UNIVERSITY OF NAIROBI

CLINICAL PROFILE AND AUDIT OF MANAGEMENT OF PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME AT THE KENYATTA NATIONAL HOSPITAL.

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2017
DECLARATION

I declare that this dissertation is my original work and has not been published elsewhere or presented for the award of a degree in any other institution.

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ABBREVIATIONS

AAP- American Academy of Paediatrics
BPD- Bronchopulmonary Dysplasia
CPAP- Continuous Positive Airway Pressure
FiO₂- Fraction of inspired oxygen
GA- Gestational Age
HMD- Hyaline Membrane Disease
KNH- Kenyatta National Hospital
MV- Mechanical Ventilation
NBU- New Born Unit
PEEP- Positive End Expiratory Pressure
RDS- Respiratory Distress Syndrome
SP- Surfactant Proteins
SRT- Surfactant Replacement Therapy
VILI- Ventilator induced lung injury
WHO- World Health Organization
DEFINITIONS

1. Respiratory Distress Syndrome: it is a condition of pulmonary insufficiency that commences at, or shortly after birth. It is characterised by features of early respiratory distress comprising tachypnea, cyanosis, grunting and retractions.

2. Preterm neonate: babies born alive before 37 completed weeks of pregnancy. Can be sub-categorised based on weeks of gestational age:
   - Extremely preterm; <28 weeks
   - Very preterm; 28 to <32 weeks
   - Moderate to late preterm; 32 to <37 weeks

3. Gestational age: measure of the period of time between conception and birth. It is a measure of the age of pregnancy calculated from the last normal menstrual period and applying the Naegele’s rule.

4. Finnström Score: A tool used to assess gestational age using 7 physical signs: breast size, nipple formation, skin opacity, scalp hair, ear cartilage, fingernails and plantar skin creases. (Appendix 1)

5. Silverman Anderson score: score of severity of respiratory distress. It measures 5 parameters: upper chest retraction, lower chest retraction, xiphoid retraction, nasal flaring and expiratory grunt. (Appendix 2)

6. Parity: total number of times a woman has been pregnant regardless of the outcome.

7. Continuous Positive Airway Pressure ventilation (CPAP): it is a form of continuous airway ventilation that applies positive end expiratory pressure to maintain the alveoli open at the end of an expiratory cycle to improve ventilation.
ABSTRACT

Background

Respiratory distress syndrome is a common disorder among preterm neonates whose incidence and degree of severity is inversely related to gestational age and birth weight. The standards of care require adequate prenatal care, immediate stabilization, thermoregulation, surfactant therapy and appropriate respiratory support. This audit will provide estimates of the current standards of care, current clinical practice and will help inform local guidelines and contribute to the adoption of the guidelines recommended by WHO and European consensus. This will help guide clinicians in implementing the guidelines towards improving patient care.

Objectives

The purpose of this study is to describe the characteristics of the preterm infants with RDS admitted at KNH, assess the level of severity and perform an audit on the initial management within the first 48 hours. The study will also determine the uptake and the extent to which the standard guidelines are being used.

Methodology

This was a descriptive cross sectional study undertaken in KNH, NBU aimed at describing the clinical profile and management of respiratory distress syndrome. The study was carried out between the months of August and December 2016. Neonates admitted at the NBU with RDS were enrolled into the study at admission and an audit on the management received at 24 and 48 hours was assessed.

Results

Of the 207 preterm neonates enrolled in the study, 67% were born in KNH and 33% from a referral facility. Male to female ratio was 1.1:1 with a median birthweight of 1650 grams. The median gestational age was 32 weeks with 58.8% of the participants having been born via spontaneous vertex delivery and 41.2% via caesarean section.

The audit revealed that RDS documentation was sub-optimal with up to 30% of preterms lacking documentation on nasal flaring and cyanosis. The average severity score of respiratory distress as per the Silverman Anderson scoring system was 4-6 (52%) with 23% of the preterms having received continuous positive airway pressure (CPAP) and 12.8% received surfactant
administration. Intravenous fluids were prescribed and administered in 97.1% and antibiotics in 89.9%, the most frequently prescribed being crystalline penicillin and gentamycin (72.5%).

**Conclusion**

The majority of neonates (52%) had a severity score of 4-6 with 56.9% of the preterms who were eligible for CPAP did not receive it. 74.1% of extreme preterms did not receive surfactant. There was suboptimal documentation of symptoms of RDS at admission.
1. INTRODUCTION AND LITERATURE REVIEW

1.1 BACKGROUND AND EPIDEMIOLOGY

Respiratory Distress syndrome also known as hyaline membrane disease is a developmental condition of pulmonary insufficiency that is characterised by features of respiratory distress at birth or shortly after birth. It is due to pulmonary deficiency in alveolar surfactant which results in increased surface tension at end expiration, reduced lung compliance and resultant alteration in ventilation and perfusion. It correlates with structural and functional immaturity of the lung. It typically affects preterms <35 weeks gestation, most common in those born less than 28 weeks of gestation.(1,2).

It commonly presents at or shortly after birth (within 4 hours). The clinical progression is seen over the first two days of life where there is increasing severity. The clinical course and progression is altered by timely surfactant use and early continuous positive airway pressure. If left untreated, it causes changes in lung function resulting in atelectasis and progressive hypoxemia. It may result in mortality due to progressive hypoxia and respiratory failure(3).

RDS is a common disorder and the most common cause of respiratory distress in premature infants. Its incidence and severity is inversely related to gestational age and birth weight. It occurs in 60-80% of infants <28 weeks, 15-30% 32-36 weeks and about 5% in those beyond 37 weeks and rarely at term(4,5).

It occurs in 20,000-30,000 infants born in the United States annually(6). In developing countries the numbers are much higher. In India, it was estimated to occur in approximately 200,000 infants per year(7). It is responsible for 30-40% of admissions in the neonatal period and accounts for about 20% of neonatal deaths(8).

The incidence of RDS is varied. Overall incidence is estimated at 1%. According to the European perinatal health report 2010, the rate for RDS among neonates with a gestational age of 24-25 weeks was 92%, 88% at 26-27 weeks and 57% at 30-31 weeks(9).

In a study done in Karachi Pakistan, the incidence was 1.2% with a prevalence of 12.8% among low birth weight infants. The overall mortality was 39% with the highest mortality rate being 68% among neonates <1000g(10). Another study done in Pakistan in a rural setting over a one year period in 2000, reported an incidence of up to 1.72% of total live births. Incidence was
100% at ≤ 26 weeks, 57.14% at 32 weeks and 3.70% at 36 weeks. Out of these 93.61% were preterm and 6.38% were term infants(11).

A study in Nigeria found the incidence of RDS among newborn infants to be 12%(12). Another study in South Africa reported a high burden of premature births with a high proportion of the mortality contributed by RDS(13).

An epidemiological survey carried out among 20 hospitals in China showed that the prevalence rate was 3.3% with an average gestational age of 33 weeks(14). A study done in Kenyatta National Hospital showed that the overall mortality rate of infants born weighing <2000grams was 37.4%. The mortality rate was; 31% among those 32-35 weeks, 73% of those 28-31 weeks and 91% among those <28 weeks. RDS was the commonest clinical syndrome seen among this population and accounted for 43% while sepsis accounted for 41%(15).

1.2 ETIOLOGY AND RISK FACTORS

RDS is primarily caused by surfactant deficiency. The greatest risk factor is prematurity. The risk of RDS increases with decreasing gestational age and birth weight. This correlates with both structural and functional immaturity of the lung(4,6,16).

Male gender: the condition is more common among boys. Sodium transport driven alveolar fluid clearance is crucial for the prevention of RDS. There exists a difference in expression of the epithelial Na+ channels (ENaC) and activity of the channels between the male and female population. There is a higher expression of hormone receptors in fetal distal lung epithelial cells; postulated reasons include the presence of estrogen and progesterone which may render the female more responsive to the ENaC subunits(17).

Maternal diabetes and macrosomia: the incidence is six times higher in infants of diabetic mothers. This is due to a delay in pulmonary maturity despite macrosomia. Hyperglycemia in the fetus results in stimulation of insulin, growth hormone and insulin-like growth factors. Insulin inhibits differentiation of type 2 alveolar cells which produce surfactant. Hyperinsulinemia also inhibits biosynthesis of surfactant. In addition, insulin also inhibits the accumulation of surfactant protein messenger RNA therefore down regulates their production. Infants born of diabetic mothers are at a higher risk of premature delivery compared to normoglycemic mothers, thus at a higher risk of surfactant deficiency(18,19).
Mode of delivery: elective caesarean section without labour. One study showed a 1.7 fold increase in the probability of RDS in babies born via caesarean section without labour and vaginal births(20). A different study found a significantly increased risk in RDS among late preterms born via elective caesarean section(21). Another study carried out in Southeast Asian countries showed no statistical difference between incidence of RDS among babies born via caesarean section and vaginal births(22). Various reasons have been postulated as the cause of increased risk of RDS in babies born via caesarean section. The absence of the physiologic events surrounding spontaneous labour such as a surge in endogenous steroids and catecholamines has been shown to increase the risk. Rapid clearance of fetal lung fluid plays a key role in transition to air breathing. Disruption of the ENaC channels may lead to retention of fluid in alveolar spaces leading to alveolar hypoventilation(23,24). Another study found absence of endogenous prostaglandins in the absence of labour causes pulmonary hypoperfusion leading to persistent pulmonary hypertension and RDS(25).

Familial predisposition: rare genetic disorders may contribute to respiratory distress. Genetic absence of apoproteins leading to deficiency in SP-B and SP-C. Mutations in the adenosine triphosphate binding cassette gene (ABCA) results in poor formation of lamellar bodies and leads to altered phospholipid metabolism and thus inactive surfactant. Mutations in the genes responsible for transporting surfactant across membranes (ABC transporter 3) has been associated with severe and often lethal forms of RDS(26).

Multiple gestation: babies born after multiple gestation are often delivered prematurely. Preterm births are seen in 50-60% of twin pregnancies, 90% of triplet and almost 100% of quadruplet pregnancies. One study showed RDS occurred in 23% of triplets, 65% of quadruplets and 75% of quintuplets(27). As the number of foetuses increases, the expected duration of pregnancy decreases. The average gestation for twins is 35 weeks, reducing to 33 weeks and 30 weeks in triplets and quadruplets respectively. Prematurity will result in primary surfactant deficiency. There is also an increased rate of caesarean deliveries among this population(28).

Asphyxia: there is a positive association between asphyxia and development of RDS. The amniotic fluid lecithin/ sphingomyelin ratio was shown to be decreased, and this relates to structural maturity of surfactant. Associated hypotension from myocardial dysfunction and acidosis have been shown to reduce surfactant production. Increased pulmonary capillary permeability causes extravasation of plasma proteins which in turn cause surfactant
inactivation(29,30). In addition, reperfusion injury following oxygen supplementation will lead to further surfactant depletion by excessive free oxygen radicals(31).

**Hypothermia:** preterm neonates with hypothermia have a two fold increase in developing RDS compared to normothermic neonates(32). Neonates with cold stress may develop sequelae like tissue hypoxia and acidosis which will reduce surfactant production(33).

Factors associated with decreased risk of RDS include: antenatal use of steroids, chronic intrauterine stress, premature rupture of membranes (PROM), maternal hypertension in pregnancy, intrauterine growth restriction and maternal use of narcotics. Antenatal use of corticosteroids stimulates developmentally regulated gene expression and physiologic functions resulting in maturation of the lungs. The mechanisms include: accelerated development of pneumocytes which increases surfactant production, stimulation of surfactant proteins and enzymes necessary for phospholipid synthesis. In addition, steroids cause induction of pulmonary beta receptors which upregulates surfactant release, induction of fetal lung antioxidant enzymes and upregulation of ENaC channels. Antenatal steroid exposure also amplifies the post neonatal response to surfactant therapy(34).

Premature rupture of membranes is associated with a reduction in the incidence of RDS. Chronic intrauterine stress such as preeclampsia, IUGR and maternal use of narcotics has been shown to increase the cortisol production therefore cause stimulation of surfactant production and accelerated fetal lung maturity(35,36). One study however postulates that in preeclampsia, the abnormal placentation and compromise in uterine blood flow results in fetal hypoxia and impedes fetal angiogenesis, alveolarization and restricts lung vessel interactions necessary for normal lung development. This may actually cause an increase in RDS and even bronchopulmonary dysplasia(37).

**1.3 PATHOPHYSIOLOGY**

The primary pathology is inadequate surfactant production resulting from lung immaturity.
### Table 1: Stages of normal foetal lung development

<table>
<thead>
<tr>
<th>Stage</th>
<th>Time of development</th>
<th>Anatomic developmental changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Embryonic</td>
<td>26 days gestation</td>
<td>- Fetal lung bud appearance as a protrusion from the foregut</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Initial main branching of lung forming prospective main bronchi</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Development of laryngotracheal groove</td>
</tr>
<tr>
<td>2. Pseudoglandular</td>
<td>5-16 weeks</td>
<td>- Continued branching to form terminal bronchioles</td>
</tr>
<tr>
<td>3. Canalicular</td>
<td>16-26 weeks</td>
<td>- Terminal bronchioles divide to form 2 or more respiratory bronchioles and alveolar ducts</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Vascular surrounding mesenchyme</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Differentiation into alveolar type 2 cells and formation of lamellar bodies</td>
</tr>
<tr>
<td>4. Saccular/terminal sac</td>
<td>26 weeks- birth</td>
<td>- Formation of terminal sacs (primitive alveoli)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Formation of type 1 and 2 pneumocytes</td>
</tr>
<tr>
<td>5. Alveolar</td>
<td>8 months- 8 years</td>
<td>- Development of more mature alveoli</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Increase in number and size of alveoli and capillaries</td>
</tr>
</tbody>
</table>

Table 1: Stages of normal fetal structural lung development

### Overview of surfactant

Surfactants/ surface active- agents are components that increase surface pressure while lowering surface tension. High surface pressure resists a decrease in alveolar surface area, while low surface tension stabilizes the lung by decreasing the pressure gradient across the alveolar lining layer. This results in splinting of the alveoli at the end of an expiratory cycle(40).

Surfactant is synthesized by type 2 pneumocytes. Phospholipid synthesis together with the lipoprotein component form the surfactant lipoprotein complex secreted into the alveolar space. Metabolism is regulated by an enzymatic and hormonal pathway. The enzymatic control is principally by cholinephosphotransferase (CPT) which is a catalyst for a rate limiting step. Hormonal regulation is by: glucocorticoids, estrogen, thyroid hormone, prolactin which increases lipid synthesis and insulin which has a dual role; low doses increase synthesis and high doses inhibit biosynthesis(41,42).
Surfactant is composed of lipids (90%) and proteins (10%). Of the lipid component, 70% is phosphatidylcholine (lecithin) of which predominates palmitoylphosphatidylcholine, the major tension lowering component, phosphatidylglycerol, phosphatidylinositol and phosphatidylethanolamine. Four surfactant proteins have been described; surfactant- specific proteins (SP) A-D. SP-B and SP-C are the predominant proteins. They are hydrophobic and enhance the adsorption of lipid to the surface of the alveoli. SP- A and SP- D are hydrophilic and participate in the innate host defence immune system.

Surfactant has many functions: facilitate diffusion of gases, maintain structural integrity of the alveoli, enhance lung compliance and have a role in host defence. SP- B and SP-C the major surfactant proteins facilitates absorption of lipids and as a result contributes to the surface tension lowering ability of surfactant. They are the constituents found in commercially prepared surfactant formulations.

SP- A and SP- D have a role in immunomodulation. They opsonise pathogens; both bacterial eg Group B streptococci and viral to facilitate phagocytosis by macrophages and monocytes and eventual clearance from the airways. They also regulate production of inflammatory mediators and possess a direct antimicrobial activity in the absence of immune effector cells.

**Sequelea of surfactant deficiency (47–49)**

Surfactant deficiency causes alveolar instability. This leads to alveolar collapse especially at low volumes and diffuse atelectasis. Preterm infants also have a decrease in the alveolar radius and a weak chest wall which increase the risk of atelectasis.

Following atelectasis, there are well perfused areas of the lung which are poorly ventilated resulting in a ventilation-perfusion (V/Q) mismatch. Subsequently, there is hypoxemia and hypercaribia as a result of intra pulmonary shunting and alveolar hypoventilation. Prolonged hypoxemia and systemic hypoperfusion results in anaerobic metabolism and lactic acidosis. The net effect is a mixed metabolic and respiratory acidosis.

Oxygenation is further impaired as acidosis and prolonged hypoxemia cause pulmonary vasoconstriction. This results in both intrapulmonary and extrapulmonary right to left shunting (at the level of the ductus arteriosus and foramen ovale).
Depletion of surfactant causes atelectasis which may lead to injury of the respiratory epithelium via a cytokine and chemokine mediated inflammatory response. There is accumulation of neutrophils in the lung causing inflammation and worsening respiratory epithelial injury. Exposure to excessive oxygenation with production of free oxygen radicals during treatment (barotraumas, volutrauma and high FiO₂) may exacerbate the injury. An increase in the endothelial permeability leads to pulmonary edema. The accumulation of an exudative fluid inactivates any surfactant present therefore worsening the deficiency. A membrane (hyaline membrane) composed of fibrinous material and cellular debris lines the airspaces.

The net effect is pulmonary compromise. There is low compliance and low functional residual capacity with an increase in dead space. Total lung resistance is increased as a result of airway compression, edema and high pressure required to prevent alveolar collapse. Hypoventilation is due to decreased tidal volume, increased dead space and decreased minute ventilation. Progressive atelectasis and altered lung mechanics leads to features of respiratory distress and increased work of breathing. If untreated, progressive hypoxemia and hypercarbia with associated acidosis ends up in respiratory failure and death may ensue.

1.4 CLINICAL PRESENTATION AND DIAGNOSIS

Clinical manifestations arise as a result of pulmonary dysfunction causing hypoxemia and hypercarbia. Symptoms typically commence at or soon after birth; usually within 4 hours. Characteristically, it presents with features of respiratory distress; tachypnea, intercostal and subcostal retractions, nasal flaring, grunting and cyanosis in room air(50).

Tachypnea (respiratory rate > 60 breaths/minute) is due to an attempt to increase minute ventilation to compensate for a decrease in tidal volume. Intercostal, subxiphoid and subcostal retractions occur due to an attempt by the infant to generate a high intrathoracic pressure to expand poorly compliant lungs in a highly compliant rib cage. Nasal flaring indicates the use of accessory muscles of respiration and lowers the total respiratory system resistance. Grunting arises due to forced expiration against a partially closed glottis in an effort to maintain the functional residual capacity to help keep the alveoli patent. Cyanosis is due to right-to-left shunting; both intra and extrapulmonary.

With worsening atelectasis and respiratory failure, there is progressive worsening of symptoms with lethargy and reduction or disappearance of grunting. The presence of irregular breathing and apnea are ominous signs. Death may occur due to severe respiratory impairment, alveolar
air leaks for example due to interstitial edema and pneumothorax, pulmonary hemorrhage, secondary sepsis and intraventricular hemorrhage.

The severity of respiratory distress is assessed by Silverman Anderson scoring system. Scoring should be done accurately, at half hour intervals and a documented chart maintained to determine progress. The score is based on: upper and lower chest retraction, xiphoid retraction, nasal flaring and expiratory grunt.

**Table 1: Silverman Anderson Score**

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper chest retraction</td>
<td>Synchronized</td>
<td>Lag on inspiration</td>
<td>See- saw</td>
</tr>
<tr>
<td>Lower chest retraction</td>
<td>No retraction</td>
<td>Just visible</td>
<td>Marked</td>
</tr>
<tr>
<td>Xiphoid retraction</td>
<td>None</td>
<td>Just visible</td>
<td>Marked</td>
</tr>
<tr>
<td>Nasal flaring</td>
<td>None</td>
<td>Minimal</td>
<td>Marked</td>
</tr>
<tr>
<td>Expiratory grunt</td>
<td>None</td>
<td>Audible with stethoscope only</td>
<td>Audible without stethoscope</td>
</tr>
</tbody>
</table>

Score 0: no respiratory distress, score ≥7: impending respiratory failure, score 10: severe respiratory distress.
On physical examination there are reduced breath sounds on auscultation with an increased heart rate. Peripheral pulses may have decreased volume with peripheral edema. There may be an accompanying oliguric phase. There is progressive worsening over 48 - 72 hours.

With worsening of the disease, blood pressure may reduce with progression of the cyanosis. If left untreated, death may occur due to progressive hypoxia and respiratory failure. The natural history is greatly modified by exogenous surfactant administration and early use of CPAP. In survivors, resolution occurs in 2 - 4 days which usually coincides with a diuretic phase after a period of oliguria. Improvement is marked by improvement in the arterial blood gas parameters and lower ventilator support such as lower FiO₂.

**DIAGNOSIS**

The diagnosis is often made by clinical evaluation recognizing the risk factors. Early onset of respiratory distress in a preterm neonate is suggestive. RDS can be predicted or anticipated prenatally using various tests of fetal lung maturity. These tests include: amniotic fluid lecithin/sphingomyelin ratio, foam stability index test and surfactant/albumin ratio.

In the foam stability index test, the more the surfactant in amniotic fluid, the greater the stability of the foam that forms when the fluid is combined with ethanol. Risk of RDS is low when
lecithin/ sphingomyelin ratio is >2:1, foam stability index = 47 or surfactant/ albumin ratio is >55mg/g.

Adjunct tests in making a diagnosis include: pulse oximetry, blood gas analysis, chest radiographs and echocardiograms. Pulse oximetry will show low saturations (<92%) correlating to low PaO₂ levels. Arterial blood gas analysis will have low PaO₂, high PaCO₂ and low pH corresponding with metabolic and respiratory acidosis.

Chest radiograph often shows reduced lung volumes, diffuse atelectasis, and a bilateral reticular granular pattern classically described as “ground- glass appearance” with bilateral air bronchograms.

An echocardiogram may be used to rule out congenital structural defects as well as to determine the direction and degree of shunting and making the diagnosis of pulmonary hypertension. If cardiomegaly is present, this may point to prenatal asphyxia, maternal diabetes or structural cardiac anomalies. Blood cultures may be done to rule out sepsis.

The Vermont Oxford Neonatal Network diagnostic criteria requires the affected neonate to have a PaO₂ <50mmHg in room air, central cyanosis in room air, or need for supplemental oxygen to maintain PaO₂ >50mmHg, as well as the characteristic chest radiograph findings(1).

Differential diagnosis: Transient tachypnea of the newborn, early onset neonatal sepsis, aspiration syndromes eg meconium aspiration syndrome, congenital diaphragmatic hernia, congenital heart disease, anaemia, neonatal congenital or acquired pneumonia, metabolic abnormalities eg hypoglycaemia, pulmonary air leaks e.g. pneumothorax and pneumomediastinum.

1.5 MANAGEMENT

The aim of management of RDS is to provide interventions that will maximize survival whilst minimizing potential adverse effects(1). Various strategies and therapies have been developed and form the guidelines used in prevention and management of RDS and shall be discussed below. This shall take into account both the European consensus guidelines on the management of neonatal RDS (1)and the WHO recommendations on interventions to improve preterm birth outcomes(51).
Prenatal care

These are interventions that are instituted before birth to prevent or reduce the severity of RDS. Preterm birth can often be predicted with prior warning signs. It is recommended that women at high risk of preterm birth should deliver in centres where skilled personnel and appropriate resources are available including various modes of respiratory support (CPAP, mechanical ventilation) preferably a neonatal intensive care unit in a tertiary facility.

Use of prenatal steroids is recommended in all pregnancies with threatened preterm labour from 23 weeks up to 34 completed weeks of gestation. They do not appear to improve outcome in pregnancies delivering between 34 and 36 weeks gestation. When given before an elective caesarean section, they reduce the risk of admission to NICU. The optimal time interval between treatment and delivery is more than 24 hours and less than 7 days from the start of steroid treatment. The benefits of antenatal steroids are diminished beyond 14 days after administration. Prenatal steroids not only reduce the risk of RDS by up to 35% but have the added advantage of reducing the mean duration of mechanical ventilation and oxygen supplementation, reducing the risk of intraventricular hemorrhage and necrotizing enterocolitis. There have been concerns on the effects of multiple steroid doses and the effects on fetal growth. A single repeat course of antenatal betamethasone given more than 1-3 weeks after the first course and if the pregnancy is <33 weeks gestation also has a benefit. The recommended steroid dose is 24mg (dexamethasone or betamethasone) given in two divided doses.

Immediate stabilization post delivery

Applying lung protective strategies such as controlled tidal volumes and use of bagging (positive pressure breaths) when needed rather than routinely right from the initiation of breathing is recommended. An initial concentration of 21-30% oxygen is recommended to start stabilization and appropriate adjustments made based on pulse oximetry. Resuscitation with 100% oxygen has been shown to increase mortality and room air is recommended. In babies with spontaneous breathing effort, initial stabilization with CPAP with 5-6 cm H₂O is recommended via mask or nasal prongs. Intubation should be reserved for babies who have not responded to positive pressure ventilation and these neonates should receive surfactant.
Thermoregulation

Appropriate temperature should be maintained throughout to sustain a thermoneutral environment maintaining a core temperature of 36.5-37.5 °C. Hypothermia is an independent risk factor for mortality. Immediate drying in the delivery room should be practiced. In addition, skin to skin warmth of the babies who are not critically ill and incubators for those who are critically ill.

Surfactant therapy

Surfactant therapy is pivotal in the management of RDS. It has been shown to reduce the risk of RDS if given prophylactically. Timing of administration of early surfactant is important. It has been shown that early administration of surfactant (within 2 hours of birth) is associated with better outcomes than delayed use, with a 13-32% reduction in mortality. Early surfactant use is associated with a reduction in the risk of pneumothorax, reduction in the incidence of pulmonary interstitial emphysema, bronchopulmonary dysplasia and mortality (52–54).

Initial studies recommended prophylactic surfactant for all extremely preterm neonates. More recent evidence has shown that early initiation of CPAP and selective surfactant administration rather than routine prophylaxis has shown better outcomes as some neonates avoided intubation.

Early rescue surfactant should be given in babies <26 weeks when FiO₂ requirements are >0.30 and babies >26 weeks when FiO₂ requirements are >0.40. The ‘INSURE’ technique (intubate, give surfactant, extubate to CPAP) has been recommended with high chance of reducing need for mechanical ventilation. At least 100mg/kg of the phospholipid content is required with 2 doses being superior to a single dose. Target oxygen saturations should be between 90-95%.

Respiratory support

This may be non-invasive or invasive. Non-invasive respiratory support includes CPAP and other modes of oxygen supplementation (face mask, nasal prongs or cannula) termed as NIPPV (nasal intermittent positive pressure ventilation). These methods are less injurious to the lungs and are recommended if the child does not need mechanical ventilation. Mechanical ventilation is a preserve of those who fail CPAP. It restores the alteration in blood gases by stabilizing the lung and optimizing lung volumes. Mechanical ventilation can be provided by intermittent positive pressure ventilation (IPPV) or high frequency oscillatory ventilation (HFOV).
Permissive hypercarbia is a strategy recommended during MV as hypocarbia is associated with increased risk of BPD and periventricular leukomalacia. Adjustments on the concentration of oxygen levels should be by FiO₂ 0.1 per 30 seconds and guided by target oxygen saturations.

CPAP use has been documented widely to have benefits and reduced mortality rates. Early use of CPAP has been shown to reduce the need for mechanical ventilation by up to 38% and reduce the rate of respiratory failure and death by up to 35%. In addition, CPAP when initiated early prevents the duration of hospital stay and long term complications of mechanical ventilation such as BPD. Early initiation of CPAP is of greater benefit compared to late CPAP(55–57). Endotracheal intubation and mechanical ventilation can cause significant damage to the premature lungs and long term sequelae such as BPD and neurodevelopmental outcomes(58).

**Antibiotic use**

Prophylactic treatment for sepsis for the shortest possible course is recommended until sepsis has been ruled out. All babies with RDS should be screened for sepsis. Blood cultures and other markers such as C-reactive protein should be determined. Combination of penicillin/ampicillin with and aminoglycoside is recommended.

**Fluid and nutritional management**

Careful fluid balance is recommended with early nutritional support using parenteral nutrition while enteral nutrition is being established. Initial intravenous fluids are started at 70-80mls/kg/day is recommended. Subsequently, the fluid requirements are adjusted according to the electrolyte levels and the percentage weight loss. Diuretic use is not recommended. Both enteral and parenteral nutrition should be commenced on day 1 to avoid growth restriction.
Table 3: Summary of the recommendations on the management of RDS

<table>
<thead>
<tr>
<th>Management principles</th>
<th>European Consensus Guideline document</th>
<th>WHO recommendations to improve preterm birth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal care</td>
<td>Strong recommendation to give steroids &gt;23 weeks and &lt;34 weeks GA.</td>
<td>Antenatal steroids recommended; when preterm birth is considered imminent 24-34 weeks, GA assessment can be done and essential and special care package can be availed.</td>
</tr>
<tr>
<td>Delivery after steroid administration</td>
<td>Within 24 hours and up to 7 days of starting treatment.</td>
<td>Within 24 hours and up to 7 days of starting treatment.</td>
</tr>
<tr>
<td>Repeat steroid dose</td>
<td>A single repeat course of antenatal betamethasone given more than 1-3 weeks after the first course and if the pregnancy is &lt;33 weeks gestation also has a benefit.</td>
<td>Recommended if delivery does not occur within 7 days after initial dose with assessment demonstrating high risk of preterm birth in the next 7 days.</td>
</tr>
<tr>
<td>Resuscitation</td>
<td>Oxygen at 21-30% (room air)</td>
<td>Use of low blended oxygen or room air</td>
</tr>
<tr>
<td>Thermoregulation</td>
<td>Radiant warmers</td>
<td>Early initiation of kangaroo mother care in a stable neonate, if unstable use of radiant warmers is recommended.</td>
</tr>
<tr>
<td>Spontaneously breathing baby</td>
<td>Initial CPAP (5-6cm H₂O) by nasal prongs or mask.</td>
<td>Early initiation of CPAP recommended as soon as diagnosis of RDS is made clinically. CPAP use via</td>
</tr>
<tr>
<td></td>
<td>Reserved in those who failed CPAP</td>
<td>Recommended for critically ill neonate.</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>----------------------------------</td>
<td>-----------------------------------------</td>
</tr>
<tr>
<td>Mechanical ventilation use</td>
<td>Nasal prongs, nasal cannula or mask.</td>
<td></td>
</tr>
<tr>
<td>Surfactant use</td>
<td>Early surfactant administration using the ‘INSURE’ technique.</td>
<td>Recommended for intubated and ventilated newborns early, within 2 hours after birth.</td>
</tr>
<tr>
<td>Antibiotic use</td>
<td>Recommended, until sepsis is ruled out</td>
<td></td>
</tr>
</tbody>
</table>
1.6 PROGNOSIS AND LONG TERM SEQUELAE

The condition worsens over the first 48 hours of life. In survivors, resolution begins between 48 and 96 hours of life. Long term sequelae may arise from: the progression of the primary disease or complications arising from therapeutic interventions.

Bronchopulmonary dysplasia (BPD): the exposure of both antenatal and postnatal factors contribute to the development of BPD. Antenatal factors include prematurity; surfactant deficiency in addition to the poorly developed airway and the underdeveloped antioxidant system all increase vulnerability of the lungs to injury and development of BPD. Post natal factors include mechanical ventilation and its effects such as volutrauma resulting from high tidal volumes. Oxygen toxicity is another mechanism that causes cellular damage from free superoxide radicals that overwhelms the immature antioxidant system. Postnatally acquired sepsis is another risk factor. Sepsis and the resultant inflammatory process will cause a secondary surfactant deficiency.

Mortality rates vary among different studies; the overall mortality in India was 39% with the highest mortality rate of 68% seen among those <1kilo gram (10). In China, the mortality was 65.3% (14). In KNH, it contributed to 43% of mortality in neonates <2000 grams (15).
2. STUDY JUSTIFICATION AND UTILITY

Globally, WHO estimates that 15 million babies are born preterm annually; that is 1 in every 10 babies born\(^2\). A study done in KNH found the prevalence of preterm births as 18.3\%^{\text{(59)}}. RDS is the most common cause of respiratory distress in preterm infants. It has a high incidence and a high mortality among preterm neonates. A study carried out in KNH among neonates <2000 grams showed that RDS accounted for 43\%^{\text{(15)}}.

There are evidence based guidelines consistently applied for management of RDS in other settings with good neonatal outcomes. These guidelines formed by the European Consensus and World Health Organisation have been implemented and have shown reduction in neonatal mortality\(^2,51\). This study will evaluate the extent to which these guidelines are being applied in a tertiary facility and serve as an advocacy tool by highlighting the experience and challenges.

Lately, there have been additions in the KNH NBU such as introduction of CPAP machines and surfactant therapy. Therefore, there has been a change in the management of RDS but this has not been well documented in a study. The audit will inform our current clinical practice and help inform local guidelines and possibly adoption of the recommended guidelines. In addition, the characterization of the clinical profile of the preterm neonates with RDS will inform the application of our findings to different facilities.

Being one of the first inpatient surveys on the management of RDS in neonates, this study will provide estimates of the current standards of care among the neonates presenting with RDS in our setting. This will provide baseline data for further studies carried out in the future in our region. In addition, this will help guide clinicians in implementing the guidelines towards improving patient care.

The study will also provide information on the burden of disease and characterise the profile of the affected neonates. Investigating the clinical profile of these neonates may reveal possible associations that may lead to expansion of the interventions.

Additionally, describing the characteristics of the neonates who present with RDS may reveal high priority areas which may inform policy makers on potential areas of improvement.
2.1 RESEARCH QUESTIONS

- What is the clinical profile of preterm infants with RDS admitted at KNH?
- What is the initial management of preterm infants with RDS at KNH?

2.2 STUDY OBJECTIVES

Primary objectives:

- To describe the clinical profile of preterm infants with RDS admitted at KNH.
- To audit the care given to preterm infants with RDS admitted at KNH.

Secondary objective:

- To determine the uptake and extent to which the standard guidelines are being used.

2.3 RESEARCH METHODOLOGY

2.3.1 STUDY DESIGN

This was a hospital based descriptive cross sectional study.

2.3.2 STUDY SITE

The study site was in the New Born Unit at the Kenyatta National Hospital.

2.3.3 STUDY POPULATION

The study population included preterm neonates either born at KNH or referred from another facility within 12 hours of delivery who presented with features of RDS.

2.4 STUDY TOOLS

A questionnaire was used to collect the data from enrolled participants. Entries made into the files of the neonates admitted, their treatment sheets and feeding charts were reviewed and audited. This was done at 24 and 48 hours after admission to the unit. The questionnaire was pretested in the new born unit in KNH among neonates with suspected RDS.
2.5 STUDY PERIOD

The study was carried out between the months of August and December 2016.

2.6 STUDY OUTCOMES

The study achieved the following outcomes:

- Determined the clinical profile of preterm neonates with RDS admitted at KNH.
- An audit of the initial management and described various aspects of the care.
- Determined the uptake and extent to which the standard guidelines are being used.

2.7 SELECTION AND ENROLLMENT OF PATIENTS

2.7.1 INCLUSION CRITERIA

- Symptoms of RDS: tachypnea, flaring, grunting, intercostal, subxiphoid and subcostal retraction, cyanosis in room air within 4 hours of birth
- For referred patients; those who presented to KNH within 12 hours of delivery
- Preterm infants born at a gestational age of <37 completed weeks determined by Finnström score.
- The patients enrolled had informed consent given by the parent.

2.7.2 EXCLUSION CRITERIA

Patients meeting any of the following were excluded from the study:

- The presence of any congenital anomalies
- Perinatal asphyxia
- Late referrals

2.8 SAMPLE SIZE DETERMINATION


The sample size necessary for estimating a population proportion \( p \) of a small finite population with \( (1−α) \) 100% confidence and error no larger than \( ε \) is:
\[ n = \frac{m}{1 + \frac{m-1}{N}} \]

where

\[ m = \frac{z^2 \sigma^2}{\varepsilon^2} \]

is the sample size necessary for estimating the proportion \( p \) for a large population.

**Assumptions**

Population size (estimated number of neonates admitted with RDS in NBU during the 5 month period of the study based on physical hospital records assessment in 2016(N): 900

Level of precision (\( \varepsilon \)): 5%

Estimated proportion of neonates with RDS in NBU who receive appropriate management (\( p \)): 50%

Critical value for a 95% Confidence level \( \alpha = 0.05 \): 1.96

Two hundred and seven neonates with RDS admitted to NBU were recruited.

2.9 **CASE DEFINITION**

- Preterm: neonate born before completion of 37 weeks gestation determined by the estimated date of delivery from the last normal menstrual period.
- Gestational age: the post conceptional age of the baby based on menstrual dates and confirmed by clinical assessment using the Finnström score.
- RDS: based on features of respiratory distress (flaring, grunting, intercostal, subxiphoid retractions, tachypnea and cyanosis in room air) at admission and severity scoring done using the Silverman Anderson scoring system.

2.10 **PATIENT RECRUITMENT PROCEDURE**

Ethical approval was sought and granted by the Kenyatta National Hospital Ethics and Research Committee (KNH ERC) under P306/04/2016. Patients who met the inclusion criteria were recruited into the study at admission. They were recruited based on the case definition of respiratory distress syndrome. The principal investigator approached the parent and explained the purpose and methods of the study allowing them to ask any questions prior to providing
voluntary informed consent. Consent was given in written form on a pre-designed consent form which was availed to the parent. The consent form provided described the purpose of the study, the study procedure to be followed and any potential benefits and risks of participating in the study. The consent obtained was voluntary.

Parents accepting to take part in the study signed the consent form which was countersigned by the investigator. A copy of the consent form was given to the parents who consented to the study. Records were kept regarding reasons for non-participation from eligible participants. Data was then collected from the eligible patients by administration of a pre-tested questionnaire.

Once the patient was enrolled into the study, demographic data of both the neonate and the mother were entered down into the questionnaire. The following information was abstracted from records:

- Gestational age assessment
- Respiratory distress severity score
FLOWCHART OF PATIENT RECRUITMENT PROCEDURE

Admission criteria based on Silverman Anderson scoring system for severity of RDS

- exclude those who do not meet admission criteria, patients with asphyxia, congenital anomalies or late referrals

At admission; prenatal steroid use, initial resuscitation measures and temperature recording

At 24 hours; documentation of surfactant administration, intravenous fluids and antibiotics

At 48 hours; documentation of repeat surfactant dose, additional laboratory tests, fluid type and dosage administered and nutritional management commenced.

Once the neonates met the inclusion criteria of RDS, they were enrolled into the study. An audit of the management was carried out. This audit was done at admission, 24 and 48 hours. 72 hours.

The audit included documentation of the following:

1. At admission;
   - Prenatal use of steroids and timing of administration.
   - Initial resuscitation measures done; whether 21-30% oxygen was used.
   - Mode of transportation to NBU.
   - Temperature recording.
2. At 24 hours:
   - Initial stabilization done with CPAP.
   - Surfactant administration; timing and dosage given.
   - Mode of respiratory support that the neonate was receiving.
   - Intravenous fluid prescribed.
   - Type of antibiotics prescribed.

3. At 48 hours:
   - Repeat dose of surfactant.
   - Additional tests and their findings; blood gas analysis, chest radiographs
   - Amount of prescribed intravenous fluids administered.
   - Nutritional management given; enteral/parenteral feeds prescribed and the amounts given.

STUDY PROCEDURES:

No invasive procedures were performed on the study participants.
3. DATA COLLECTION, MANAGEMENT AND ANALYSIS

3.1 DATA COLLECTION

Following selection of the study participants, data was collected from the identified neonates by checking the medical records in the files. All the mothers of the neonates recruited were interviewed using the questionnaire which assessed the following aspects regarding the patient: the patient’s demographic data, clinical assessment and an audit of the management given at admission, 24 hours and 48 hours post admission.

3.2 DATA MANAGEMENT AND ANALYSIS

The categories of variables assessed for and collected were as follows:

Categorical data was summarized as frequency distributions and tabulated. Proportions were represented graphically as pie charts and bar graphs.

Data entry and analysis was done by both EpiInfo and SPSS software packages.

3.3 ETHICAL CONSIDERATIONS

The following ethical considerations were met:

- Permission was sought from the Kenyatta National Hospital Ethics Research Committee to carry out this study as part of the thesis dissertation. Copies of this protocol, the informed consent form as well as any modifications that were likely to arise were presented to this committee for written approval prior to commencing the study.
- The study was fully explained to the parent prior to obtaining consent to participate in the study and verified by a signature by the parent.
- All information was handled with uttermost confidentiality throughout the tenure of the study, held in trust by the investigator and the study institution. The participants were given study identification numbers and no information concerning the study subjects was released to an unauthorized third party without prior written approval of the study institution or the Ethics Research Committee.
- Any information necessary for the management of the child was communicated to the clinician overseeing the management of the patient.
4. RESULTS  
**General characteristics of the mothers and neonates**

During the study period, 207 records were audited. Of these, 105 (51%) were male. Most patients were assessed at a mean of thirteen hours post-delivery as depicted below.

**Table 4: Birth parameters of neonates admitted**

<table>
<thead>
<tr>
<th>Characteristics of neonates</th>
<th>Median [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in hours</td>
<td>6 [4 - 8]</td>
</tr>
<tr>
<td>Gestational age by dates</td>
<td>32 [28 - 36]</td>
</tr>
<tr>
<td>APGAR score at 1 min</td>
<td>6 [4 - 8]</td>
</tr>
<tr>
<td>APGAR score 5 min</td>
<td>8 [6 - 10]</td>
</tr>
<tr>
<td>APGAR score 10 min</td>
<td>8.5 [7 - 10]</td>
</tr>
<tr>
<td>Birth weight</td>
<td>1650 [800 - 2890]</td>
</tr>
<tr>
<td>Current weight</td>
<td>1687 [840 - 2970]</td>
</tr>
</tbody>
</table>

The median gestational age was 32 weeks and median birth weight of 1650 grams.

Forty three percent of the preterm neonates were moderate pre terms, 21.3% late pre terms, 43% very pre term and 13% extreme pre terms as illustrated below.

**Table 5: Distribution of preterm neonates according to gestational age (n=207)**

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Proportions</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 28 weeks</td>
<td>27</td>
<td>13.0</td>
</tr>
<tr>
<td>28 to &lt;32</td>
<td>47</td>
<td>22.7</td>
</tr>
<tr>
<td>32 to &lt;34</td>
<td>89</td>
<td>43.0</td>
</tr>
<tr>
<td>34 to &lt;37</td>
<td>44</td>
<td>21.3</td>
</tr>
</tbody>
</table>
Table 6: Characteristics of neonates on admission (n=207)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Category</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender of baby</td>
<td>Male</td>
<td>105</td>
<td>51.0</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>101</td>
<td>49.0</td>
</tr>
<tr>
<td>Place of delivery</td>
<td>KNH (inborn)</td>
<td>132</td>
<td>67.0</td>
</tr>
<tr>
<td></td>
<td>Referring facility</td>
<td>65</td>
<td>33.0</td>
</tr>
<tr>
<td>Mode of delivery</td>
<td>SVD</td>
<td>120</td>
<td>58.8</td>
</tr>
<tr>
<td></td>
<td>CS</td>
<td>84</td>
<td>41.2</td>
</tr>
<tr>
<td>Type of gestation</td>
<td>Single</td>
<td>145</td>
<td>74.0</td>
</tr>
<tr>
<td></td>
<td>Twins</td>
<td>48</td>
<td>24.5</td>
</tr>
<tr>
<td></td>
<td>Triplets</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Quadruplets</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Most of the preterm neonates were delivered in KNH; however, 65 of them (33%) were from referral facilities; whose distribution of frequency is depicted below. Two neonates did not have documentation of the referral centres.

Table 7: Referring facilities

<table>
<thead>
<tr>
<th>Referral centre</th>
<th>Number of preterms received at KNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mama Lucy</td>
<td>13</td>
</tr>
<tr>
<td>Machakos</td>
<td>9</td>
</tr>
<tr>
<td>Mbagathi</td>
<td>9</td>
</tr>
<tr>
<td>Pumwani</td>
<td>8</td>
</tr>
<tr>
<td>Kangundo</td>
<td>7</td>
</tr>
<tr>
<td>MSF Kibera</td>
<td>6</td>
</tr>
<tr>
<td>Shalom Athi River</td>
<td>6</td>
</tr>
<tr>
<td>Uhai Neema</td>
<td>5</td>
</tr>
</tbody>
</table>

Majority of the referring facilities were government county hospitals (57.1%) that is Mama Lucy, Machakos, Mbagathi, Pumwani and Kangundo.

The median age of mothers was twenty six years with the youngest being 16 years and the oldest 44 years. Of the 207 mothers, the majority were para 2+0. The maternal characteristics is as shown below.
Table 8: Maternal characteristics

<table>
<thead>
<tr>
<th>Maternal characteristics</th>
<th>Median [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>26 [16 - 44]</td>
</tr>
<tr>
<td>Parity</td>
<td>2 [1 - 3]</td>
</tr>
<tr>
<td>Duration of labour (hours)</td>
<td>12 [8 - 14]</td>
</tr>
<tr>
<td>Duration of rupture of membranes (hours)</td>
<td>1 [0 - 4]</td>
</tr>
</tbody>
</table>

Figure 2: Antenatal use of steroids

Of the audited records 32% of the women had documentation of having received antenatal steroids. Other parameters were observed and recorded as whether documented or not. These include: gestational age, level of severity of respiratory distress (Silverman Anderson scoring system), oxygen saturation and temperature recording as shown below. (figure 3)
The symptoms of RDS observed at admission were recorded as either having been documented as present or absent from the admission notes. Majority of the patients presented with intercostal and subcostal retractions (75%) The rest presented with grunting (48.3%) and nasal flaring (45.3%). Of those documented, the average severity score was 4-6 (52%).

Table 9: Symptoms of RDS at admission (n=207)

<table>
<thead>
<tr>
<th>Symptoms of RDS at admission</th>
<th>Documented</th>
<th></th>
<th></th>
<th>Not documented</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Nasal flaring</td>
<td>92</td>
<td>38</td>
<td>45.3</td>
<td>18.7</td>
</tr>
<tr>
<td>Grunting</td>
<td>98</td>
<td>58</td>
<td>48.3</td>
<td>28.0</td>
</tr>
<tr>
<td>Cyanosis in room air</td>
<td>55</td>
<td>90</td>
<td>26.6</td>
<td>44.3</td>
</tr>
<tr>
<td>Intercostal &amp; subcostal retractions</td>
<td>153</td>
<td>19</td>
<td>73.9</td>
<td>9.2</td>
</tr>
</tbody>
</table>

The least documented clinical findings were nasal flaring (37.2%) and cyanosis in room air (30.5%).
Audit of care and assessment of initial management:

Of the neonates received in the new born unit during the study period, 22% received initial stabilisation with CPAP. Surfactant administration was done in 12.8%. The surfactant was administered after 24 hours of admission.

The majority of the neonates who required respiratory support received oxygen supplementation via face mask with a non re-breather bag. (39.6%). The second most frequent mode of oxygen supplementation was CPAP (23.2%). None of the preterm neonates received oxygen via nasal catheter.

Table 10: Audit of initial management

<table>
<thead>
<tr>
<th>Initial management</th>
<th>n=207</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of respiratory support and oxygen delivery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal prongs</td>
<td>22</td>
<td>10.6</td>
</tr>
<tr>
<td>Plain face mask</td>
<td>7</td>
<td>3.4</td>
</tr>
<tr>
<td>Face mask + Nonrebreather mask</td>
<td>82</td>
<td>39.6</td>
</tr>
<tr>
<td>Continuous positive airway pressure (CPAP)</td>
<td>68</td>
<td>32.8</td>
</tr>
<tr>
<td>Mechanical ventilation done</td>
<td>21</td>
<td>10.1</td>
</tr>
<tr>
<td>IV fluid and antibiotics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intravenous fluids given</td>
<td>201</td>
<td>97.1</td>
</tr>
<tr>
<td>Antibiotics given</td>
<td>186</td>
<td>89.9</td>
</tr>
</tbody>
</table>

Of the study population, 76.8% of the neonates received appropriate intravenous fluids as recommended that is 10% dextrose and 72.5% received 1st line antibiotics; crystalline penicillin and gentamycin. The different prescribed fluids and antibiotics are depicted below.
Figure 4: Types of fluids and antibiotics prescribed

The figure below depicts the management instituted at 48 hours.

Figure 5: Management at 48 hours
The table below illustrates the uptake of the guidelines based on provision of surfactant and CPAP versus the eligibility based on gestational age and respiratory distress (RD) score.

Table 21: Neonates who received CPAP and MV versus eligibility based on RD score

<table>
<thead>
<tr>
<th>RD score</th>
<th>CPAP</th>
<th>MV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Eligible</td>
<td>Received</td>
</tr>
<tr>
<td>4 to 6</td>
<td>102</td>
<td>44</td>
</tr>
<tr>
<td>&gt;6</td>
<td>0</td>
<td>24</td>
</tr>
</tbody>
</table>

Of the neonates eligible for CPAP based on the RD score 4 to 6, 43.1% received CPAP. It was also noted that 17.6% received mechanical ventilation in this group. Of the neonates who scored >6 making them eligible for MV, 23.4% received that intervention. Thirty-one percent received CPAP instead.

The table below depicts uptake of surfactant administration and CPAP based on gestational age in various categories.

Table 32: Uptake of surfactant and CPAP based on GA

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Surfactant administration</th>
<th>CPAP delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Eligible</td>
<td>Received</td>
</tr>
<tr>
<td>&lt;28</td>
<td>27</td>
<td>7</td>
</tr>
<tr>
<td>28 to &lt;32</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>32 to &lt;34</td>
<td>32</td>
<td>6</td>
</tr>
<tr>
<td>34 to &lt;37</td>
<td>28</td>
<td>1</td>
</tr>
</tbody>
</table>

The total number of neonates who received surfactant were 26. The preterms between 28 to <32 weeks accounted for majority of the group who received surfactant at 46.2%. The extreme preterms and borderline preterms received surfactant in 26.9% and 23.1% respectively.
5. DISCUSSION

This study sought to determine the clinical profile of preterm neonates with RDS and perform an audit of the management they received in a large tertiary Kenyan hospital. Previous local research addressing this question were conducted prior to the introduction of the CPAP machines in KNH.

The majority of the neonates were moderate preterms (32 to less than 34 weeks); with a smaller proportion of extreme and late preterms. The relatively low contribution of late preterms may eb due to the fact that we targeted infants with RDS whose prevalence and severity correlates inversely with gestational age. On the other hand, the low contribution of extreme preterms may reflect the less than optimal survival experienced by this group in our setting. A previous study by Wagura et al found that 62% of all preterm babies born in the same facility were late preterms.

The Caesarian section delivery rate was 41.2%, which has increased from 28.3% in a previous study which probably indicates changing practice that sets a lower threshold for elective CS delivery for preterm infants. The mean maternal age was 27 years. This is comparable to another study in KNH by Ondari et al that showed the mean age range was 26 to 30 years.

In this study 67% of the pre term neonates were delivered at KNH; of the ones delivered in other facilities, public county hospitals provided the highest numbers (Mama Lucy, Machakos and Mbagathi hospitals). This suggests that KNH remains an important referral site for public hospitals and thus practices in the institutions will have wide reaching effects. (impact beyond the facility). It is also evident that these public hospitals serve catchments areas that are densely populated.

Nearly one third (32%) of the mothers recruited to the study were documented to have received antenatal steroids prior to delivery. This low uptake of antenatal steroids probably reflects gaps in implementation of evidence based guidelines at various levels, poor identification and follow-up of women at risk of preterm delivery and a high levels of spontaneous preterm deliveries in otherwise normal pregnancies. Both the WHO and European consensus highly recommend administration of antenatal corticosteroids when preterm delivery is imminent.

In our study only 12.8% of the neonates admitted with RDS received surfactant administration within 24 hours of delivery and a further 5.4% at 48 hours. Ten percent of the neonates received
mechanical ventilation. The WHO guidelines recommend surfactant replacement therapy for intubated and ventilated neonates with RDS while the European consensus guideline document recommends early surfactant administration using the ‘INSURE’ technique (intubate, give surfactant and extubate to CPAP). Based on the severity of RDS observed, a larger proportion would meet the criteria for both surfactant administration and mechanical ventilation but these were limited by availability suggesting the urgent need to improve the infrastructure of neonatal facilities in our setting.

None of the neonates received surfactant prior to the onset of respiratory distress; this is in keeping with the guidelines which do not recommend administration of surfactant before the onset of respiratory distress (prophylactic administration).

The respiratory support given to the preterm neonates depends on the severity score (Silverman Anderson scoring system) where a score of 4-6 requires CPAP and a score greater than that requires mechanical ventilation. Of the neonates who scored 4-6, 23% received CPAP and those who scored >6, 10.1% received mechanical ventilation. WHO recommends CPAP therapy for treatment of preterm neonates with RDS as this was associated with a significantly lower risk of respiratory failure requiring assisted ventilation. These findings are comparable to a survey in Kijabe where there was reduction in the number of days required for supplemental oxygen therapy in neonates who received CPAP as an intervention.

Intravenous fluids were prescribed and given in 97.1%. This is comparable to the recommended guidelines which recommend starting parenteral fluids prior to commencement of feeds. 89.9% of the neonates received antibiotics; 72.5% receiving crystalline penicillin and gentamycin which is in keeping with the recommendations to give antibiotics until sepsis is ruled out. 5.8% received 2nd line antibiotics and 2.9% received 3rd line antibiotics.

An audit on adherence of the European consensus guidelines carried out in UK by Tanney et al, showed that 75% of the neonates were managed as per guidelines which correlated with a reduction in the duration of mechanical ventilation. Complete adherence to the guidelines was shown to minimise consequences of RDS. Another audit of practice done by Brooke et al in London revealed similar results with a reduction in mechanical ventilation duration and consequences of prolonged mechanical ventilation such as BPD being minimal.
In addition, it was demonstrated that the effectiveness of early CPAP and surfactant administration using the ‘INSURE’ technique reduced the adverse pulmonary outcomes of prolonged mechanical ventilation.

6. CONTROL OF BIASES AND ERRORS
The following measures were taken to reduce different forms of bias and errors:

- Measurement bias was reduced as the questionnaire was pretested to ensure the questions were sensitive enough to detect the differences in the variables of interest.
- Information bias was reduced by assessment of the responses given to the questionnaires daily during data entry to ensure validity of collected data.
- Recall bias was minimised by obtaining the relevant record from documented data.

7. STUDY STRENGTHS AND LIMITATIONS
The study has several strengths:

- The findings of this study provide valuable information for improving management of RDS among preterm neonates.
- The audit will guide uptake and implementation of the management guidelines.
- The study revealed other referral hospitals which may be included in adoption of the guidelines.

The following study limitations were encountered:

- Poor documentation in the treatment sheets and fluid charts.
- Incomplete record keeping in the files.
- Prior knowledge of the audit by the members of the staff.

8. CONCLUSION

- 67% of preterm neonates were born in KNH, majority via SVD.
- The highest number of referrals came from Mama Lucy hospital.
- The mean gestational age was 32 weeks with a median maternal age was 26 years.
- There was suboptimal documentation of symptoms of RDS at admission.
- Majority of the neonates (52%) had a severity score of 4-6.
- 12.6% received surfactant replacement therapy, 43.1% received CPAP and 36.4% mechanical ventilation.
- IVF were given in 97.1% and IV antibiotics in 89.9%.

9. RECOMMENDATIONS

- There is need to adhere to the guidelines in our setting; in respiratory support (mechanical ventilation, CPAP administration) and surfactant administration.
- Improve documentation of clinical findings in preterms with respiratory distress.
- Adequate supply of surfactant and availability of CPAP machines and ventilators.
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APPENDICES

APPENDIX I: QUESTIONNAIRE

CLINICAL PROFILE AND AUDIT OF CLINICAL CARE OF PRETERMS WITH RESPIRATORY DISTRESS SYNDROME IN KENYATTA NATIONAL HOSPITAL

Questionnaire number ____ Date ________________

Instructions to the participant:

1. This questionnaire contains 4 sections (sections A to D).
2. Tick your response in the boxes provided.
3. Provide one response per question asked for sections A and B.
4. Sections C and D shall be filled by the investigator or research assistant.

SECTION A: SOCIODEMOGRAPHIC DATA INFORMATION OF THE CHILD

1. Gender of baby: Male ☐ Female ☐
2. Age in hours: _______
3. Gestational age by dates:
4. Place of delivery: KNH ☐ Referring facility ☐
5. Mode of delivery: SVD ☐ C/S ☐
6. Type of gestation: single ☐ twin ☐ triplet ☐
7. APGAR score at birth: 1min ____ 5min ____ 10min ____
8. Birth weight (grams): ______
9. Current weight (grams) : ______

SECTION B: SOCIODEMOGRAPHIC DATA OF THE MOTHER

1. Maternal age (years): ______
2. Parity: ______
3. Duration of labour (hours): ______
4. Duration of rupture of membranes (hours): ______
5. Antenatal use of steroids: Yes ☐ No ☐
**SECTION C: EXAMINATION FINDINGS ON ADMISSION**

<table>
<thead>
<tr>
<th>Gestational Age (Finnström score)</th>
<th>Documented</th>
<th>Not documented</th>
<th>Value</th>
</tr>
</thead>
</table>

1. Symptoms of RDS at admission
   - Nasal flaring
   - Grunting
   - Cyanosis in room air
   - Intercostal& subcostal retractions

<table>
<thead>
<tr>
<th>Level of severity (Silverman Anderson scoring system)</th>
<th>Documented</th>
<th>Not documented</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Oxygen saturation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Temperature recording</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Incubator care</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5. Other tests done:
   a. Blood Gas Analysis

<table>
<thead>
<tr>
<th>BGA</th>
<th>pH</th>
<th>pCO2</th>
<th>pO2</th>
<th>HCO3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
b. Chest radiograph

<table>
<thead>
<tr>
<th>Normal radiograph</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reticular granular pattern “ground glass appearance”</td>
</tr>
<tr>
<td>Air bronchograms</td>
</tr>
<tr>
<td>Total lung white out</td>
</tr>
</tbody>
</table>

SECTION D: ASSESSMENT OF INITIAL MANAGEMENT GIVEN

At 24 hours:

1. Was initial stabilization done with CPAP? Yes ☐ No ☐
2. Was surfactant administered? Yes ☐ No ☐
3. If Yes;
   a) How many hours post delivery was the 1st dose given? _____
   b) What was the dose given (in mg/kg)? _____
4. What mode of respiratory support is the neonate currently receiving?

<table>
<thead>
<tr>
<th>Mode of Respiratory Support</th>
<th>Oxygen flow rate (L/min)</th>
<th>Oxygen saturation measurement (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal prongs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal catheter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face mask (plain)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face mask+NRM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FiO2</th>
<th>PEEP</th>
<th>PIP</th>
<th>O₂ saturation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MV</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5. Which intravenous fluids were prescribed?
   *Indicate type of fluid ______________________________
   *Dosage (mls/kg) _________
6. Which antibiotics were prescribed?

*Indicate generic name ________________________________

*Dosage (mg/kg) _______________

At 48 hours:

1. Was a repeat dose of surfactant given? Yes ☐  No ☐
   If yes, what was the dose administered (in mg/kg) ___________

2. Were the prescribed intravenous fluids administered? Yes ☐  No ☐
   *(correlate with the fluid chart including the balance)*

3. Were there any additional tests carried out? Yes ☐  No ☐. If yes indicate here

<table>
<thead>
<tr>
<th>BGA</th>
<th>pH</th>
<th>PCO₂</th>
<th>PO₂</th>
<th>HCO₃⁻</th>
<th>BE</th>
<th>O₂ sat</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. Was a chest radiograph done? Yes ☐  No ☐
   If yes, did it show features suggestive of RDS? Yes ☐  No ☐

5. Was nutritional management commenced? Yes ☐  No ☐
   a) Were enteral feeds given? Yes ☐  No ☐
      *If yes please indicate the volume in mls/kg ___________
   b) Were parenteral feeds started? Yes ☐  No ☐
      *If yes please indicate the volume in mls/kg ___________
APPENDIX II: CONSENT FORM-ENGLISH

CLINICAL PROFILE AND AUDIT OF MANAGEMENT OF PRETERM INFANTS WITH RESPIRATORY DISTRESS SYNDROME AT KNH

Date: ______________

Investigator: Dr. Priscilla Njeri Ng’ang’a

Paediatric resident, University of Nairobi

Mobile number: 0735073788

Supervisors:

Prof. Christine Jowi,
Associate Professor Department of Paediatrics and Child Health,
University of Nairobi

Prof. Dalton Wamalwa,
Associate Professor Department of Paediatrics and Child Health,
University of Nairobi

Prof. Fredrick Were,
Professor Department of Paediatrics and Child Health,
University of Nairobi.

Dr. Florence Murila,
Senior Lecturer Department of Paediatrics and Child Health,
University of Nairobi.
Investigators statement:

We are requesting you and your child to kindly participate in this research. The purpose of this consent form is to provide you with the information that you will need to help you decide whether to participate in the study. Please read the information in this consent form carefully and ask any questions or clarifications on any matter pertaining to the study. This process is termed ‘informed consent’.

Introduction:

Respiratory distress syndrome (RDS) is a common disorder among preterm neonates and is characterised by features of respiratory distress. There are varying degrees of severity that guide on the management options. There are various aspects of management which when implemented improve the outcome of the affected neonates. This study seeks to determine the clinical profile, assess the severity and audit the management instituted for your child.

Purpose of the study:

The purpose of this study is to describe the clinical profile of preterm infants with RDS and audit the management offered to them in KNH.

Benefits:

An audit of the management of your child will help inform future guidelines and policies used to help improve the care for other hospitalized children.

Risks:

There will be no risks to you or your child during the study. No invasive procedures carried out during the study will harm your child.

Refusal to participate in the study will not alter the treatment of your child in any way.

Confidentiality:

The information obtained about you and your child will be kept in strict confidence. No information regarding you or your child will be released to any person without your written permission. The overall findings following the assessment of all the children will be discussed but not specific to your child. We will not reveal the identity of your child in these discussions.
Compensation:

There shall be no compensation or remuneration provided to you during the period of the study.

Study procedures:

The only procedures to be undertaken during the study period are those offered in the routine care of your child’s condition. No additional tests or procedures will be performed. The procedures performed may include oxygen supplementation, chest radiographs and blood gas analysis and will not harm your child.

Voluntariness:

The study will be fully voluntary. There will be no financial rewards or tokens given to you for participating in the study. One is free to participate or withdraw from the study at any given point. Refusal to participate will not compromise the care given to your child in any way.

Concerns or questions:

If you have any queries about the study or about the use of the results, feel free to contact the principle investigator, Dr Priscilla Ng’ang’a on 0735073788.

If you have any questions on your rights as a research participant you can contact the Kenyatta National Hospital Ethics and Research Committee using the number 2726300 ext. 44355.
Consent Form: Participant’s Statement:

I ___________________________ having received adequate information regarding the study, risks and benefits hereby agree/ disagree (circle appropriate answer) to participate in the study with my child. I understand that our participation is fully voluntary and that I am free to withdraw at any given time. I have been given adequate opportunity to ask questions and seek clarification on the study and these have been addressed satisfactorily.

Parents Signature: _____________ Date: ______________

I ___________________________ declare that I have thoroughly explained to the above participant regarding the study, risks and benefits and given her time to ask questions and seek clarification regarding the study. I have answered all questions and addressed their queries to the best of my ability.

Interviewers Signature: ______________ Date: ______________

APPENDIX III: FOMU LA IDHINI- KISWAHILI

UTAFITI WA UKAGUZI WA UTARATIBU UNAOFUATILIWA KATIKA TIBA WA MARADHI YA KUPUMUA KWA WATOTO WASIOTIMIZA UMRI WA KUZALIWA

Tarehe: ______________

Mpelelezi: Dr. Priscilla Njeri Ng’ang’a

Paediatric resident, University of Nairobi

Mobile number: 0735073788

Supervisors: Prof. Christine Jowi,

Associate Professor Department of Paediatrics and Child Health,

University of Nairobi

Prof. Dalton Wamalwa,

Associate Professor Department of Paediatrics and Child Health,

University of Nairobi
Prof. Fredrick Were,
Professor Department of Paediatrics and Child Health,
University of Nairobi.

Dr. Florence Murila,
Senior Lecturer Department of Paediatrics and Child Health,
University of Nairobi.

Semi la Wachunguzi
Tunatoa ombi kutoka wewe ili kushiriki katika utafiti. Sababu ya idhi ni hii ni kukupa mawaidha ya kukusaidia kuamua kama utajihusisha na utafiti huu. Tafadhali soma maelezo kwa makini, naukiwa na swali sikia huru kuuliza.

Kianzishi
Watoto ambao hawajatimiza umri wa kuzaliwa wanapata maradhi ya kupumua. Ukaguzi wa utaratibu unaofuatiliwa katika tiba wa maradhi ya kupumua ni muhimu. Utafiti huu utasaidia kupata kujua hali ya matibabu ambao watoto hawa wanapata.

Faida:
Majibu ya utafiti yatatumiwa na wahudumu wa afya kusaidia kutengeneza sera za afya.

Hatari:
Hamtakuwa na hatari lolote litakalomkabili mtoto wako katika utafiti huu.
**Kujitolea:**


**Taratibu za utafiti:**

Taratibu ambazo zitanywa ni zile atakazopata kama matibabu ya maradhi ya kupumua. Hakuna taratibu zingine zitakazofanywa. Taratibu zitakazofanywa ni kama tiba ya oksijeni, picha ya xray na uchambuzi wa gesi ya damu.

**Usiri:**

Maswali yote utakayojibu kuhusu wewe na mwanawe yatawekwa kwa siri.

**Maswali au shida?**

Ukiwa na swali au tatizo lolote kuhusu utafiti huu, kuwa huru kuwasiliana na msimamizi wa utafiti huu Daktari Priscilla Njeri Ng’ang’a kwa kupiga simu nambari 0735-073788.

Ukiwa na swali kuhusu kujiunga na utafiti huu wasiliana na Kenyatta National Hospital Ethics and Research Committee (KNH-ESRC) kwa kupiga simu nambari 2726300 Ext. 44355.

**Fomu la idhini la mlezi**

Mimi ____________________________ nimepewa mawaidha ya kutosha kuhusu utafiti huu na nina KUBALI/KATAA (Futa kama inavyofaa) kujihusisha na utafiti huu.

Idhini ya mlezi: _____________________ Tarehe __________________

Mimi ____________________________ natangaza ya kwamba nimemshauri mshiriki wa utafiti yote kuhusiana na utafiti huu na kujibu maswali yote aliyouliza.

Sahihi la mchunguzi ___________________ Tarehe ___________________