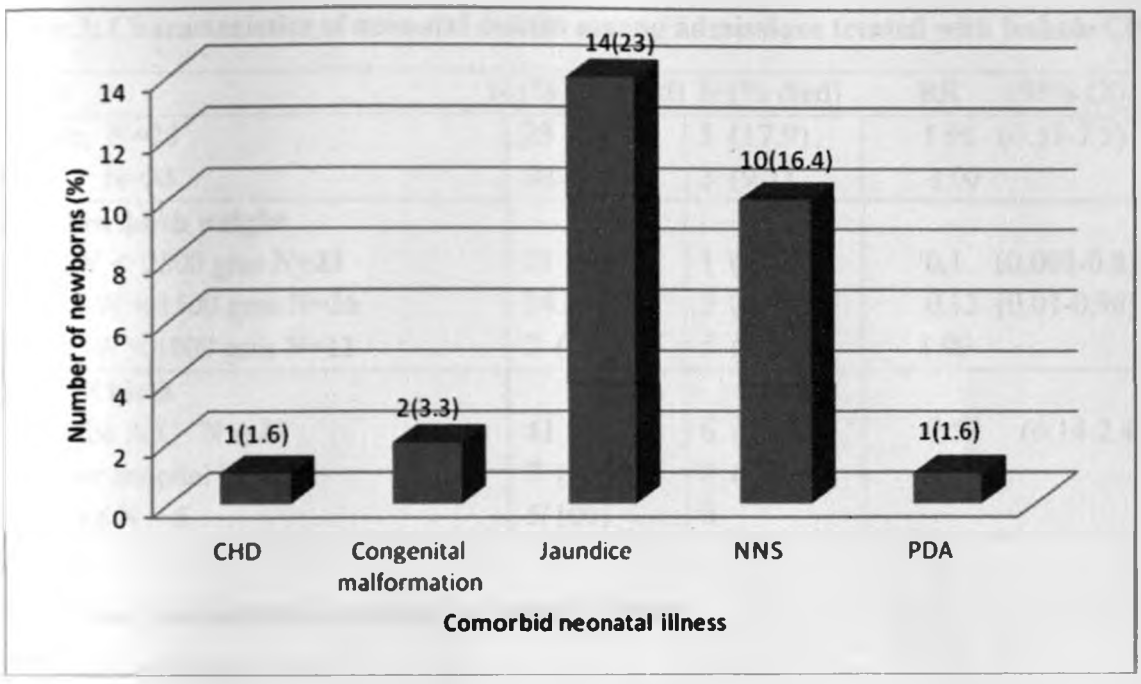

Figure 2: Comorbid illnesses among preterm newborns admitted with RDS at Kijabe AIC Hospital

Mortality rate in preterm babies treated with Bubble CPAP for RDS

The mortality rate among the preterms treated with Bubble CPAP during the study was 13.1%.

The characteristics of pretems who died during hospital stay are presented in table 3. Neonatal death was significantly associated with Birth weight.

Table 3: Characteristics of neonatal deaths among admissions treated with bubble CPAP

Factor	N (% survived)	N (% died)	RR (95% CI)	P value
Female, **N=28**	23 (82.1)	5 (17.9)	1.96 (0.51-7.5)	0.45
Male, **N=33**	30 (90.9)	3 (9.1)	1.00	
Very low birth weight				
LBW < 2500 gms **N=23**	21 (95.5)	1 (4.5)	0.1 (0.001-0.81)	0.007
VLBW < 1500 gms **N=26**	24 (92.3)	2 (7.7)	0.12 (0.01-0.96)	0.012
ELBW < 1000 gms **N=12**	7 (58.3)	5 (41.7)	1.00	
Place of birth				
Kijabe AIC **N = 47**	41 (87.2)	6 (12.8)	0.57 (0.14-2.40)	0.64
Other hospital **N = 9**	7 (77.8)	2 (22.2)	1.00	
Home **N = 5**	5(100)	0		

Respiratory outcomes in patients on bubble CPAP

Duration on bubble CPAP

The median duration of Bubble CPAP treatment was 5 days (interquartile range 3 to 7 days).

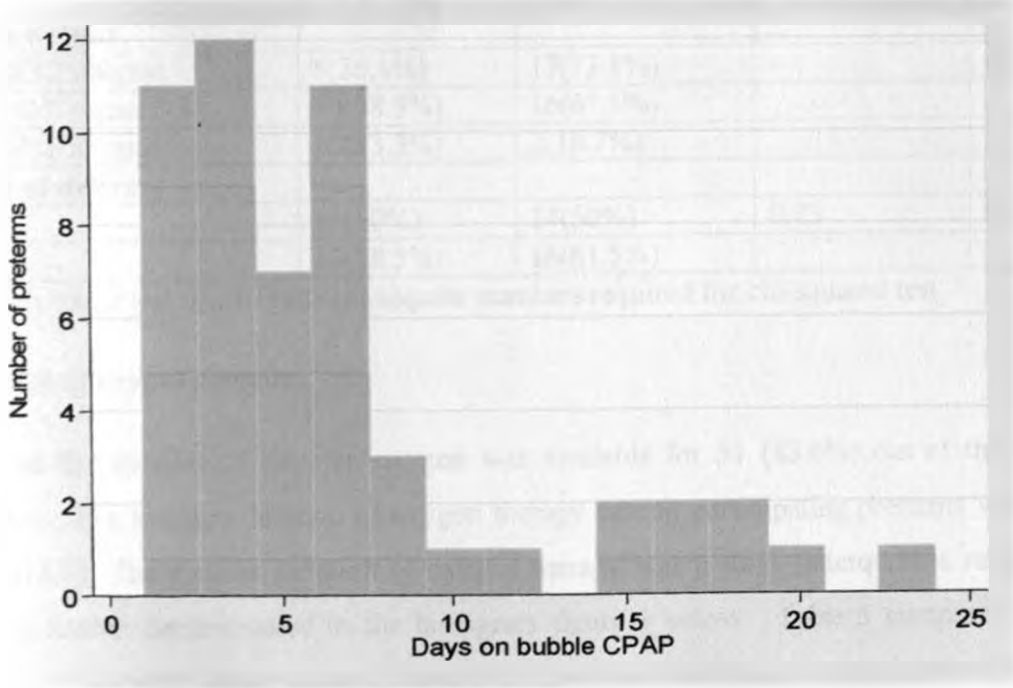

Figure 3: Histogram showing the duration of Bubble CPAP

As shown in Table 4 the median duration of bubble CPAP treatment was significantly associated with birth weight (p = 0.044). The median length of bubble CPAP treatment was significantly longer among very low birth weight preterms compared to preterms weighing > 1750 gms.

Table 4: Characteristics of preterm babies and median duration of bubble CPAP therapy

	Duration of CPAP therapy greater than median duration (5 days)		Chi square	P value
	Yes	No		
Sex				
Male	11(36.7%)	19(63.3%)	1.65	0.27
Female	13(54.2%)	11(45.8%)		
Surfactant administered				
Yes	2(25%)	6(75%)	-	0.43*
No	20(47.6%)	22(52.4%)		
Birth place				
Kijabe AIC	21(48.8%)	22(51.2%)	-	0.29*
Other hospital	3(37.5%)	5(62.5%)		
Home	0(0%)	2(100%)		
Antenatal steroids				
Yes	5(33.3%)	10(66.7%)	0.70	0.54
No	17(45.9%)	20(54.1%)		
Birth weight				
VLBW<2500gms	6(26.1%)	17(73.1%)	-	0.044*
LBW<1500gms	10(38.5%)	16(61.5%)		
ELBW<1000gms	10(83.3%)	2(16.7%)		
Mode of delivery				
SVD	14(50%)	14(50%)	0.73	0.43
CS	10(38.5%)	16(61.5%)		

*Fishers exact test – cells with inadequate numbers required for chi squared test

Duration of oxygen support

Data on the number of days on oxygen was available for 51 (83.6%) out of the 61 preterm neonates. The average duration of oxygen therapy among participating preterms was 14.2 days (SD ±18.9). The median duration of oxygen therapy was 6 days (interquartile range 4 to 17). This is further demonstrated in the histogram figure 3 below. Table 5 compares the median duration of oxygen therapy among babies with different clinical and demographic characteristics using chi square test.

There was a statistically significant association between birth weight and median duration of oxygen therapy (p = 0.006). The mode of delivery also showed a significant association with duration of oxygen therapy. On further multivariate analysis the birth weight seemed to be the independent correlate. This is demonstrated in table 6 (p = 0.017).

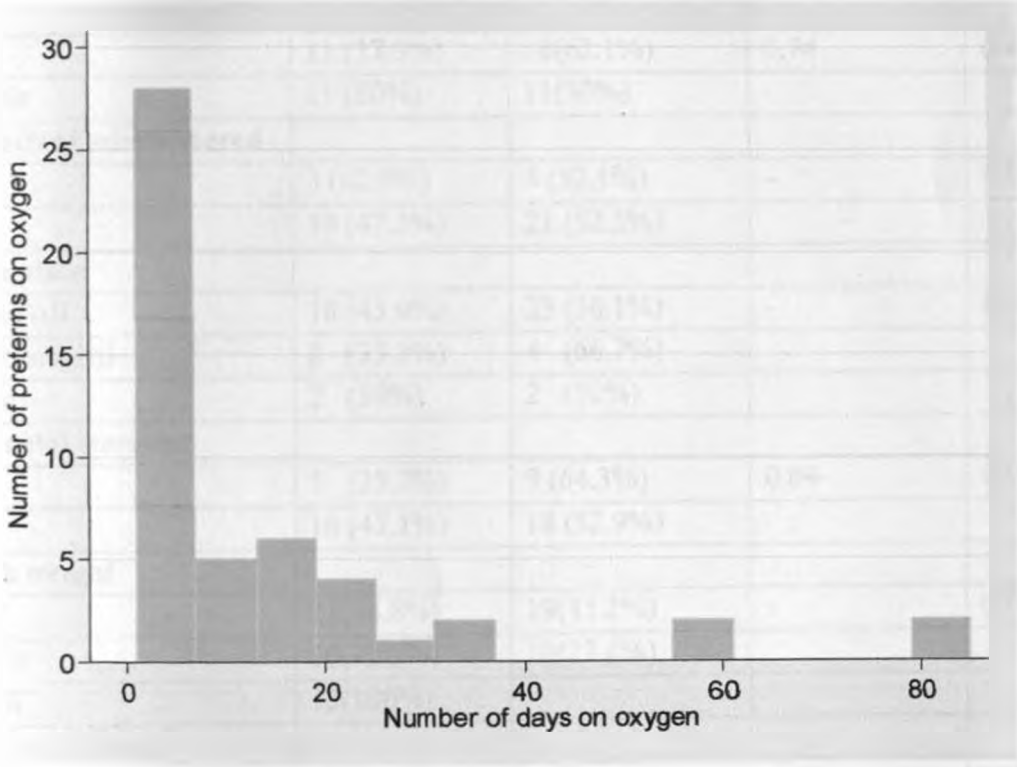

Figure 4: Histogram showing the duration of oxygen therapy.

Table 5: Characteristics of preterm babies managed using bubble CPAP and median duration of oxygen therapy

	Duration of oxygen therapy greater than median duration (6 days)		Chi square	P value*
	Yes	No		
Sex				
Male	11 (37.9%)	18(62.1%)	0.74	0.41
Female	11 (50%)	11(50%)		
Surfactant administered				
Yes	3 (42.9%)	4 (57.1%)	-	0.99*
No	19 (47.5%)	21 (52.5%)		
Birth place				
Kijabe AIC	18 (43.9%)	23 (56.1%)	-	0.99*
Other hospital	2 (33.3%)	4 (66.7%)		
Home	2 (50%)	2 (50%)		
Antenatal steroids				
Yes	5 (35.7%)	9 (64.3%)	0.04	0.92
No	16 (47.1%)	18 (52.9%)		
Birth weight				
LBW	23(54.8%)	19(45.2%)	-	0.006*
VLBW	26(72.2%)	10(27.8%)		
ELBW	12(100%)	-		
Mode of delivery				
SVD	15 (68.2%)	7 (31.8%)	4.58	0.048
CS	11 (37.9%)	18 (62.1%)		

*Fishers exact test – cells with inadequate numbers required for chi squared test.

Table 6: Multivariable analysis

	Odds Ratio	P value	[95% Conf.Interval]	
Gender	1.74	0.52	0.32	9.53
Birth place.				
Kijabe hospital	0.80	0.90	0.03	23.14
Other hospital	1.96	0.74	0.04	98.76
Surfactant use.	0.23	0.20	0.03	2.13
ANC steroids	1.15	0.87	0.21	6.14
Mode of delivery	8.37	0.02	1.33	52.86
LBW	1.00			
ELBW/VLBW	2.03	0.017	1.36	11.39

Oxygen administration at 36 weeks

Out of the 61 newborn babies 50 (82%) were aged less than 36 weeks hence data on oxygen administration at 36 weeks for 82% of the sample. Out of the 50 newborns delivered before 36 weeks GA 10 (20%) required oxygen administration at 36 weeks. Table 6 below compares the characteristics of newborns requiring oxygen at 36 weeks to newborns not on oxygen administration.

The factors that showed in Table 6 did not show a significant association with oxygen administration at 36 weeks.

Table 7: Characteristics of preterm babies managed using bubble CPAP and oxygen requirements at 36 weeks

	Oxygen requirement at 36 weeks		P value
	Yes	No	
Sex			
Male	7(25.9%)	20(74.1%)	0.31*
Female	3(13.0%)	20(87%)	
Surfactant administered			
Yes	4(40%)	6(60%)	0.18*
No	6(15.4%)	33(84.6%)	
Birth place			
Kijabe AIC	7(17.5%)	33(82.5%)	0.12*
Other hospital	1(14.3%)	6(85.7%)	
Home	2(66.7%)	1(33.3%)	
Antenatal steroids			
Yes	0(0%)	14(100%)	0.085*
No	8(23.5%)	26(76.5%)	
Birth weight			
LBW	7(16.7%)	42(83.3%)	0.99*
VLBW	1(12.5%)	8(87.5%)	
ELBW	2(66.7%)	1(33.3%)	
Mode of delivery			
SVD	7(25.9%)	20(74.1%)	0.3*
CS	3(13%)	20(87%)	

*Fishers exact test – cells with inadequate numbers required for chi squared test.

Non-respiratory outcomes in patients on bubble CPAP

Complications of bubble CPAP

During the study all 61 newborn babies on bubble CPAP were monitored for development of pneumothorax, CPAP belly or nasal trauma. There was no major complication of bubble CPAP reported during the study.

Age at full-enteral feeding

The outcome of age at full enteral feeding was available for 33 (54.1%) of the newborn babies in the study. The median age at full enteral feeds was 18 days (interquartile range 12 to 25 days).

7.0 DISCUSSION

This was a short prospective cohort study describing the use of a new technique for ventilatory support for preterm neonates with respiratory distress syndrome in a rural hospital in a developing country. Bubble CPAP was feasible and safe in this hospital that had nurse patient ratios less than normally required by neonatal intensive care units as well as one medical officer and clinical officer who out of hours covers all other pediatric areas in the hospital.

The role of Bubble CPAP has been well documented[27,30,31,32-36]. In this study, 86.9% of the preterms who were treated with Bubble CPAP survived to discharge. These results are similar to reports of effective Bubble CPAP as was found by Prashanth Urs[35] who reported an 80% effective Bubble CPAP and Bassinouy et al a 61 % success rate among the 50 and 44 newborns studied in India respectively. Again, the outcome did not vary between genders in this study, Sandri et al[42] in their study found that there was a high need for respiratory assistance in the male preterms. Another significant finding was that 91.8% of the prematures had Bubble CPAP initiated on the first day of life hence there was no delay in the institution of respiratory support.

The mortality rate in preterm babies treated with Bubble CPAP was 13.1%. With regard to gender, gestational age, birth weights and place of birth, none of these factors showed a statistically significant association with death. Although this study was not powered to detect an association, data on the significant effect of Bubble CPAP on mortality is consistent with findings in other studies. De Klerk and De Klerk[33] found a significant reduction in the incidence of death or CLD at 28 days of 16% vs 3% where Bubble CPAP was used as the mode of respiratory support. Other studies from neonatal intensive care units in developing countries have reported high mortality rates, for example, forty-six percent (46%) overall mortality

among two hundred and thirty-four (234) neonates in Zimbabwe, and an odds ratio for death of 12 if babies required mechanical ventilation compared to those who received conventional CPAP.

Of the respiratory outcomes, the duration of Bubble CPAP treatment median was 5 days (interquartile range 3 to 7 days) and was significantly associated with birth weight. Gupta et al found a median of 2 days with an interquartile range of 1 to 3 days. In their study, the neonates had weights in the range of 600gms – 1500gms. Meyer et all similarly found that less than 10% of the study population – preterms of weights <1000gms required any form of respiratory support at 36 weeks GA.

In this study, the median duration of oxygen therapy was 6 days with an interquartile range of 4 to 17 days. This was significantly associated with neonates who had GA of less than 32 weeks. De klerk and De Klerk found a twofold decline in the number of days on oxygen, median duration of 2 days with an interquartile range of 1 to 3 days. The two populations of neonates studied are comparable are theirs were VLBW of 1000-1499gms similar to the population in this study.

The incidence of CLD was (20%). This study did not show any significant association between oxygen administrations with use of surfactant or antenatal steroids. This is probably because the study was not powered to detect this effect even on multivariate analysis. Meyer et al[45] found that fewer of the Middlemore cohort, were on Oxygen at 28 days (odds ratio 0.17 with 95%CI 0.07–0.32) and fewer infants were discharged home on oxygen (odds ratio risk 0.38 95% CI 0.16–0.90).

The non respiratory outcome of age at full enteral feeding was in this study at a median of 18 days (interquartile range of 12 to 25 days). The study by Chan and Chan[34] found that the babies on Bubble CPAP reached full enteral feeding faster and hence were on total parenteral feeds for a shorter duration. This was at a mean age of 16.4 days. De Klerk[33] reported similar results in that infants reached full enteral feeds faster and there was no change in days to regain birth weight. This suggests that abdominal distention and or increased work of breathing and caloric expenditure, both potential adverse effects of CPAP did not adversely affect the infants in the study.

During this study, all the babies were monitored for development of pneumothorax, CPAP belly or nasal trauma. None of these complications was reported. This is similar to what Chan and Chan[34] reported in that no infant had injury or trauma to the nose, and no significant air leak was encountered in the study period.

This is one of the few prospective studies on the role of Bubble CPAP for RDS in preterm neonates in our setting. In terms of study design, it varies from previous studies that have been retrospective analytical surveys with historic cohorts or multicentre randomized control trials. These have the advantage of comparing two time periods before and after Bubble CPAP introduction in the units. This was possible in that, the two time periods were directly comparable in terms of staffing as well as the availability of standardized admission criteria so that preterms admitted and managed in the two periods were comparable. Again, the study settings were different. This study was conducted in a resource poor setting with limited number of staff with an equally high turn overrate and frequently had a period of on the job training rather than a specific training on Bubble CPAP. Further, mechanical ventilation was not

available round the clock in the event that a neonate failed Bubble CPAP and hence required mechanical ventilation. This was significant as previous studies were conducted in equipped neonatal units with specifically trained staff attached to the unit and available mechanical ventilation in the event of failed Bubble CPAP. This study aimed at describing the immediate short term outcomes of neonates on Bubble CPAP. A longer study period that allows the description and follow up of the long term outcomes for instance the neurocognitive development would be useful in the further description of this mode of respiratory support. Studies on the effectiveness of Bubble CPAP in Africa are mainly those that have been described in South Africa.

This study in Kenya has allowed the description of this treatment modality and the results are encouraging in that Bubble CPAP is safe and feasible. Safe mechanical ventilation requires a high level of expertise and the constant availability of trained medical staff. This is rarely a reality in provincial or district hospitals in our setting, which receive the bulk of these neonates. Thus, it's highly advantageous if a cheaper and simpler intervention can significantly reduce the need for mechanical ventilation. Perhaps an initial step in development of neonatal services should be the provision of Bubble CPAP.

7.1 STUDY LIMITATIONS

The study was underpowered due to the limited number of preterm neonates admitted into the unit. This may account for the lack of statistical correlation with the commonly acknowledged associations with good outcomes e.g. use of surfactant and antenatal steroids.

Some caution is required in the interpretation of these results. This was not a randomized trial and hence other factors confounding mortality rates are possible.

We did not collect data on the severity of illness in terms of the respiratory distress and hence it's possible that more neonates of lower severity of illness were admitted and only a randomized trial could fully compensate for other confounding.

7.2 CONCLUSION

- Bubble CPAP is a safe and effective mode of respiratory support for preterm neonates with RDS and can be safely applied in primary care facilities.
- The mortality rate of preterms treated with Bubble CPAP was 13.1%.
- Bubble CPAP was not associated with any complications during the study period specifically pneumothorax, CPAP belly and nasal trauma.
- 10(20%) of the preterm neonates required continued oxygen administration at 36 weeks Gestational Age.

7.3 RECOMMENDATION

This study has shown that Bubble CPAP is a simple, safe and effective mode of respiratory support for neonates with RDS which can be applied in primary levels of care in our setting and we suggest that it be adopted as a primary respiratory support in all levels of care that admit and manage neonates.

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APPENDIX 1: QUESTIONNAIRE

(Inclusive of data from ICU)

Study ID number _____
Date of Birth:_____
Date of Admission: _____
Left Hospital (Date)_____
- ◊ Discharged
- ◊ Died in Hospital
- ◊ Transferred to other hospital
- ◊ Unknown

Gestational Age (Birth): _____ weeks.
New Ballard score for GA_____ weeks.
Birth Weight (g): _____ grams
Admission Weight (g): _____ grams
Discharge Weight (g): _____ grams
Sex M F Unknown_____

BIRTH DETAILS

Location of Birth
- ◊ Kijabe _____
- ◊ Home_____
- ◊ Other Hospital (Name)
- ◊ Health Center (Name)
- ◊ Unknown

Mode of Delivery
- ◊ SVD _____
- ◊ CS
- ◊ AVD(Vacuum/forceps)
- ◊ Other
- ◊ Unknown _____

APGAR score (NA if not available)_____
- ◊ 1 minute: _____
- ◊ 5 minutes:
- ◊ 10 minutes:

Antenatal Steroids
- ◊ None
- ◊ Partial(1-3 doses)
- ◊ Complete (4 doses)
- ◊ Unknown

Respiratory
- ◊ Bubble CPAP
  - o # Days on CPAP_____
  - o CPAP started Hour of life _____
- ◊ Surfacant Y N unknown _____
- ◊ Mech Vent Y N Unknown _____

Prematures
- ◊ Weight at 36/40 PMA (gms)_____
- ◊ O2 at 36/40 PMA Y N Unknown_____
- ◊ No of days on O_2 therapy_____
- ◊ Age at full enteral feeds (DOL) _____
- ◊ Highest PEEP _____
- ◊ Highest FIO2_____
- ◊ Episodes of significant apnea_____
- ◊ Weaning off from CPAP(DOL)_____
- ◊ Procedure for weaning

_____
_____
_____

Complications of CPAP
- ◊ Pneumothorax_____
- ◊ CPAP belly_____
- ◊ Nasal Trauma_____

DIAGNOSIS

Tick all that apply – IN NOT TICKED, ASSUME "NO"
- ◊ Asphyxia
- ◊ Aspiration Pneumonia (not MAS)
- ◊ Congenital Heart Dz
- ◊ Congenital Malformations – NOS
- ◊ Hydrocephalus
- ◊ Hypoglycemia
- ◊ IVH (Intraventricular Hemorrhage)
- ◊ Jaundice – neonatal
- ◊ MAS (Meconium Aspiration Syndrome)
- ◊ NEC (Necrotizing Enterocolitis)
- ◊ PDA (Patent Ductus Arteriosus)
- ◊ RDS (Respiratory Distress Syndrome)
- ◊ Seizures
- ◊ Sepsis neonatal
  - o Culture positive? Y N Unknown
- ◊ Sepsis – suspected (R/O sepsis): Criteria:
  - o Fever
  - o MAS
  - o PROM (<18hrs prem; <24hrs term) _____
  - o Prematurity
  - o Other
  - o Unknown _____
- ◊ Spina bifida
- ◊ TTN (Transient Tachypnea of Newborn) _____
- ◊ Other Dx _____
- ◊ Other 2nd Dx
- ◊ Other 3rd Dx

APPENDIX 2: DATA COLLECTION FORM

Newborn Feeding And Observations

Baby's Hospital Number: _____
Baby of: _____
Baby's Name: _____

Date: _____ Gest Age: _____ Day of life: _____ Head Circum: _____

VITALS	Weight: _____ gram ↑ / ↓ _____ gm Time weighed: _____																							
Time of Day	0600	0700	0800	0900	1000	1100	1200	1300	1400	1500	1600	1700	1800	1900	2000	2100	2200	2300	2400	0100	0200	0300	0400	0500
Temp Ax																								
Temp Skin																								
Temp Isolette																								
Heart Rate																								
Respirations																								
Resp Asses (1)																								
O_2 Sat. %																								
O_2 litre./min.																								
O2 % Blended																								
Rm/Can/Mask CPAP																								
PEEP																								
Skin Color (2)																								
Position (3)																								
FLUIDS	**INTAKE**																							
Breast Feed (4)																								
Order ml x h																								
Feed Type (5)																								
Syringe ml																								
NG Feed ml																								
Aspirate ml																								
Aspirate color(6)																								
NGT changed																								
Total Oral (Syr+NG)																								
IV Fluid (7)																								
Buretrol ml																								
Infused ea. hr.																								
IV 2/ Blood																								
IV site/change (8)																								
IV tubing/sol change																								
OUTPUT																								
Vomitus (6)																								
Stool (9)																								
Urine (9)																								
Nurse Initials																								

APPENDIX 3: CONSENT FORM

THE SHORT TERM OUTCOMES OF PREMATURE INFANTS TREATED WITH BUBBLE CPAP FOR RDS AT THE AIC KIJABE HOSPITAL, KENYA

Introduction

My name is Dr. Omoding Anastasia Amokola. I am a post graduate student in the department of pediatrics and child health at the University of Nairobi. School of Medicine. As part of my postgraduate studies, am required to carry out a research project. My research study is intended to find out the short term outcomes of preterm infants with RDS(Respiratory Distress Syndrome) who are treated with . Bubble CPAP(Continous Positive Airway Pressure) at the AIC Kijabe Hospital. These are clinical parameters that are used to monitor the babies progress using this form of treatment. I would like to include your child as part of the study.

Purpose of the study.

RDS stands for Respiratory Distress Syndrome which is one of the most common disease process that is seen in babies who are born before term also refered to as preterms. RDS occurs because the baby has been born before they have matured adequately in the lungs to allow them to be able to breath on their own. The baby does not have the necessary lung protein that is important in keeping the airways open or it may be in very small amounts. Because of this, the baby will require to be assisted in breathing and hence the use of Bubble CPAP. This treatment is currently not available in the tertiary and other Government hospital facilities for babies with RDS in Kenya. It has however been used widely in the West with good results. There have been no studies done in our setting to evaluate this form of treatment.

Study procedures.

If you decide to participate in this study, you will be asked several questions about the babies health and period during the pregnancy-Antenatal Period. A doctor will then examine the baby and the baby will be started on the treatment-Bubble CPAP. The baby will subsequently monitored as per the normal routine as well as the progress on Bubble CPAP which includes respiratory function, feeding pattern and weight gain pattern.

Risks and or discomforts.

The baby may experience some mild discomfort during the administration of the nasal prongs. They will be adjusted to allow for the correct size fit.

Benefits.

If your baby is found to have any illness that was previously not diagnosed.I will liase with the primary doctor and ensure appropriate and prompt advice and treatment is given. You and others will benefit in future from the information learned in this study. The results of this study will help in identifying the benefits and success of this modality of treatment and by so doing give the information that will help it to be used in other hospitals.

Other information.

Costs to you.

There is no cost to you for being in this study.

Confidentiality.

Efforts will be made to keep all personal information related to you and the baby confidential. Any publication of this study will not use your name or the babies name or identify you or the child personally.

Withdrawal.

You are free to withdraw or refuse to participate in the research study at any one time.

Problems or questions.

If you have any questions about the study you should contact Dr. Omoding Anastasia at KNH on 0720834124.

If you have any questions regarding your rights as aresearch participant you should contact the chair of the KNH ethics and research comitee at 2726300.

NAMES	TITLE	CONTACTS.
Dr. Omoding Anastasia Amokola	Principal investigator.	Tel-0720834124.Email-mokolading@yahoo.com.
Prof. Ezekiel Wafula.	Supervisor.	Tel-0722366077. Email-wafulaem@yahoo.com
Dr. Florence Murilla.	Supervisor.	Tel-0729430022. Email-murilaf@gmail.com

CONSENT FORM

I Mr./Mrs./Miss_____ being a person aged 18 years and over, having read/been explained to the above, and in the knowledge that it's voluntary, do hereby give consent for my child to participate in this study.

I understand that my child has the right to be withdrawn from the study without any penalty or harm.

_____ Parent / guardian signature_____ date.

_____ Investigators signature _____ date.

_____witness signature_____date.

APPENDIX 4: BUDGET

PARTICULARS	UNIT COST(KSHS)	TOTAL COST (KSHS)
Human resources.		
Statisticians pay	15000	15,000
Transport costs	350x5dysx36wks	63000
MATERIALS AND SUPPLIES		
Foolscaps- 1 ream	300	300
Folders/clipboard	100	100
Stapler	250	250
Staples	50	50
Duplicating paper	350	350
Stationery(ball pens. pencils. pens)	-	500
PROPOSAL		
Typing	300/=	300
Printing	500x5	2500
Proposal binding 5 copies	50/=	250
Photocopying questionnaires and consent 3 pages	3x 3x80	720
Printing final report 3 copies	500x3	1500
Photocopying final report 5 copies	3x60x5	900
Data analysis	-	3000
Report binding 5 copies	50	250
SUB TOTAL		**90470**
10% Contingencies		**9047**
GRAND TOTAL		**99517**

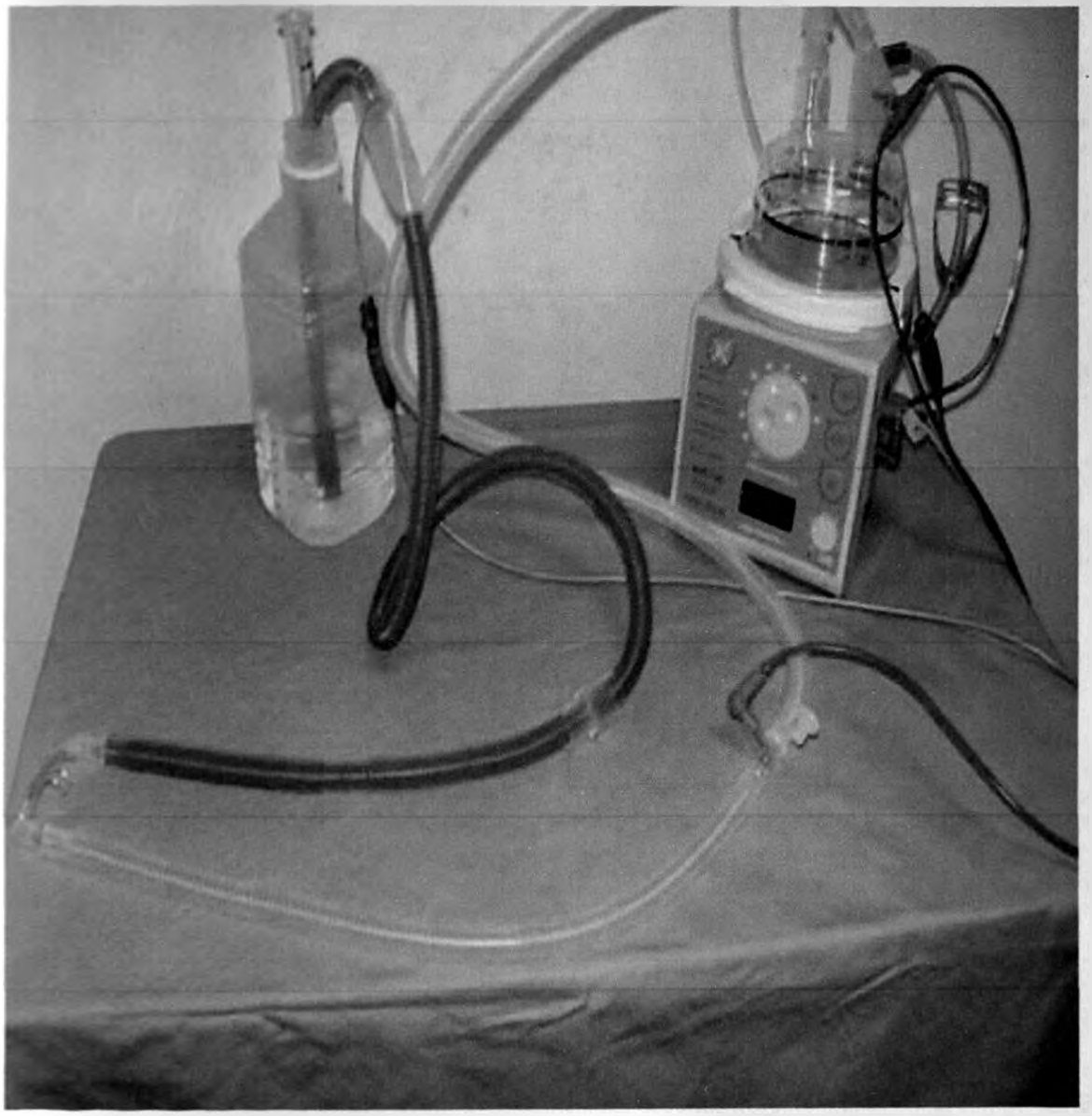
There is no external source of funding. The cost of the study will be footed solely by the principal investigator.

APPENDIX 5: TIME FRAME

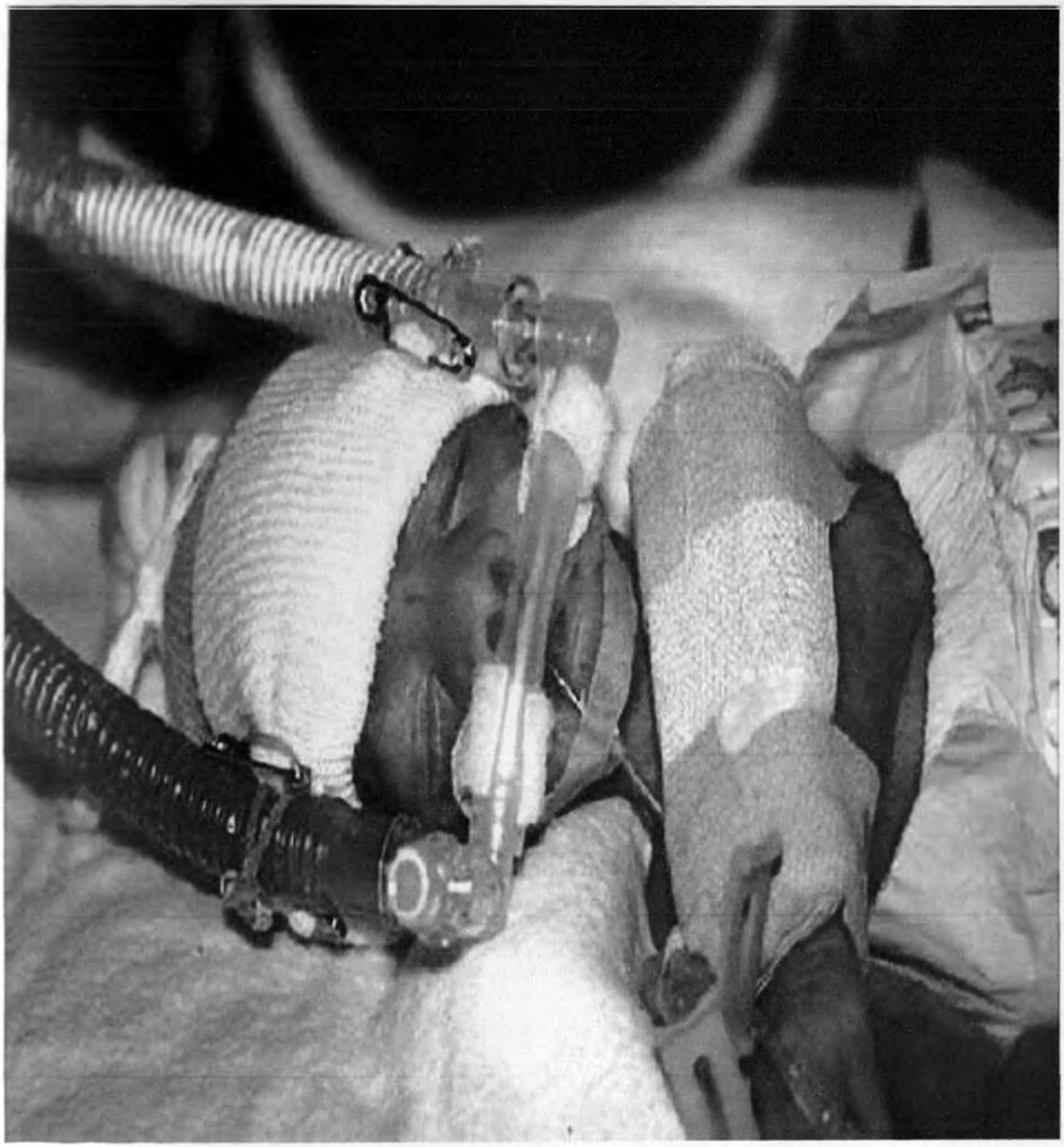
GHANT CHART

MONTHS	Month 1				Month 2				Month 3				Month 4				Month 5				Month 6			
WEEKS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16								
ACTIVITIES																								
Proposal development	■	■	■	■	■																			
Ethical clearance						■	■	■	■															
Actual study										■	■	■	■	■	■	■	■	■	■	■				
Data processing																					■			
Data analysis																					■	■		
Report presentation																							■	■

APPENDIX 6: BUBBLE NASAL CPAP AND INTERFACE



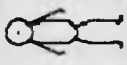
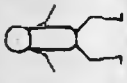
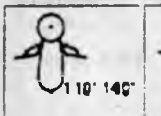
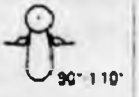
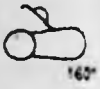
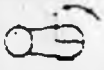
APPENDIX 7: PRETERM BABY ON BUBBLE CPAP



APPENDIX 8: THE NEW BALLARD SCORE

At the end of the examination, the total score determines the gestational maturity in weeks.

NEUROMUSCULAR MATURITY

SIGN	SCORE							SIGN SCORE
	-1	0	1	2	3	4	5	
Posture								
Square Window								
Arm Recoil								
Popliteal Angle								
Scarf Sign								
Heel To Ear								
							TOTAL NEUROMUSCULAR SCORE	

PHYSICAL MATURITY

SIGN	SCORE							SIGN SCORE
	-1	0	1	2	3	4	5	
Skin	Sticky, friable, transparent	gelatinous, red, translucent	smooth pink, visible veins	superficial peeling &/or rash, few veins	cracking, pale areas, rare veins	parchment, deep cracking, no vessels	leathery, cracked, wrinkled	
Lanugo	None	sparse	abundant	Thinning	bald areas	mostly bald		
Plantar Surface	heel-toe 40-50mm: -1 <40mm: -2	>50 mm no crease	faint red marks	anterior transverse crease only	creases ant. 2/3	creases over entire sole		
Breast	imperceptable	barely perceptable	flat areola no bud	stippled areola 1-2 mm bud	raised areola 3-4 mm bud	full areola 5-10 mm bud		
Eye / Ear	lids fused loosely: -1 tightly: -2	lids open pinna flat stays folded	sl. curved pinna; soft; slow recoil	well-curved pinna; soft but ready recoil	formed & firm instant recoil	thick cartilage ear stiff		
Genitals (Male)	scrotum flat, smooth	scrotum empty, faint rugae	testes in upper canal, rare rugae	testes descending, few rugae	testes down, good rugae	testes pendulous, deep rugae		
Genitals (Female)	clitoris prominent & labia flat	prominent clitoris & small labia minora	prominent clitoris & enlarging minora	majora & minora equally prominent	majora large, minora small	majora cover clitoris & minora		
							TOTAL PHYSICAL MATURITY SCORE	

MATURITY RATING

TOTAL SCORE (NEUROMUSCULAR + PHYSICAL)	WEEKS
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Ballard JL, Khoury JC, Wedig K, et al: New Ballard Score, expanded to include extremely prematureinfants. J Pediatrics 1991; 119:417-423

APPENDIX 9: ETHICAL APPROVAL

KENYATTA NATIONAL HOSPITAL
Hospital Rd. along, Ngong Rd.
P.O. Box 20723, Nairobi.
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP", Nairobi.
Email: KNHplan@Ken.Healthnet.org

27th June 2011

Ref: KNH-ERC/ A/148

Dr. Omoding A.A.
Dept. of Paediatrics & Child Health
School of Medicine
University of Nairobi

Dear Dr. Omoding

Research Proposal: "Short-term outcomes of premature infants treated with bubble Continuous Positive Airway Pressure (CPAP) for Respiratory Distress syndrome at the AIC – Kijabe Hospital" (P107/4/2011)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and **approved** your above revised research proposal . The approval periods are 27th June 2011 26th June 2012.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

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

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH/UON-ERC

c.c. The Deputy Director CS, KNH
The Dean, School of Medicine, UON
The Chairman, Dept. of Paediatrics & Child Health, UON
The HOD, Records, KNH
Supervisors: Prof. Wafula Ezekiel, Dept.of Paediatrics & Child Health, UON
Dr. Murilla Florence, Dept.of Paediatrics &Child Health, UON