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The Magnitude and Risk Factors of Acute Respiratory Distress Syndrome among Newborn Admitted To Neonatal Intensive Care Unit at Benghazi Medical Center

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Hyaline Membrane Disease (HMD)/Respiratory Distress Syndrome (RDS) is the most common lung condition affecting premature babies. The inadequate amount of surfactant causes alveoli to collapse when the baby breathes out. It is hard for your baby to re-inflate the collapsed alveoli when he breathes. The lack of surfactant and resulting inflammation is called. Hyaline Membrane Disease (HMD)/Respiratory Distress Syndrome (RDS).
Aim of the Study: To determine the magnitude of Hyaline membrane disease or respiratory distress syndrome and identify the risk factors and complication among newborn babies in neonatal intensive care unit at Benghazi medical center (BMC).
Materials and Methods: Case series study. The study was conducted during the period between March 2017 to March 2018 of HMD cases at Benghazi medical center. A convenient sample of 120 cases diagnosed as HMD. Studied variables include the following; gestational age, birth weight, gender, type of pregnancy and type of delivery also the data for mothers such as (diabetes mellitus, preeclampsia hypothyroidism, receiving of Dexamethasone injection and premature rupture of membrane). Also investigation and treatment and finally the outcomes of babies.

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Statistical Methods: Data were analyzed with SPSS version 17, analysis of associations was made with application Chi - square test for categorical variables comparison, was applied for test of association *P* <0.25. *P* was considered statistically significant if ≤ 0.05.
Results: Female gender was predominant (52%). Most of cases of HMD were between 1000 - 2000 kg. Among the 120 cases we have (15%) sever HMD and the majority of cases have moderate –to sever Hyaline membrane disease 39 (32.5%) whereas very sever HMD were observed in nearly 27% of cases. The risk factors were history of maternal preeclampsia, maternal diabetes mellitus, prematurity and low birth weight babies and neonatal sepsis, all these were found to be very common risk factors of HMD. Pearson chi-square test p value highly significant of female gender with complications of HMD. Our results observed more than half of babies were died.
Conclusion: The risk factors were history of maternal preeclampsia, maternal diabetes mellitus, prematurity and low birth weight babies and neonatal sepsis all these were found to be very common risk factors of HMD. Also we concluded that the cases had premature rupture of membrane, which identified as risk factors of hyaline membrane disease. Furthermore, we concluded that highly significant of female gender with complications of HMD, such as Pneumothorax, bronco pulmonary, dysplasia, intra ventricular hemorrhage and congenital heart diseases were common co- morbidities with respiratory distress syndrome, all these could be have an association with the development of hyaline membrane disease, finally we observed more than half of babies were died this is a warning sign for health services.

Keywords: Risk factors; acute respiratory distress syndrome; newborn; Intensive care unit; neonatal health.

1. INTRODUCTION

Respiratory Distress Syndrome (RDS) or Hyaline Membrane Disease (HMD) is one of the most common causes of neonatal respiratory failure. According to the National Neonatal Perinatal Database 2003, HMD was found to affect 1.2% of total live births and contributed to 13.5% of total neonatal deaths [1].

Respiratory distress syndrome or hyaline membrane disease is a main cause of morbidity and mortality in the early neonatal period. Related to the degree of prematurity, it occurs in 7% - 50% of neonates. It is also responsible for 30% - 40% of newborns' hospital admission [2,3].

Respiratory distress syndrome is one of the potential risk factors that affect the survival time of premature infants [4].

Whereas Hyaline membrane disease (HMD) is one of the most challenging problems in neonatal period both in developing and in industrial countries [5].

The global number of neonatal deaths declined from 5.0 million in 1990 to 2.5 million 2018. 7,000 deaths every day in 2018 compared with 14,000 in 1990, the risk of a child dying before completing the first year of age was highest in the WHO African Region (52 per 1000 live births), over seven times higher than that in the WHO European Region (7 per 1000 live births) [6].

In addition, the infant mortality rate is around 12.6/1,000 live births, It has to be reported that, the high rate of the neonatal death is one of the reasons that Millennium Development Goal (MDG-4) for reducing under-five mortality by two thirds by the year 2015 may not be achieved [7]. Whereas, the infant mortality is the most sensitive indicator of population health. High infant mortality rate (IMR) reflects the presence of unfavorable social, economic, and environmental conditions during the first year of life [8].

In an effort to reduce infant and child mortality, massive investment has been made to improve access to health-care, nutrition, hygiene and sanitation, and promote exclusive breastfeeding. As a result, all regions of the world have shown reductions in infant mortality rate (IMR) and under-five. However, these achievements are challenged by disparities that persist among regions and within countries [8].

About 12 percent of babies born in the United States are preterm, which is higher risk of

Respiratory distress syndrome (RDS) than in other developed countries [9]. About 10 percent of premature babies in the United States develop RDS each year. The risk of RDS rises with increasing prematurity. Babies born before 29 weeks of gestation have a 60 percent chance of developing RDS, but babies born at full term rarely develop this condition. Maternal risk factors for preterm birth include previous preterm birth, periodontal disease, low maternal body mass, poor prenatal care, poverty, being uninsured, and being a member of a minority group [10,11,12].

Therefore, in this study we aimed to determine the magnitude of the of Respiratory Distress Syndrome and identify the risk factors and complications among newborn babies in neonatal intensive care unit in Benghazi Medical Center (BMC) at Benghazi city to achieve the goal of reduction neonatal deaths via policy efforts to promote health of the infant and under 5 children in Benghazi – Libya.

2. LITERATURE REVIEW

2.1 Definition

RDS, formerly known as hyaline membrane disease, occurs in incompletely developed lungs and is, therefore, a disease of prematurity. Immature lungs are functionally deficient in mature surfactant. The absence of surfactant in the liquid film lining of alveoli causes an increase in surface tension and alveolar collapse. If not treated, such atelectasis causes an increased work of breathing, intrapulmonary shunting, ventilation-perfusion mismatch, hypoxia, and eventual respiratory failure [13].

2.2 Epidemiology

Hyaline membrane disease, neonatal infection and prematurity are responsible for high morbidity and mortality rates among neonates [2,3,5].

RDS is seen almost exclusively in preterm infants, before the lungs begin to manufacture adequate amounts of surfactant. In fact, the risk of RDS decreases with increasing gestational age: 60% of babies born at fewer than 28 weeks' gestation, 30% of babies born between 28 and 34 weeks' gestation, and fewer than 5% of babies born after 34 weeks' gestation develop RDS, Other factors that increase the risk of RDS include male sex, maternal gestational diabetes, perinatal asphyxia, hypothermia, and multiple gestations. With the advent of therapies for RDS, including antenatal steroids and surfactant replacement therapy (SRT), mortality from RDS has decreased from nearly 100% to less than 10% in recent years [13].

For example in Indonesia Hyaline Membrane Disease (HMD) is the leading cause of perinatal morbidity and mortality. It is estimated that in Indonesia alone, not less than 150,000 prematurely born babies suffer from neonatal respiratory distress syndrome each year, most of them due to HMD [5].

Path physiology, causes: genetic, environment. Through the ages, infant death has been attributed to an inability of the newborn to adapt to life outside the uterus. In the early 20th century, "hyaline membranes were found during autopsy in the lungs of infants who died shortly after birth, but never in stillborns. In the 1920s, Dr. Kurt von Neergaard, a Swiss physiologist, postulated the existence of a substance in the lungs that reduces surface tension, allowing the lungs to open. In the 1950s, Dr. John Clements, a U.S. pulmonary physiologist, showed that this substance was surfactant. Finally, in 1959, Drs. Mary Ellen Avery and Jere Mead, both working at Harvard at the time, demonstrated that surfactant was lacking in the lungs of premature babies, which was the base cause of the respiratory failure seen in some of these infants [14]. Further study on infant respiratory distress syndrome (RDS) found that the deficiency of surfactant was a consequence of either insufficient production by the immature lungs or a genetic mutation in one of the surfactant proteins, SP-B. The rarer genetic form of the disease is not associated with premature birth and occurs in full-term babies [15].

Surfactant is necessary for the tiny lung alveoli to overcome surface tension and remain open. Without adequate surfactant, the pressure exerted trying to open these alveoli by either the baby's desperate breathing or by a mechanical ventilator ruptures the alveoli, producing an emphysema-like picture, or Pneumothorax, if the air escapes outside the lung and is trapped in the chest wall. Extremely premature babies may suffer from bleeding into the brain (intraventricular hemorrhage), sepsis, and other complications of their immature systems, including neurological and developmental damage. In survivors, broncho-pulmonary

dysplasia (a chronic scarring lung disease marked by prolonged oxygen need) may develop due to oxygen toxicity and mechanical ventilation. These complications are related to the severity of the disease, birth weight, and gestational age of infants. Smaller babies are at greater risk of developing broncho-pulmonary dysplasia [16].

From literature there are many causes of infant mortality, so among very low birth weight infants, the greatest lethal risk is extreme prematurity and hyaline membrane diseases [5].

Respiratory Distress Syndrome (RDS): is the most common lung condition affecting premature babies. Premature babies can have both immature lung tissue and a lack of surfactant, Hyaline membrane disease due to lung surfactant deficiency in the preterm newborn is an important cause of neonatal morbidity and mortality. Exogenous lung surfactant has transformed HMD therapy in developed countries, but an equivalent benefit has not been accomplished in developing countries due to a variety of factors [17,18].

One of the main causes of respiratory distress was Hyaline membrane disease (HMD), Hyaline Membrane Disease (HMD)/ /Respiratory Distress Syndrome (RDS), the inadequate amount of surfactant causes alveoli to collapse when the baby breathes out. It is hard for your baby to re-inflate the collapsed alveoli when he breathes. The lack of surfactant and resulting inflammation is called. Hyaline Membrane Disease (HMD)/ /Respiratory Distress Syndrome (RDS), the lung of the preterm baby is morphologically and functionally immature. Surfactant deficiency in the immature lungs causes alveolar instability and collapse, capillary edema and the formation of hyaline membrane [18].

Respiratory distress syndrome is the primary cause of mortality and morbidity in preterm newborns. Rate and degree are related to the gestational age (GA) and weight of the newborn baby [18,19].

One of the most common reasons for admission of term neonates to a neonatal intensive care unit (NICU) is respiratory distress. The cause may be of pulmonary or non-pulmonary origin. The non-pulmonary causes include cardiac, infectious, metabolic, central nervous system, and miscellaneous conditions [19].

2.3 Causes of RDS in Neonates [19]

2.3.1 Parenchymal conditions

Transient tachypnea of the newborn:

- Meconium aspiration syndrome and other aspirations
- Respiratory distress syndrome
- Pneumonia
- Pulmonary edema
- Pulmonary hemorrhage
- Pulmonary lymphangiectasia

2.3.2 Developmental abnormalities

Lobar emphysema:

- Pulmonary sequestration
- Cystic adenomatoid malformation
- Congenital diaphragmatic hernia
- Tracheoesophageal fistula
- Pulmonary hypoplasia

2.3.3 Air way abnormalities

Choanal atresia/stenosis:

- Laryngeal web
- Laryngotracheomalacia or bronchomalacia
- Subglottic stenosis Mechanical abnormalities

2.3.4 Mechanical abnormalities

Rib cage anomalies (eg, Jeune syndrome):

- Pneumothorax
- Pneumomediastinum
- Pleural effusion
- Chylothorax [19].

Several maternal and neonatal factors are known to the development of HMD in preterm infants. Since the cause of HMD is surfactant deficiency, factor that consistently associated with the consistently associated with the development of HMD is gestational age of HMD is gestational age. The younger the gestational age, the higher possibility of an infant to suffer from HMD, in term infants, the incidence of HMD is 0.01%, while in infants less than 30 weeks of gestational age, the incidence is approximately 30%. Other risk factors include sex {male to female ratio = 1,5 to 2: 1), asphyxia, history of previous HMD, antepartum bleeding twins, cesarean section, maternal diabetes [5].

Furthermore, a recent study in Ethiopia 2017 conducted by Million *et al,* reported premature infants come early into the world and they are born fragile, small and weighing less than full term infants. Many of the babies who survive face greater risks of significant health problems and disability throughout their lives (i.e, learning disabilities, visual and hearing problems, chronic lung disease and other long-term diseases) which translate into significant increased costs to healthcare, the economy and the broader society [5]. Premature is one of the major causes of infants' death which is not an acute disease and compared to term infants experience more difficulty with feeding, blood glucose control, jaundice, temperature instability, respiratory distress and sepsis either singly or in combination [5].

Globally, an estimated 13 million infants are born before 37 completed weeks of gestation annually. Rates are generally highest in low and middle income countries and increasing in some middle and high income countries , more than 1 in 10 of the world's babies born in 2010 were born prematurely, making an estimated 15 million preterm births, of which more than 1 million died as a result of their prematurity [4].

Preterm birth accounts for 3.1% of all Disability Adjusted Life Years (DALYs) in the Global Burden of Disease, more than for HIV and malaria. Also, deaths constitute 28% of the 4 million annual new born deaths with 99% of these deaths occurring in developing countries. Morbidity, mortality and prolonged hospital stay of preterm babies result in significant cost to the health sector, parents and the society [4].

In Ethiopia, according to report of United Nations of children fund, one of the main causes of neonatal death is preterm birth accounts for 23% of all other causes of neonatal death. Also, Ethiopian Demographic and Health Survey in 2011, high rate of neonatal mortality (37 deaths per 1000 live births) is reported and preterm birth is believed to be a major and direct cause of neonatal mortality [4]. One in every 13 babies born in Ethiopia did not survive to celebrate its first birth day and one in every eight children died before its fifth birth day. Preterm birth has multiple factors whose solutions will not come through a single discovery but rather from an array of discoveries addressing multiple biological, clinical, and social behavioral risk factors, causal factors linked to preterm birth include medical conditions of the mother or fetus, genetic influences, environmental exposure, infertility treatments, behavioral and socio-economic factors as well as iatrogenic prematurity. Approximately 45–50% of preterm births are idiopathic, 30% are related to preterm rupture of membranes and another 15–20% result from medically indicated or elective preterm deliveries [4].

On the other hand, in study in Indonesia reported that maternal illness causing chronic fetal distress, such as hypertension or eclampsia, may have a protective effect for the development of HMD. Similarly, premature rupture of the membrane, especially rupture before the initiation of delivery process, may decrease the incidence of HMO. Some of the risk and protective factors are still controversial and have not been confirmed in medical literature [5].

Chronic neonatal lung disease (CNLD) is likely to remain a serious problem despite the introduction of surfactant treatment and the use of antenatal corticosteroids [20].

The Factors associated with CNLD can be conveniently divided into four groups. The first group relates to birth parameters: young gestational age and male sex. The second group relates to the severity of hyaline membrane disease. Severity can be gauged by radiographic appearances and ventilator settings during the first 48 hours, providing the latter are adjusted in a standard way. The third group relates to failed recovery from hyaline membrane disease, occurring from day. Abnormal healing should manifest as a delay in improvement in ventilator status towards the end of the first week. Patent ductus arteriosus is also often seen during this period, and is associated with CNLD. The fourth group relates to abnormal radiological gas patterns. Neonates developing air leaks are at greater risk of developing CNLD. Terminal airway distension may also represent a more minor degree of lung barotrauma [20].

A previous study conducted in University College Hospital, London-UK reported the methods and indications of mechanical ventilation for hyaline membrane disease by the use of continuous positive airway pressure (CPAP) reduces but does not abolish the need for mechanical ventilation in infants who are very severely affected by hyaline membrane disease, (the idiopathic respiratory distress syndrome of the newborn). Both forms of therapy should be available in units caring for the infants [21].

Regarding the indications for Mechanical Ventilation Because of the complications of ventilator therapy, always been very reluctant to use it unless the infant's prognosis for intact survival was seriously jeopardized. From experience, infants with very severe impairment of gas exchange often survive without mechanical ventilation (or CPAP), if carefully managed, and are normal children at follow up. The study found that 40% of infants with an arterial oxygen tension (Pao2) less than 50 mmHg while breathing more than 90% oxygen survived, as did 75 % of those with an arterial carbon dioxide tension (Paco2) above 70 mmHg.

The study concluded that with advances in prenatal detection and treatment of infants at risk, and with improved management of infants during spontaneous breathing, it is to be hoped that the need for mechanical ventilation for hyaline membrane disease will steadily diminish. In the meantime it is important to develop techniques of ventilation which will prevent fatal or crippling lung damage while at the same time preserving an adequate circulation and oxygen supply to vital organs to solve the problem ventilate the infants at much lower peak airway pressures than in the past and to reduce the inspired oxygen concentration below 100%. The application of this approach appears to have resulted in a large increase in survival rate among ventilated infants, and the virtual disappearance of broncho-pulmonary dysplasia [21].

Ethiopia study also demonstrated the major factors that affect the survival time of preterm are prenatal Asphyxia, Sepsis, hyaline membrane disease, jaundice, Gestational age, temperature and respiratory distress syndrome for time to death of premature infants. Preterm infants having prenatal asphyxia, Sepsis, Jaundice, Hyaline membrane and respiratory distress syndrome have higher death rate. Similarly, preterm with poor health indicators like lower gestational age (26–28) weeks and initial temperature, were less likely to survive. To predict and model the survival time of premature infants, various baseline parametric regression models were applied. Among these, parametric model with log logistic baseline distribution is best fitted to predict the survival time of the premature infants [4].

The study recommended that study the main predictive factors for the survival time of premature infants are more of clinical variables. So, health workers should be cautious when mother's born preterm which has prenatal asphyxia, Sepsis, Jaundice, hyaline membrane disease and respiratory distress syndrome. The log- logistic regression model provides better predictions to the survival probability of premature infants'. So, future researchers could make use of this model. Future studies also need to assess the level of awareness, treatment and control of these risk factors [4].

A retrospective Indian study in 2008-2014 for 100 babies with hyaline membrane disease who were ventilated who required mechanical ventilation for HMD concluded that the survival rate in study was 82%. Survival improved with increasing gestational age and birth weight. Sepsis, disseminated intra vascular coagulation (DIC) and pulmonary hemorrhage were significantly associated with a poor outcome and septicemia was the commonest cause of mortality. There was a reduced incidence of intra ventricular hemorrhage (IVH) and Pneumothorax [1].

Many studies confirmed an inverse relationship between RDS and gestational age. In contrary much progress in perinatal care, respiratory distress syndrome still remains a major neonatal problem [22].

It is may have several of the following symptoms:

- Rapid breathing (tachypnea)
- Blue color to skin (cyanosis)
- Pulling in of the ribs and center of the chest with each breath (retraction)
- Uneven abdominal breathing/seesaw breathing
- Grunting (an "ugh" sound with each breath)
- Widening of the nostrils with each breath (nasal flaring).

There are risk factors of HMD/RDS:

- Premature
- low and very low birth weight
- Hypertensive mother or preeclampsia
- Hypothyroidism mother
- Infant of Diabetic Mother
- Male Gender
- Multiple Gestations

Specific treatment for the baby depends on baby's medical history, severity of HMD/RDS:

- In mild cases, it can be managed by giving extra oxygen to the baby through a tiny catheter placed in baby's nostrils to deliver oxygen, called a nasal cannula.
- In moderate cases, the baby may need Continuous Positive Airway Pressure (CPAP). CPAP is oxygen delivered under a small amount of pressure usually through little tubes that fit into the nostrils. Delivering oxygen under pressure helps keep the baby's air sacs or alveoli open.
- In moderate or severe cases, the baby may need mechanical help with breathing. This is done by inserting a tiny tube into his wind pipe. This process is called intubation. Once incubated, the baby may be placed on a breathing machine (Mechanical Ventilator) to administer breaths to the baby.
- Once the baby is on the Mechanical Ventilator, surfactant (a medication that replaces the substance that is lacking in the baby's lungs) may be administered through the airway tube in his wind pipe. This helps the alveoli expand more easily [22].

The recovery period is different for all babies. The condition is most severe in the first 2 to 3 days after birth [22]. Then the baby gradually needs less added oxygen.

If a baby has mild disease and has not needed a breathing machine, he may be off oxygen in 5-7 days. If a baby has more severe disease, the condition may last 2 to 3 weeks. The speed of recovery depends on the following:

- The birth weight and prematurity of the baby.
- The severity of the condition.
- Presence of any infection.
- Presence of any heart condition.

There are short term complication of HMD/RDS: [22]

- Pneumothorax
- Patent Ductous Arterios
- Pulmonary Hemorrhage.
- Intraventricular Hemorrhage

Long term effects are more likely if the condition has been severe or if there have been complications. Possible problems may include:

- Increased severity of colds or other respiratory infections, especially for the first two years.
- Increased sensitivity to lung irritants such as smoke and pollution.
- Greater likelihood of wheezing or other asthma-like problems in childhood.
- Greater likelihood of hospitalization in the first two years of life due to respiratory synchial virus (RSV).
- If the RDS was severe, the baby may have injury and scaring of the lung called Chronic Lung Disease [22]

2.3.5 Clinical assessment of severity and oxygen therapy

Signs of respiratory distress syndrome (RDS) include:

- Tachypnea with RR > 60/minutes
- Nasal flaring
- Expiratory grunting
- Retraction of the chest wall (sternal, intercostal, sub-costal) or chest in drawing
- Central cyanosis (visible when SpO2 is < 85%) (acrocyanosis is quite common after birth and it is not related to hypoxemia; difficult to be evaluated in case of anemia) [18]

Abnormal respiratory sounds can also be associated:

- Inspiratory stridor
- Expiratory wheezing / Whistles
- Various rales at auscultation
- HR (pulses) and SpO2 measurement by pulse oximeter
- Re-calibration 1 x/day
- Change the measurement site every 4-6 hours

The measure is poorly reliable in case of poor perfusion due to shock, acidosis or hypoxia and in case of edema or anemia.

The pulse oximeter is the best tool to guide oxygen therapy in children, regardless the age. Oxygen should be given to all neonates (at term and premature babies) with a saturation **<**90% in room air.

An excessive or inappropriate use of oxygen (high oxygen flow rate or high oxygen saturation) can directly lead to pulmonary lesions and can be related to pre- term retinopathy [18]

When oxygen is being administered, the flow rate should be adjusted to provide the minimum

flow of oxygen while maintaining the following saturations:

- 90 to 95% in babies born at term (≥ 37 weeks of pregnancy).
- 90 to 95% in preterm babies (< 37 weeks of pregnancy).

If the newborn's SpO2 is > 95%, the flow has to be progressively reduced.

Once the SpO2 is > 95% in room air, oxygen can be stopped [18].

2.3.6 Prevention, treatment and prognosis

By far the biggest risk factor for respiratory distress syndrome (RDS) is prematurity. Preventing premature births could nearly eliminate RDS. Several causes of premature birth are preventable by good prenatal care. If the birth cannot be delayed beyond 34 weeks, the mother may be given corticosteroid therapy before birth, which accelerates fetal lung maturation. High-risk and premature infants require prompt attention by a pediatric resuscitation team [16]. Healthcare providers may deliver the baby and administer surfactant down the infant airways, either as soon as the premature baby is born or when RDS is diagnosed [16].

The babies can be given respiratory support by mechanical ventilators with continuous positive airway pressure (CPAP) designed to prevent the alveoli from collapsing. The use of oxygen has improved the life of many persons with respiratory disease. In the 1950s, however, its harmful effects were manifest when blindness occurred in premature infants given pure oxygen. As mechanical ventilation and critical care became more sophisticated in the 1960s and 1970s, neonatal intensive care unit beds became filled with RDS survivors. Although these premature infants could be kept alive longer on ventilators, many still died, and those who lived often developed broncho-pulmonary dysplasia [16].

One of the greatest breakthroughs in the fight against lung disease was the development of surfactant replacement therapy, which saves these premature infants from an almost certain death. Its use has led to a dramatic decrease in mortality from nearly 100 percent to less than 10 percent. Typically, infants are able to breathe more easily within a few hours of receiving surfactant, and complications such as lung rupture are less likely to occur. There is a risk of bleeding into the lungs from surfactant treatment, especially in extremely low birth weight infants (those weighing less than 1,000 grams). In addition, inhaled nitric oxide can improve oxygenation and reduce pulmonary inflammation. When begun soon after birth in these premature infants, nitric oxide administration improves the acute disease and also reduces the chance of chronic lung disease. As with most drugs, it can also have side effects, including an increased risk of bleeding [16].

2.4 Management

As management of respiratory distress syndrome (RDS) advances, clinicians must continually revise their current practice. The fourth update of "European Guidelines for the Management of RDS" by a European panel of experienced neonatologists and an expert perinatal obstetrician based on available literature up to the end of 2018 [23]. Optimizing outcome for babies with RDS includes prediction of risk of preterm delivery, need for appropriate maternal transfer to a perinatal center and timely use of antenatal steroids. Delivery room management has become more evidence based, and protocols for lung protection including initiation of CPAP and titration of oxygen should be implemented immediately after birth. Surfactant replacement therapy is a crucial part of management of RDS, and newer protocols for its use recommend early administration and avoidance of mechanical ventilation. Methods of maintaining babies on non-invasive respiratory support have been further developed and may cause less distress and reduce chronic lung disease [23].

As technology for delivering mechanical ventilation improves, the risk of causing lung injury should decrease, although minimizing time spent on mechanical ventilation using caffeine and, if necessary, postnatal steroids are also important considerations. Protocols for optimizing general care of infants with RDS are also essential with good temperature control, careful fluid and nutritional management, maintenance of perfusion and judicious use of antibiotics all being important determinants of best outcome [23].

Currently recommended treatment modalities for HMD include oxygen therapy, Continuous

Positive Airway Pressure (CPAP), surfactant therapy and mechanical ventilation. Though most babies can be successfully managed with non- invasive therapy like nasal cannula oxygen and CPAP, mechanical ventilation is required for severe RDS. With the establishment of tertiary neonatal units, these treatment modalities are practiced both in the private and government sector in the country. Studies from apex institutes in the country have reported the profile and outcome of babies with hyaline membrane disease needing assisted ventilation. Here have been no studies from regional medical college. It is in this background that this study was undertaken to analyze the short term outcome of both preterm and term babies requiring assisted ventilation for HMD and report the complications contributing to morbidity and mortality of these patients from a regional medical college with limited resources [1].

According to European Consensus Guidelines on the management of RDS surfactant therapy reported that surfactant therapy plays an essential role in management of RDS as it reduces Pneumothorax and improves survival. However, intratracheal administration requires skill and may cause harm, particularly if uncontrolled positive pressure is applied to the newborn lung. Prior to 2013, prophylactic surfactant was recommended for the smallest babies as it improved survival in clinical trials from the pre-CPAP era. After 2013, with increased use of antenatal steroids and early initiation of CPAP, outcomes are best if surfactant is reserved for infants showing clinical signs of RDS, and for the smallest infants early initiation of CPAP may avoid the harmful effects of intubation and mechanical ventilation (MV) during the transitional phase [23].

The overall aim is to avoid invasive MV if possible whilst endeavoring to give surfactant as early as possible in the course of RDS once it is deemed necessary [23]. From a previous research in Australia for Variability is an inherent property of many biological systems, demonstrated the variable breathing is especially evident in newborn infants , particularly those born premature for whom sigh breaths with tidal volume (*V*T) more than twice the average breath volume are critical to the maintenance of resting lung volume. Current ventilator strategies advocated for the preterm infant focus on tightly regulating the size of each breath using volume guarantee or volume targeting of ventilator assisted/controlled breaths [24].

An alternative approach, variable ventilation (VV), maintains a constant breath-to-breath minute volume throughout the study but distributes delivered *V*T and respiratory rate (RR) such that the lung may receive *V*T less than or greater than the average *V*T. In adult animal models, VV improves oxygenation and enhances gas exchange as compared with controlled conventional mechanical ventilation (CV), the researchers found VV enhanced both respiratory mechanics and gas exchange in preterm lambs as compared with CV that tightly regulated both breath size and rate, similar to findings of studies in adult animal models. However, unlike the adult animal studies, VV did not improve oxygenation in the preterm lambs, most likely due to shunting across fetal channels, the study concluded that VV improves ventilation efficiency and *in vivo* lung compliance in the ovine preterm lung without increasing lung inflammation or lung injury [24].

The literature originating from Bulgaria for frequency of hyaline membrane disease in preterm infants after prenatal corticosteroid prophylaxis. A retrospective study of 167 preterm infants was conducted, of which 89 (53.3%) had prophylaxis with Dexamethasone, in 25 (15%) of preterm infants, there was a Hyaline Membrane Disease (HMD) and 101 (60.5%) developed other forms of Respiratory Distress Syndrome (RDS). The results obtained show that the incidence of HMD in preterm infants is mediated by the early gestational age and advanced age of the mother, and decreased by corticosteroid therapy [25]. The study showed that the premature birth is a serious medical, social and economic problem. Its consequences are multiple health complications leading to high neonatal mortality worldwide. Respiratory insufficiency and surfactant deficiency significantly increase the risk of developing Hyaline Membrane Disease (HMD) and other forms of Respiratory Distress (RDS). These are the most common causes of death in premature babies [25].

The study also reported that in prenatal and neonatal medicine, new and adaptive prophylaxis is being implemented to reduce the risk of death of premature babies and reduce the development of health complications, the study also mentioned the goal of effective corticosteroid prophylaxis is to reduce mortality, reduce complications in prenatal newborns, and shorten their stay in neonatal and intensive units respectively [25].

While in n Brazil study, found that the neonatal component of the infant mortality rate remains higher than the post-neonatal one and most of deaths occur in the first seven days of life (early neonatal period). At that stage breathing problems are a major cause of death especially among preterm newborns. In these newborns, lung immaturity determines deficiency of surfactant, a substance responsible for reducing the surface tension within the alveoli that prevents collapse at low lung volumes, and the use of exogenous surfactant is indicated for preterm newborns with established or presumed diagnosis of respiratory distress syndrome (RDS) because it reduces mortality, disease severity and complications due to RDS [26].

Advantages related to the use of this technology are well established in the literature. It is known that newborns with RDS receiving treatment with surfactant have reduced risk of Pneumothorax, pulmonary interstitial emphysema, death and broncho-pulmonary dysplasia or death (in combination) in comparison to those who do not receive this treatment [26].

Furthermore, Brazil study reported Although individual clinical features remain having greater weight in determining the use of exogenous surfactant replacement therapy in infants with Respiratory Distress Syndrome, factors linked to the institution are also of great importance. Interventions aimed at modifying institutional factors associated with lower surfactant use are to be encouraged, so that better results on perinatal care could be achieved. It was possible to identify units underperforming the average and to pinpoint that surfactant use is less likely in infants with Intrauterine Growth Restriction (IUGR) or with lower disease severity, all of which require corrective interventions. Special attention needs to be given to promote greater use of surfactant in lower technological complexity units and hospitals with fewer beds, since all infants with RDS have indication for surfactant use in the first two hours of life [26].

A study in Canada conducted by Joan Crane & St. John's to assess the benefits and risks of antenatal corticosteroid therapy for fetal maturation All pregnant women between 24 and 34 weeks' gestation who are at risk of preterm delivery within 7 days should be considered candidates for antenatal treatment with a single course of corticosteroids. Also treatment should consist of two 12 mg doses of betamethasone given IM 24 hours apart, or four 6 mg doses of Dexamethasone given IM 12 hours apart and there is no proof of efficacy for any other regimen and because of insufficient scientific data from randomized clinical trials regarding efficacy and safety, repeat courses of corticosteroids should not be used routinely [27].

According to Warren & Anderson Summary of recommendations 1994 and 2000 National Institutes of Health Consensus Conference regarding Antenatal Steroid [13].

1. The benefits of prenatal corticosteroids outweigh any risks that have been identified. The benefits include decreased death and decreased incidence of respiratory distress syndrome and intraventricular hemorrhage.
2. All fetuses at 24 to 34 weeks' gestation are candidates for corticosteroid therapy.
3. Prenatal corticosteroid therapy should be used without consideration of fetal sex, race, or the availability of surfactant treatments for respiratory distress syndrome.
4. Prenatal corticosteroids should be administered if tocolytics are used.
5. Because of probable benefit for treatment to delivery intervals of less than 24 hours, prenatal corticosteroids are indicated unless delivery is imminent.
6. Repeated courses of corticosteroids may not be safe and should not be administered outside of clinical trials [13].

2.5 Prenatal Care

Lack of antenatal care increases risk of death or severe morbidity. There are no generally effective means to prevent spontaneous or elective preterm births. However, in pregnant women at risk of spontaneous preterm birth due either to previous preterm birth or where a shortened cervix has been identified, use of progesterone is associated with reduced preterm delivery rates and reduced neonatal mortality) [23]. Routine cervical length measurements may be advised in populations at risk of preterm birth but not in populations with an overall low risk and/or very low incidence of short cervix. Cervical cerclage may also reduce preterm birth in high-risk singleton pregnancies. The present challenge is to identify high-risk pregnancies early and aim for effective prevention of preterm birth. Interventions to improve outcome and prevent RDS begin before birth. There is often warning of impending preterm delivery, and in

these cases a need to consider interventions to prolong gestation or reduce risk of an adverse outcome by "preparing" the fetus [23].

Cervical length measurement possibly in combination with a biomarker may determine which women are actually at risk of delivery within 7 days and allow more judicious use of antenatal treatments. Extremely preterm babies should, if possible, be transported in utero to tertiary centers where appropriate skills are available; best outcomes are achieved for babies born in centers with a high throughput of very low birth weight babies.

In cases of prenatal pre-labour rupture of membranes, antibiotics can delay preterm delivery and reduce neonatal morbidity, although co-amoxiclav should be avoided because of its association with increased risk of necrotizing enterocolitis (NEC) [23].

Magnesium sulphate (MgSO4) given to women with imminent preterm delivery reduces cerebral palsy at 2 years of age by about 30% , although longer- term benefits are less clear. Tocolytic drugs can be used in the short-term to delay birth, permit safe transfer to a perinatal center and allow prenatal corticosteroids time to take effect, although tocolytics have no direct beneficial effect on the fetus. Given their limited value, only drugs that are safe for the mother should be considered, that is oxytocin antagonists or Ca-channel blockers [23].

A single course of prenatal corticosteroids given to mothers with anticipated preterm delivery improves survival, reduces RDS, NEC and intraventricular hemorrhage and does not appear to be associated with any significant maternal or short-term fetal adverse effects. Prenatal corticosteroid therapy is recommended in all pregnancies with threatened preterm birth before 34 weeks' gestation where active care of the newborn is anticipated [23].

From the literatures describe the prevention of RDS by avoiding early labor and delivery is the best way to prevent premature birth and respiratory distress syndrome. In many cases, this is beyond the control of the mother or doctor. In some cases, if early delivery seems unavoidable, treating the mother with a steroid drug called betamethasone may reduce the risk and severity of respiratory distress in the infant [23].

2.6 Aim of the Study

1. To determine the magnitude of hyaline membrane disease (HMD) or respiratory distress syndrome among newborn babies in neonatal intensive care unit in Benghazi medical center (BMC) at Benghazi city, during the period from March 2017 to March 2018.
2. To identify the risk factors and complication of hyaline membrane disease (HMD) among of newborn admitted to neonatal intensive care unit in Benghazi medical center 2017 - 2018.

3. MATERIALS AND METHODS

3.1 Design and Settings of the Study

An observational descriptive case series study, Hospital based study.

3.2 Duration of the Study

The study was conducted during the period between March 2017 to March 2018.

3.3 Study Population

HMD cases at Benghazi medical center.

3.4 Sampling

None random sampling technique was used. A convenient sample of 120 cases diagnosed as HMD.

3.5 Variables of the Study

Studied variables include the following; gestational age , birth weight , gender , type of pregnancy and type of delivery (spontaneous vaginal delivery or caesarean section) also the data for mothers such as (diabetes mellitus, Preeclampsia, hypothyroidism, receiving of Dexamethasone injection and premature rupture of membrane).

Also investigation and treatment for them include (Chest X ray and uses of Surfactant, continuous passive airway pressure, mechanical ventilator M.V). Complications were noted such as (sepsis, intra-ventricular hemorrhage, Pneumothorax and chronic lung disease), and finally the outcomes of babies.

3.6 Statistical Methods

The data were gathered and analyzed, simple descriptive statistics of some parameters such as mean, standard deviation. Data were analyzed with SPSS version 17, analysis of associations was made with application Chi - square test for categorical variables comparison, was applied for test of association *P* <0.25. *P* was considered statistically significant if ≤ 0.05.

4. RESULTS

Female gender was predominant (52%) as shown in Fig. 1.

4.1 Birth Weight and Gestational Age

Most of cases of HMD were between 1000 kg to 2000 kg were seen in Fig. 2.

All the cases of HMD were preterm. Gestational age 32-33 weeks were seen in 33.3% of newborn infants with HMD followed by 22.5 % of newborn infants 30 - 31 weeks and gestational age 34 weeks in 20 % of newborn infants with HMD as seen in Table 2.

The vast majority of cases delivered by caesarean section 80%, while only 20 % normal vaginal delivery as shown in Fig. 4.

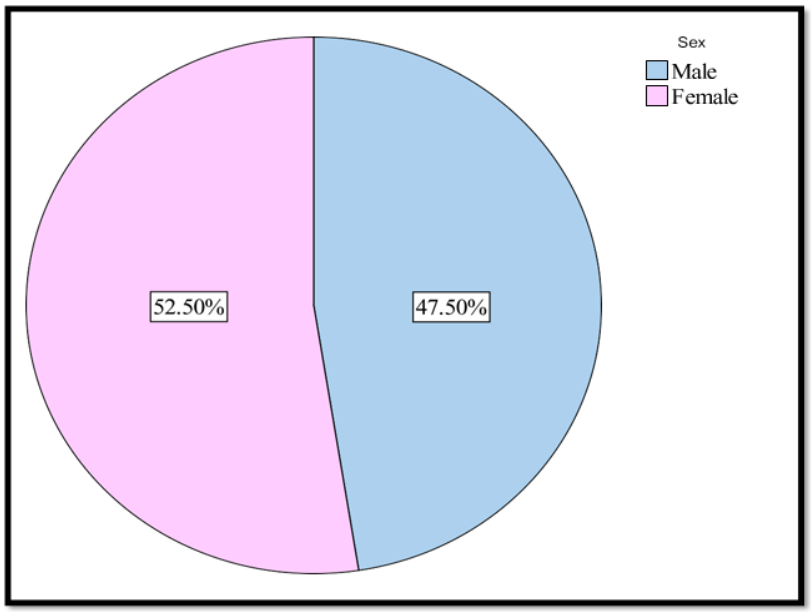

Fig. 1. Distribution of hyaline membrane disease cases (HMD) Respiratory Distress Syndrome) according to gender at Benghazi medical center 2017-2018 (N= 120)

Table 1. Descriptive statistics of some parameters in hyaline membrane disease cases (HMD) at Benghazi medical center 2017-2018 (N= 120)

Parameters	Minimum	Maximum	Mean	Std Deviation.	Number
Birth weight (kg)	500 kg	3400 kg	1460.50	532.289	120
Gestational age (weeks)	25 weeks	34weeks	31.07	2.514	120

Table 2. Neonatal gestational age of cases respiratory distress syndrome Benghazi medical center 2017-2018 (N= 120)

Gestational age (weeks)	Frequency	Percent %
24- 25 weeks	2	1.7
26- 27 weeks	6	5
28- 29 weeks	27	22.5
30-31 weeks	21	17.5
32-33 weeks	40	33.3
34 weeks	24	20

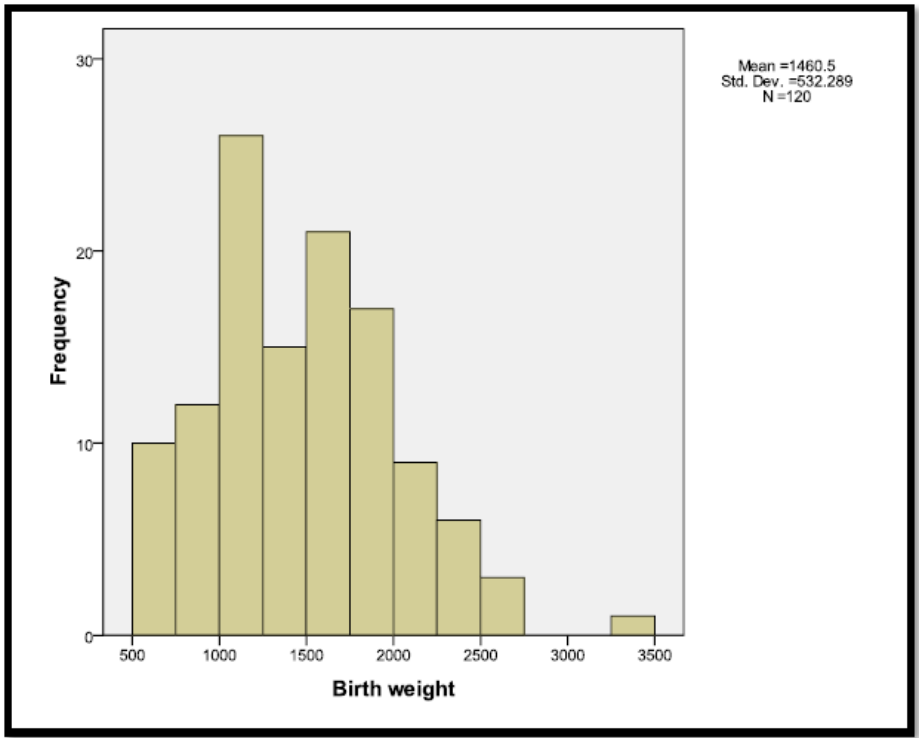

Fig. 2. Distribution of hyaline membrane disease cases (Respiratory Distress Syndrome) according to birth weight at Benghazi medical center 2017-2018 (N= 120)

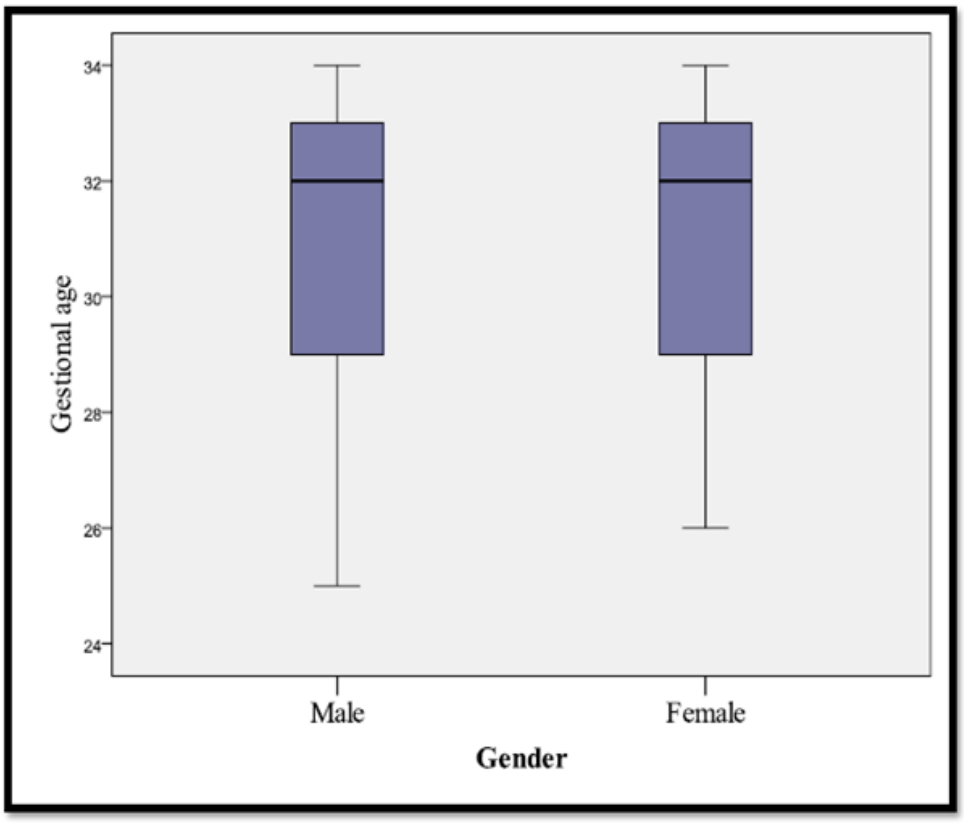

Fig. 3. Neonatal gestational age with gender

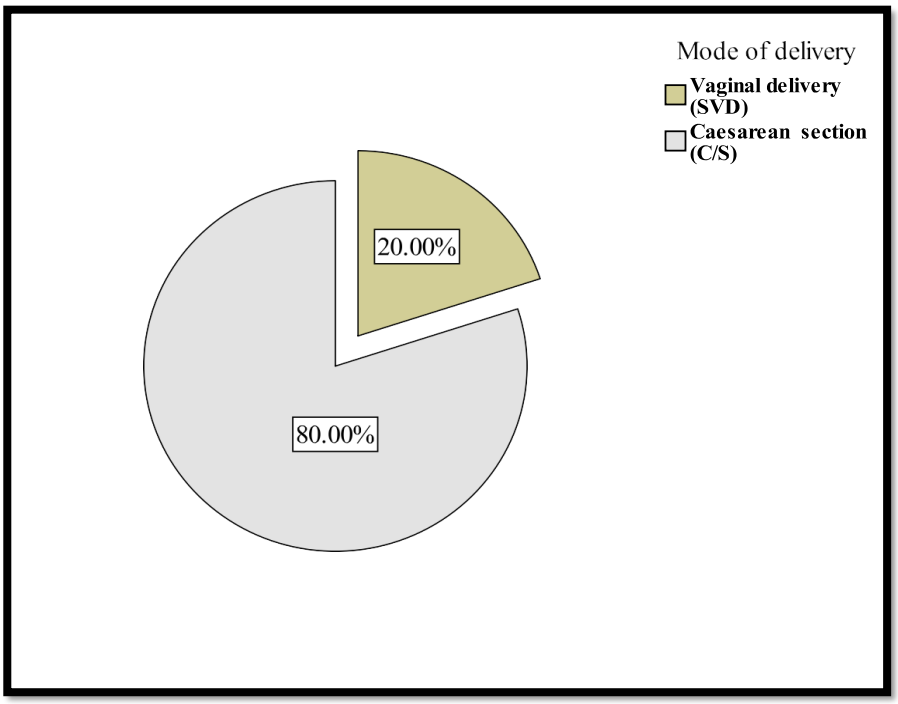

Fig. 4. Distribution of newborns of hyaline membrane disease according to mode of delivery (N= 120). H/o C/s df= 2 p value = p= 0.021 (statistically significant)

Most of cases were single 68% and 15% first twin as shown in Fig. 5.

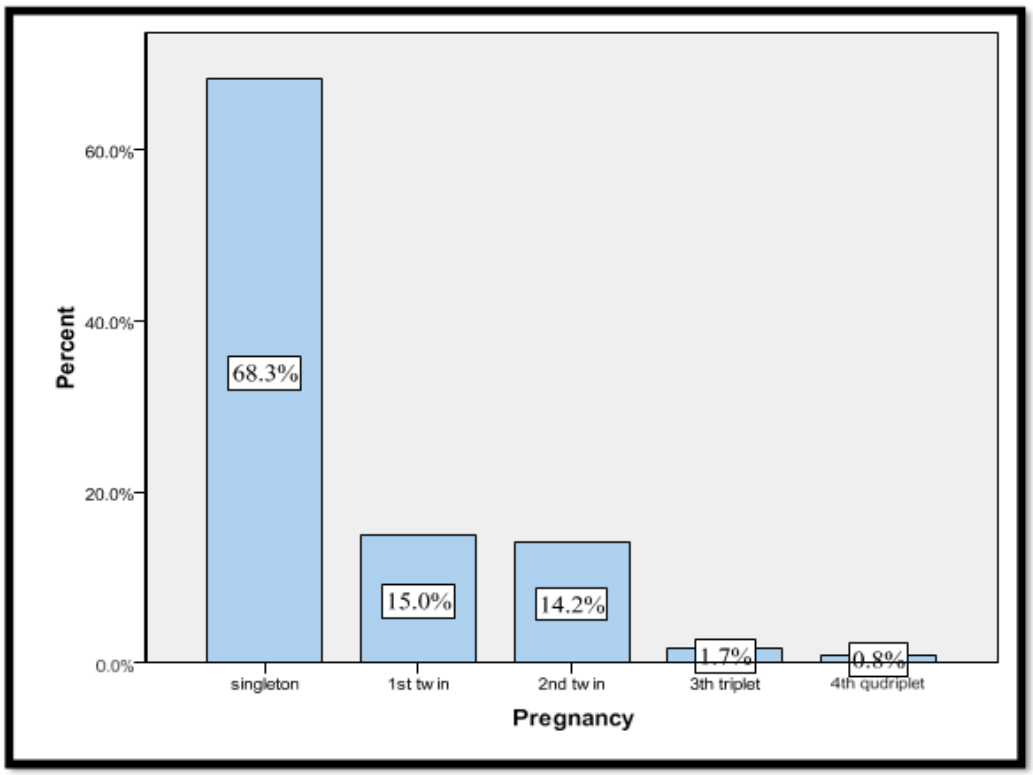

Fig. 5. Distribution of newborns of hyaline membrane disease according to type of delivery at Benghazi medical center 2017-2018 (N= 120)

Table 3. Clinical characteristics, details of 120 cases of hyaline membrane syndrome at (BMC) 2017-2018

Characteristics/Parameters	Details		Number	Percentage
Diagnosis by chest x rays	Diagnosis by x rays	Yes	120	100
	chest x rays done	Less than 6 hours after birth	1	0.8
		More than 6 hours	119	99.2
	received at 30 weeks		19	15. 8
Dexamethasone	received at 31 - 34weeks		47	39.2
	Not received		54	45
Surfactant therapy	Yes		53	44.2
	No		67	55.8
	Day one		32	26.7
Time of receive surfactant	Day two		17	14.2
	Day three		4	44.2
Nasal oxygen *	Yes		120	100
	Day one		35	29.2
Mechanical ventilation (MV) * *	Day two		14	11.7
	Day three		5	4.2
	Not connected to mechanical ventilation		48	40
Mechanical ventilation ***Td	Less than 6 days		37	30.8
	More than 6 days		19	15.8

*Therapeutic surfactant 53 out of 120 cases (44.2%), More than half of newborns babies with HMD not received surfactant in 67 (56%), all cases received *oxygen whereas mechanical ventilation ** 102 out of 120 (85%), Mechanical ventilation. ***Td, 64 out of 120 cases (53.3%). Continuous positive air way pressure not given for any case*

Among the 120 cases we have 18 (15%) sever HMD and the majority of cases have moderate to sever Hyaline membrane disease 39 (32.5%) whereas very sever HMD were observed in 32 (nearly 27%) all these finding were seen in Fig. 6.

Complications in 76 cases out of 120 which represent 63.3% whereas 44 cases (nearly 37 %) no complications with HMD. The most prevalent complications were Pneumothorax, intra ventricular hemorrhage and neonatal sepsis which represent approximately 19%, 15% & 14.2 % respectively as shown in Table 4.

12 cases preeclampsia and 2 cases diagnosis as essential hypertension were the most co-morbidities of mothers and 62 (51.6%) not associated no diseases during pregnancy in mothers this was observed in Table 5.

According to Table 4, complications present in 76 cases out of 120 which represent 63.3% whereas 44 cases (nearly 37 %), no complications with HMD Pearson chi- square =98.48, df= 2, p value = .000 exhibited highly significant of female gender with complications of HMD.

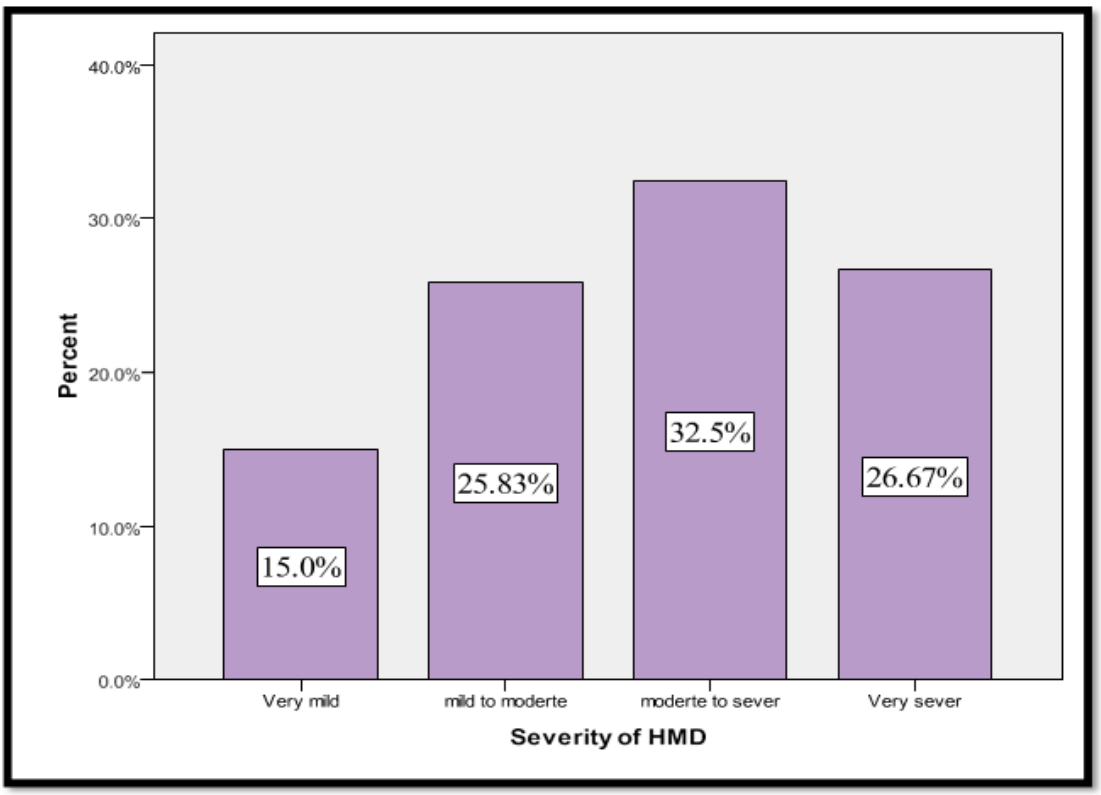

Fig. 6. Distribution of newborns of hyaline membrane disease (HMD) according to severity of disease 2017-2018 (N= 120)

Table 4. The complications of respiratory distress syndrome neonates

Complications of Hyaline membrane disease	Associated co-morbidities	Frequency.	%
	Pneumothorax	19	15.8
	Congenital pneumonia	5	4.2
	Neonatal sepsis	17	14.2
	Intra ventricular haemorrhage(IVH)	18	15
	Congenital heart diseases		
	Patent ducts arthrosis (PDA)	6	5
	Bronco pulmonary displasia	10	8.3
	Necrotizing enterocolitis (NEC)	1	0.8
	Total	76	63.3

Table 5. Distribution of maternal characteristics at Benghazi medical center 2017-2018

Maternal morbidities	Yes			No morbidities	
	No.		%	No.	%
Preeclampsia Hypertension	14		12	106	88
Diabetes mellitus	6		5	114	95
Hypothyroidism	0		0	120	100
Premature rupture of membrane (leaking)	< 18 Hours	5	4.2		
	> 18 hours	33	27.5	82	68.3
No associated diseases during pregnancy	58		48.3	62	51.6

Table 6. Cross tabulation of complications of neonates diagnosed as HMD and gender.

Gender	Complications of HMD		Total
	Yes	No	
Male	34	23	57
	59.6%	40.3%	100%
Female	42	21	63
	66.6%	33.3%	100%

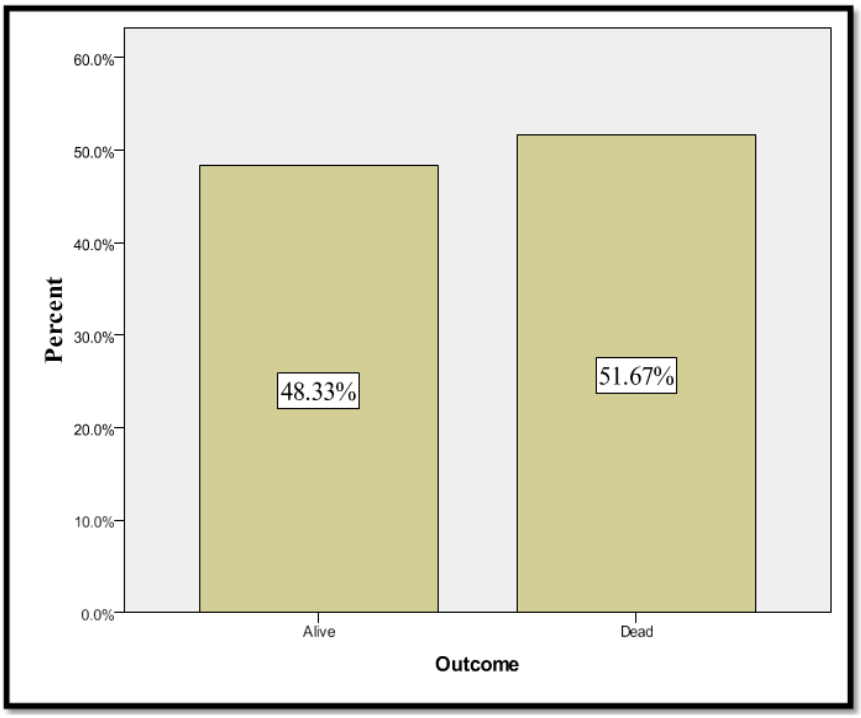

Fig. 7. Distribution of newborns of hyaline membrane disease (HMD) according to outcome (N= 120)

5. DISCUSSION

The study was conducted on 120 neonate of hyaline membrane disease were female gender was predominant and the vast majority of neonates with HMD delivered by caesarean section exhibited statistically significant, and majority newborns of hyaline membrane disease were single delivery according to Figs. 4,5.

Furthermore, in this study most of cases of HMD were between 1000 kg to 2000 kg were seen in Fig. 2, same results from other studied most of babies with HMD were low birth weight and premature [4,5].

All the cases of HMD were preterm. Gestational age 32-33 weeks were seen in 33.3% of newborn infants with HMD followed by 22.5 % of

newborn infants 30 -31 weeks and gestational age 34 weeks in 20 % of newborn infants with HMD as seen in table 2, these finding same to Indonesia study that reported the younger the gestational age, the higher possibility of an infant to suffer from HMD [5].

In our study the risk factors were history of maternal preeclampsia, maternal diabetes mellitus, prematurity and low birth weight babies and neonatal sepsis all these were found to be very common risk factors of HMD, while multiple pregnancy also is frequently associated with HMD. Also we concluded that the cases had leaking (premature rupture of membrane), was identified as risk factors of hyaline membrane disease.

From literature there are many causes of infant mortality, so among very low birth weight infants, the greatest lethal risk is extreme prematurity Sepsis hyaline membrane diseases [5].

Kathleen study in 2005 reported sepsis, especially during the first five days of life and in low and middle-income countries (28). The neonatal mortality rate was significantly higher with E coli sepsis, compared with group B Streptococcus (GBS) sepsis. E coli sepsis occurred in a more premature patient population in comparison to GBS and was associated with higher morbidity and mortality rates [28,29].

According to the results of this study highly significant of female gender with complications of HMD, such as Pneumothorax, bronco pulmonary, dysplasia, intra ventricular hemorrhage (IVH) and congenital heart diseases (patent ducts arterosis) were common co-morbidities with respiratory distress syndrome, all these could be have an association with the development of hyaline membrane disease, finally we observed more than half of babies were died this is a warning sign for health services. These results are similar to the data reported by Sudigdo in Indonesia study that confirmed poor health services such as antenatal care and maternal illness causing chronic fetal distress [5].

Regarding management in this study, all cases received oxygen whereas mechanical ventilation in 85% of babies, mechanical ventilation in more than half of newborns babies. Among 120 cases the majority of cases have moderate –to sever hyaline membrane disease, followed by very sever HMD this finding were seen in Fig. 6.

From literature originating from European Consensus Guidelines on the management of RDS surfactant therapy reported that surfactant therapy plays an essential role in management of RDS as it reduces Pneumothorax and improves survival (23)' also nearly less than half of cases were treated with surfactant More than half of newborns babies with HMD not received surfactant.

According to recent Indian experience 2016 treatment modalities for HMD include oxygen therapy, Continuous Positive Airway Pressure (CPAP), surfactant therapy and mechanical ventilation and most babies can be successfully managed with non-invasive therapy like nasal cannula oxygen and CPAP, mechanical ventilation is required for severe RDS [1].

Assisted ventilation in neonates for hyaline membrane disease neonates in our study was used as shown in table 3, whereas, a previous study conducted by Meharban in New Delhi, which aimed to study the outcome and complications of assisted ventilation in neonates with hyaline membrane disease of seventy five premature neonates with HMD needing assisted ventilation born over a period of five years, the main outcome measures was survival rate among those ventilated and complications of assisted Ventilation the study, concluded that outcome of neonates needing assisted ventilation for HMD has shown consistent improvement over the period of study. Nosocomial infections continue to be a major complication of assisted ventilation in neonates [30].

The complications of respiratory distress syndrome in neonates, the most prevalent complications were Pneumothorax then intra-ventricular hemorrhage followed by neonatal sepsis as shown in Table 4.

According to a previous study, the researchers found that ventilated who required mechanical ventilation for HMD survival rate increases Survival improved with increasing gestational age and birth weight. Sepsis, DIC and pulmonary hemorrhage were significantly associated with a poor outcome and septicemia was the commonest cause of mortality [1].

In this study Pearson chi-square test p value highly significant of female gender with complications of HMD. Outcome newborns of hyaline membrane disease were dead in more

than half of the sample (52%), Bulgaria study in 2018 mentioned the goal of effective corticosteroid prophylaxis is to reduce mortality, reduce complications in prenatal new-born babies same results in this study in which Dexamethasone was used [25].

Our study showed that around 20% of cases of HMD were died, this is a warning sign for health services many studies have shown poor outcomes in neonates in developing countries such as Indian study [1].

In this study we record newborns babies with HMD not received steroids in (45%), this could lead to death of neonates while, Jamie study reported long-term prognosis survival of infants who have RDS has improved greatly with the use of antenatal steroids. Preliminary data in infants treated with antenatal steroids suggest the possibility of less neuro -developmental delay [13]. Antenatal steroids and prolonged rupture of membranes decrease the risk of RDS [31].

Some of this study results confirmed previous results, and some were not in accordance. From Sudigdo study for risk factors for the development of Hyaline Membrane Disease in Preterm Infants, was proven that maternal morbidity, antepartum bleeding, delivery method, gender, gestational age, birth weight and the first minute Apgar score had a significant association with the incidence of HMD. On the other hand, maternal age, use of contraceptive, passive cigarette smoking, and the duration of fetal membrane rupture had no significant association with the incidence of HMD [5]. Outcome of admitted neonates in Indian study by Iyer et al, (2017) showed, third quarter of cases were discharged after improvement, death due to respiratory distress syndrome was common in preterm and male neonates [3].

Furthermore, maternal age has been known as one of the risk factors in HMD incidence, from both univariate and multivariate analysis no significant association was found between maternal age and incidence of HMD. Maternal age has been an association with premature delivery, but does not any association with the incidence of HMD in preterm infants [5].

6. CONCLUSION

From the results female gender was predominant, also we found that both maternal and neonatal factors had contributed to the risk of hyaline membrane disease. The vast majority of neonates with HMD delivered by caesarean section exhibited statistically significant. The risk factors were history of maternal preeclampsia, maternal diabetes mellitus, prematurity and low birth weight babies and neonatal sepsis all these were found to be very common risk factors of HMD, while multiple pregnancy also is frequently associated with HMD. Also we concluded that the cases had leaking (premature rupture of membrane), was identified as risk factors of hyaline membrane disease.

Furthermore, we concluded that highly significant of female gender with complications of HMD, such as Pneumothorax, bronco pulmonary, dysplasia, intra ventricular hemorrhage (IVH) and congenital heart diseases (patent ducts arterosis) were common co- morbidities with respiratory distress syndrome, all these could be have an association with the development of hyaline membrane disease, finally we observed more than half of babies were died this is a warning sign for health services.

7. LIMITATION OF THE STUDY

This study has some limitations, the results might lack of generalizability the reason due to the study was conducted in short period of time between 2017- 2018 and small sample size. The design of the study was an observational descriptive case series could not allow for establishing relation between the risk factors associated with HMD and morbidity and mortality. Therefore, a thorough follow-up of patients with HMD by cohort study.

8. RECOMMENDATION

It is therefore recommended to have more skilled health personnel and advanced equipment while providing maternal and neonatal health care services; including ,mange the pregnant mothers well such as preeclampsia, diabetes mellitus and premature rupture of membrane to the recommended antenatal schedule and take prompt action in seeking medical help during pregnancy to avoid development of sepsis after delivery and provision of community health education would encourage pregnant women to abide to obstetric emergencies.

Health care providers should adhere to aseptic precautions while performing invasive procedures. We recommend future research is needed to verify these finding for a large size sample.

CONSENT

It is not applicable.

ETHICAL APPROVAL

After formal approval taking from the authority providing Hospital (Benghazi medical center) Confidentiality of data was guaranteed.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Prabha NPC, Pillai SKS, Rahman JMI. Outcome of ventilation in hyaline membrane disease: the Indian experience. J. Evolution Med. Dent. Sci. 2016;5 (52):3378-3381.
   DOI: 10.14260/jemds/2016/780.
2. Amorim Melo ERA, de Barros Lima Filho A, Furtado Ferreira AC, de Sousa Carvalho G, da Conceição Brito JJ, et al. Prevalence of Meningitis in Patients with Late Neonatal Sepsis in a Reference Maternity. Ann Pediatr Child Health. 2018;6(3):1148.
3. Chandrakala R. Iyer, Naveen G, Suma HR, Kumarguru BN, Swetha K, Janakiraman. Clinical profile and outcome of neonates with suspected sepsis form a rural medical college hospital of South India. International Journal of Contemporary Pediatrics *Iyer* CR et al. Int J Contemp Pediatr. 2018;5(1):55-60.
   Available:http://www.ijpediatrics.com
4. Million Wesenu, Sudhir Kulkarni,Tafere Tilahun. Modeling Determinants of Time-To-Death in Premature Infants Admitted to Neonatal Intensive Care Unit in Jimma University Specialized Hospital Ann. Data. Sci. 2017;4(3):361–381.
5. Sudigdo Sastroasmoro. Risk Factors for the Development of Hyaline Membrane Disease in Preterm Infants. Paediatric Indonesia J. 1998;38:243-254.
6. WHO, Unicef, World Bank Group & united Nation. Report 2019. Levels & Trends in Child Mortality. Estimates developed by the UN Inter-agency Group for Child Mortality Estimation.
7. Bashir M. Ashour, Anwar Gassier, Yosef Shami, Jalal A. Bilal &, Ishag Adam. Neonatal out come in Misurata central Hospital – Libya. Journal of Science. 2014;4(2):87-89.
8. Berhe Weldearegawi, Yohannes Adama Melaku, Semaw Ferede Abera, Yemane Ashebir, Fisaha Haile, Afework Mulugeta et al. infant mortality and causes of infant deaths in rural Ethiopia: a population-based cohort of 3684 births. BMC Public Health. 2015;15(Article no. 770).
9. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet. 2008;371:75–84.
10. National Heart, Lung, and Blood Institute Web site. What is respiratory distress syndrome? Accessed January 21, 2010. Available:http://www.nhlbi.nih.gov/health/dci/Diseases/rds/rds_all.html.
11. Robertson PA, Sniderman SH, Laros RK Jr, Cowan R, Heilbron D, Goldenberg RL, Iams JD, Creasy RK. Neonatal morbidity according to gestational age and birth weight from five tertiary care centers in the United States, 1983 through 1986. Am J Obstet Gynecol. 1992;166:1629 – 1641.
12. Angus DC, Linde-Zwirble WT, Clermont G, Griffin MF, Clark RH. Epidemiology of neonatal respiratory failure in the United States: projections from California and New York. Am J Respir Crit Care Med. 2001; 164:1154–1160.
13. Jamie B. Warren& Jo Dee M. Anderson, Core Concepts: Respiratory Distress Syndrome Neo Reviews. 2009;10 (7):351-361.
14. Halliday HL. Surfactants: past, present and future. J Perinatol. 2008;28:S47–S56.
15. Nkadi PO, Merritt TA, Pillers DA. An overview of pulmonary surfactant in the neonate: genetics, metabolism, and the role of surfactant in health and disease. Mol Genet Metab. 2009;97:95–101.
16. UCSF Children's Hospital .Intensive Care Nursery House Staff Manual. Respiratory distress syndrome. The Regent of the University of California. 2004;Chapter 9:79-84.
17. Melchor Sánchez-Mendiola,a Octavio C. Martínez-Natera, Nazarea Herrera-Maldonado,c Jesús Ortega-Arroyoc Estudio controlado del tratamiento de la enfermedad de membrana hialina del recién nacido pretérmino con surfactante pulmonary exógeno (porcino *vs.* bovino Gac Méd Méx. 2005;141(4)
    Available: (www.anmm.org.mx).

18. Advanced Neonatal Care Clinical & Therapeutic guideline. Available:https:/ /ftp.ocg.msf.org/data/public/2b1f7b.php Version – Janvier 2015: 97-100
19. Orna Flidel-Rimon, Eric S. Shinwell. Respiratory Distress in the Term and Near-term Infant. Neo Reviews. 2005;6(6):290-289. Available:http://neoreviews.aappublications.org/ at McMaster University on July 27, 2012.
20. Steven W Ryan, Nicholas J Wild, Rosemary J Arthur, Ben N J Shaw. Prediction of chronic neonatal lung disease in very low birth weight neonates using clinical and radiological variables. Archives of Disease in Childhood. 1994;71 :F36-F39. Available:http://fn.bmj.com/ on June 22, 2017 - Published by group.bmj.com
21. Reynolds E 0 R. Proc. r-oy. Soc. Med Journal. 1974;67:10.
22. Robert M. Kliegman**.** Respiratory distress syndrome. Nelson Textbook of pediatric. 20 th ed. Published by Elsevier. 2016;528-231.
23. David G. Sweet, Virgilio Carnielli, Gorm Greisen , Mikko Hallman Eren Ozek, Arjan te Pas *et al.* European Consensus Guidelines on the Management of Respiratory Distress Syndrome – 2019 Update Neonatology. 2019;115:432–450. Available: www.karger.com/neo
24. Clare A. Berry, Béla Suki, Graeme R. Polglase and J. Jane Pillow Variable ventilation enhances ventilation without exacerbating injury in preterm lambs with respiratory distress syndrome. Pediatric Research. 2012;72(4):384-391.
25. Anna Mihaylova, Stanislav Gueorguiev, Nikoleta Parahuleva, Emilia Karaslavova, Milena Sandeva, Elina Petkova-Gueorguieva *et al.* Frequency of hyaline membrane disease in preterm infants after prenatal coid prophylaxis Biomedical Research . 2018;29(6):1115-1119.
26. Ceane Cunha Rios Lessa, Fernando Lamy Filho, Zeni Carvalho Lamy Antônio Augusto Moura da Silva, Maria Elizabeth Lopes Moreira Maria Auxiliadora de Souza Mendes Gomes. Prevalence and factors associated with surfactant use in Brazilian Neonatal Intensive Care Units: A multilevel analysis Ciência & Saúde Coletiva. 2018;23(9):3067-3076.
27. Joan Crane & St. John's. Antenatal corticosteroids therapy for fetal maturation. Journal obtet Gynaecol Can. 2003;25 (1):45-8.
28. Kathleen Mayor-Lynn, Vı´ctor Hugo Gonza´lez-Quintero, Mary Jo O'Sullivan, Alan I. Hartstein &Sonia Roger & Madeline Tamayo. Comparison of early-onset neonatal sepsis caused by Escherichia coli and group B Streptococcus. American Journal of Obstetrics and Gynecology. 2005;192:1437–9. Available: www.ajog.org
29. Foad Al Magri, Abdellatif Amnaina, Omar El Shourbagy, and Yakut El Senosy, Neonatal Sepsis in Derna, Libya. Sebha MJ. 2009;8(2):63-68.
30. Meharban Singh, Ashok K. Deorari, Rajiv Aggarwal & Vinod K. Paul. Assisted ventilation for hyaline membrane disease. India Institute of Medical Sciences, New Delhi. Department of Pediatrics. 1995; 1268 -1274.
31. Stevens TP, Sinkin RA. Surfactant replacement therapy. Chest.2007;131: 1577–1582.

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