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Review Article

### RESPIRATORY DISTRESS IN NEONATES

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**Abstract:**

**Introduction:** Respiratory distress is considered a very common in the early neonatal stages. The incidence is estimated to be more than seven percent of newborn infants. There have been many studies conducted that focused on respiratory distress syndrome and chronic lung disease of prematurity in preterm infants however every year a marked number of term-born infants are admitted to neonatal units for treatment of their respiratory distress. Many clinical conditions could lead to respiratory distress in term newborn infants. Clinical conditions like surfactant protein deficiency syndromes or alveolar capillary dysplasia are seldom and there have been many reviews on them. A study showed that a trending in the incidence of respiratory distress of all neonates admitted to neonatal units between 1974 and 2004 relating three possible explanations: an increase in extremely low birth weight infants, modifications in admission guidelines and higher numbers of infants delivered by caesarean section. The effect of elective caesarean sections has particularly grew the incidence of respiratory distress in term infants. This has been established for several years. A study estimated that more than two thousand patients are diagnosed per year that needed neonatal admission for pulmonary diseases following caesarean section prior to the onset of labor in the UK alone. There were 706,248 live births in England and Wales in 2009 and approximately more than ninety percent of these were full term deliveries. Between 1990 and 2002, it is estimated that the admission rate to a busy neonatal unit in England was more than eight percent of all live births. The most common reason for admission was respiratory distress. There is an obvious inverse relationship between gestational age and incidence of respiratory distress most notably by transient tachypnoea of the newborn (TTN) and respiratory distress syndrome (RDS).

**Aim of work:** In this review, we will discuss the most recent evidence regarding respiratory distress syndrome in neonates.

**Methodology:** We did a systematic search for respiratory distress syndrome in neonates using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

**Conclusions:** We summarized the most common causes of respiratory distress in term infants. TTN and RDS are considered very common particularly in infants delivered after elective caesarean sections however, they have good prognosis. Even delivery at 37 weeks gestation, is linked with higher respiratory morbidity so should be avoided wherever possible. Clinical conditions like pulmonary arterial hypertension that could be primary or secondary to RDS, MAS or CDH will respond in most cases to oxygen therapy, mechanical ventilation including high frequency ventilation, inhaled nitric oxide or inotropes but ECMO should be considered if the respiratory failure does not respond to maximum medical therapy. The early recognition and initiation of appropriate management is important to ensure the optimal outcome for all infants presenting with respiratory distress.

**Key words:** Respiratory Distress Syndrome, Neonates, Presentation, Management.

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**INTRODUCTION:**

Respiratory distress is considered a very common in the early neonatal stages. The incidence is estimated to be more than seven percent of newborn infants. [1] There have been many studies conducted that focused on respiratory distress syndrome and chronic lung disease of prematurity in preterm infants [2] however every year a marked number of term-born infants are admitted to neonatal units for treatment of their respiratory distress. [3]

Many clinical conditions could lead to respiratory distress in term newborn infants. Clinical conditions like surfactant protein deficiency syndromes or alveolar capillary dysplasia are seldom and there have been many reviews on them. A study showed that a trending in the incidence of respiratory distress of all neonates admitted to neonatal units between 1974 and 2004 relating three possible explanations: an increase in extremely low birth weight infants, modifications in admission guidelines and higher numbers of infants delivered by caesarean section. [4] The effect of elective caesarean sections has particularly grown the incidence of respiratory distress in term infants. This has been established for several years. A study estimated that more than two thousand patients are diagnosed per year that needed neonatal admission for pulmonary diseases following caesarean section prior to the onset of labor in the UK alone. There were 706,248 live births in England and Wales in 2009 and approximately more than ninety percent of these were full term deliveries. Between 1990 and 2002, it is estimated that the admission rate to a busy neonatal unit in England was more than eight percent of all live births. The most common reason for admission was respiratory distress. There is an obvious inverse relationship between gestational age and incidence of respiratory distress most notably by transient tachypnoea of the newborn (TTN) and respiratory distress syndrome (RDS). [5] Another study also found that a major risk factor for severe respiratory distress in term infants was elective caesarean section at 37–38 weeks

gestation however with meconium stained liquor being most often found at 39–41 weeks gestation. So, avoiding routine elective caesarean sections prior to 38 weeks of gestation would markedly decrease the incidence of respiratory problems in the term infant.

In this review, we will discuss the most recent evidence regarding respiratory distress syndrome in neonates.

**METHODOLOGY:**

We did a systematic search for respiratory distress syndrome in neonates using PubMed search engine (<http://www.ncbi.nlm.nih.gov/>) and Google Scholar search engine (<https://scholar.google.com>). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: respiratory distress syndrome, neonates, presentation, management.

**ASSESSMENT:**

Respiratory distress can be diagnosed as any signs of breathing difficulties in the neonate. Helpful history taking can lead to accurate diagnosis. The best way to start the assessment of any infant with respiratory distress is to order blood tests (full blood count, C reactive protein, blood culture and blood gases), pulse oximetry and chest radiography. The early management's goals are to reverse the hypoxia, hypercapnia and acidosis that may have progressed.

**TRANSIENT TACHYPNOEA OF THE NEWBORN:**

TTN was initially referred by by Avery in 1966 and is now known as the most common cause of respiratory distress in newborn term infants. It is due to the delay in the absorption of fluid in the lungs after birth. So, TTN is often noticed in new born after elective caesarean section. It often presents with grunting and mild signs of respiratory distress, which can last for up to 2 days and is considered a self-limiting disorder. But, some infants progress to

develop an oxygen requirement that lead to admission to the neonatal unit for a couple of days accounting for about more than ten percent of all newborn term admissions. [6]

### Pathophysiology

The lungs in utero secrete fluid to aid lung growth and development in a constant fashion. But the rate of lung fluid production and volume of fetal lung lumen lowers before birth, remarkably during labor. [7] The mechanism for fluid absorption starts by neuroendocrine hormones, which can cause lymphatic vessel dilatation. As the lung pulmonary circulation increases after the first breath, the fluid in the lungs is cleared thus interruption of this process of clearing fluid from the lungs could lead in respiratory distress.

### Risk factors

The most common risk factor for TTN is delivery after elective caesarean section. The usual mechanisms to clear fluid, which happen following the beginning of labor, are not activated after elective caesarean section so there is usually insufficient clearance of pulmonary fluid, which could lead to TTN. [8] Other known risk factors involve delivery prior to 38 weeks of gestation, male sex, low birth weight and macrosomia and maternal diseases like gestational diabetes and asthma. [9]

### Prevention

The Burgundy Perinatal Network has concluded that the incidence of TTN that need ventilation is markedly decreased for each extra week in utero. A new multicenter pragmatic randomized trial concluded that administration of antenatal steroids before elective caesarean delivery at 37–39 weeks' gestation reduces the incidence of TTN. [10]

### Management

It is highly critical to establish the diagnosis by taking a thorough history and performing a physical examination. TTN usually presents within the first few hours of life and is frequently treated conservatively involving RDS and pneumonia which could progress rapidly in newborn infants. Chest radiographs often show “a wet silhouette” around the heart with fluid in the horizontal fissures. [11] Some infants might need oxygen therapy or other forms of respiratory support for several days to aid recovery. Antibiotics are usually routinely used.

### Prognosis

Infants who progress to TTN usually recover fully and are nursed in air within a few days of delivery.

but, TTN could be linked with development of asthma later in childhood, particularly in males. [12] Adams & Doull discuss the association of birth by caesarean section and asthma.

### RESPIRATORY DISTRESS SYNDROME:

RDS is believed to be caused by a deficiency of surfactant and is often also called hyaline membrane disease, which is considered a histological diagnosis. Newborn infants with RDS often present during the first four hours of life. It is often seen in preterm infants; but researches have concluded that infants with a birth weight of >2500 g account for 9.9% to 11.5% of infants with RDS and those with gestational age of <37 weeks gestation account for 7.8%.

### Pathophysiology

It is extremely challenging to differentiate between RDS and TTN, particularly in newborn term infants. It has been proposed that both these clinical conditions are part of one spectrum of respiratory disease that occur during adapting to postnatal life at birth. The production of surfactant by type 2 pneumocytes commences around 24–25 weeks gestation reaching adequate levels to support breathing after birth by 36–37 weeks gestation. [13]

### Risk factors

The risk of RDS grows inversely with decreasing gestational age so the most common patients at-risk group are preterm infants. Dani et al. showed that gestational age, low birthweight, maternal age, elective and emergency caesarean section and male sex are all risk factors for RDS.

### Prevention

A guideline recently reported that the risk of RDS declines with each week of gestation until 38 weeks, even at the relatively mature age of 37 weeks gestation, the chances of developing RDS were 3 fold greater than at 39–40 weeks gestation. The use of antenatal corticosteroids to improve fetal lung surfactant and antioxidant enzyme production is now given routinely in threatened preterm labor between 24- and 34-weeks' gestation and is occasionally considered at 35–36 weeks gestation. [14]

### Management

The preliminary treatment will go along with the standard method of taking the history and performing the physical examination. The requirement for respiratory support will need to be assessed from clinical observations, chest radiographs and blood gas results. The chest radiograph in RDS often reveal air

bronchograms and reticulonodular shadowing throughout the lung fields. In several neonatal units there are well-established guidelines for the treatment of RDS in newborn infants, involving the use of exogenous surfactant. Newborn infants produce their own surfactant very quickly, so that the respiratory distress usually resolves completely in untreated infants after 72 – 96 hours of age. The management of infants with RDS is hugely supportive until enough surfactant synthesis starts. The occasional unresponsive infant should be examined further to exclude rare clinical conditions such as alveolar capillary dysplasia and genetic abnormalities of the surfactant system.

### Prognosis

Engle et al. examined the outcome of infants given surfactant for RDS and found that ‘the risk of respiratory abnormalities later in infancy and early childhood continues to be high for preterm infants with respiratory distress syndrome’. [15]

### MECONIUM ASPIRATION SYNDROME:

The passage of meconium in utero leads to meconium-stained amniotic fluid (MSAF), which could be inhaled by the fetus particularly if the infant is compromised. If the infant has symptoms from the inhalation the clinical condition is usually referred to as meconium aspiration syndrome (MAS). MAS is a disease of term and post-term born infants but an infective etiology particularly from *Listeria* should be suspected in preterm deliveries associated with MSAF. MAS can lead to respiratory distress of different severity immediately after birth. MSAF is found in five to thirty percent of term and post-term deliveries of which two to ten percent will develop MAS. Pulmonary hypertension commonly presents in severe cases and should be aggressively treated.

### Pathophysiology

MSAF seems to occur in utero because of fetal hypoxia from fetal distress. The passage of meconium prior to 37 weeks is considered uncommon thus MAS is hugely confined to term and post-term deliveries. [16] The inhaled meconium can lead to mechanical obstruction of the airways leading to mismatched ventilation/ perfusion; chemical pneumonitis and infection which inhibit surfactant function and leads to inflammation and swelling, which also can block small airways.

The respiratory distress observed at birth from inhaled meconium is mostly to be due to the mechanical obstruction; but the distress that develops after a few hours of life is likely to be secondary to

chemical pneumonitis and infection. The combination of ventilation/perfusion mismatch and pulmonary inflammatory can lead to vasoconstriction of the pulmonary vasculature leading to pulmonary hypertension.

### Risk factors

Risk factors involve higher MSAF density, post-term gestational age, fetal distress, male sex, Apgar score of less than seven and oligohydramnios. [17] The Australian and New Zealand Neonatal Network have shown that fetal distress and low Apgar scores can elevate the risk of MAS. [18] There is also an apparent relationship between maternal ethnicity and the risk of developing MAS with black Americans and Africans being at highest risk.

### Prevention

A study concluded a marked decrease in the incidence of perinatal asphyxia and improved Apgar scores at one minute following the introduction of neonatal resuscitation programs for labor ward staff. decreasing post-term deliveries has also been shown to decrease the incidence of MAS.

### Management

It is considered a very common practice to perform ‘meconium observations’ for between 12 to 24 hours on all new born after MSAF. [19] Any signs of respiratory distress in these infants can indicate the early development of MAS and requires urgent assessment. Most cases of MAS will recover within 2–3 days and only require supportive therapy. But some infants will progress to develop severe MAS requiring intubation and ventilation.

The early chest radiograph is usually similar to the findings linked with pneumonia with bilateral patchy infiltrates and possible pleural effusion. Distinguishing MAS from pneumonia can be difficult thus antibiotics are usually prescribed either as treatment or as prophylaxis to prevent progression to infection. Available management options for MAS, depending upon the severity, including conventional or high frequency oscillatory ventilation, surfactant.

### Prognosis

The incidence of MAS remains to decline greatly because of improved obstetric care. Moreover, mortality has decreased significantly but few studies have concluded long term outcomes although there is some evidence of lasting neurodevelopmental abnormalities and persisting respiratory abnormalities. [18]

### CONCLUSIONS:

We summarized the most common causes of

respiratory distress in term infants. TTN and RDS are considered very common particularly in infants delivered after elective caesarean sections however, they have good prognosis. Even delivery at 37 weeks gestation, is linked with higher respiratory morbidity so should be avoided wherever possible. Clinical conditions like pulmonary arterial hypertension that could be primary or secondary to RDS, MAS or CDH will respond in most cases to oxygen therapy, mechanical ventilation including high frequency ventilation, inhaled nitric oxide or inotropes but ECMO should be considered if the respiratory failure does not respond to maximum medical therapy. The early recognition and initiation of appropriate management is important to ensure the optimal outcome for all infants presenting with respiratory distress

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