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Incidence of Respiratory Distress Syndrome and Its Associated Factors Among Preterm Neonates: Study From West Java Tertiary Hospital

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Abstract

Respiratory distress syndrome (RDS) or hyaline membrane disease is the most frequent cause of respiratory failure and mortality in preterm infants. As a result, many infants are brought to a neonatal intensive care unit (NICU). There may also be other factors that affect the incidence rate of RDS as well. Our research goals are to find out the incidence rate of RDS among three preterm groups and its related factors. In a cross-sectional-descriptive analytical study, newborn data was gathered and assessed by using hospital medical records. One hundred forty-two preterm infants with gestational age ≤ 36 weeks were hospitalized in the NICU. All participants were divided into three groups: extremely preterm (< 28 weeks), very preterm (28 to < 32 weeks), and moderate-to-late preterm (32 to 36 weeks). The frequency of RDS and some related factors were compared among three groups. Finally, we analyzed the relationship between variables by SPSS statistics software version 19. The level of significance was considered P< 0.05. Respiratory distress syndrome was observed in 64.68% of all participants; RDS is more common in infants within 28-32 weeks of gestation (81%), while infants with < 28 weeks of gestation and 33-36 weeks of gestation have lower rates (50% and 52 Our study shows a positive correlation between birthweight and RDS as well as between birthweight and gestational age. (P value: 0.001, 0.003). Infants between 28 to 32 gestational age have a higher risk of RDS. The risk of RDS also increases in low birth weight and male infants.

Keywords: Respiratory distress syndrome (RDS), preterm infants, neonatal intensive care unit (NICU)

Background

Many infants are admitted to a neonatal intensive care unit (NICU) due to respiratory distress syndrome (RDS), (Liu *et al.*, 2014; Zennitaet *et al.*, 2018) also known as hyaline membrane disease, which is the most common cause of respiratory failure and death, especially in preterm infants (Luca, 2020; Stylianou-Riga, 2021). Gestational age and birth weight have an inverse connection with the incidence of RDS. There are 15-30% of preterm infants between 32-36 weeks of gestational age and 60-80% of preterm infants < 28 weeks of gestational age that has RDS, while infants > 37 weeks of gestational age rarely to get RDS.5 Additionally, RDS also occurs in 42% of deficient birthweight infants,(Roberts *et al*., 2017) and 9.9-11.5% of infants with birthweight >2500 g. (Roberts *et al*., 2017)

The developmental immaturity of the lung is the etiology of RDS, which causes the lack of pulmonary surfactant. Newborn dyspnea can occur because of pulmonary surfactant deficit, which increases the alveolar wall surface tension and lowers pulmonary compliance (Wang *et al* ., 2020). To improve the infant's chances of survival, respiratory support and surfactant replacement therapy are required (Course and Chakraboty, 2020). Most infants with RDS recover with surfactant and nasal continuous positive air pressure treatment without any long-term effect. To lower the risk of RDS, antenatal corticosteroids (ACS)

can also be administered between 24 and 34 weeks of gestation(Christian *et al* ., 2015).

The risk of getting a life-threatening disease is great during the neonatal period. The most common cause of infants' morbidity and mortality is a respiratory disease. One of the studies shows that RDS is the most common respiratory disease and premature labor is the most common risk factor for RDS (Abdel *et al* ., 2020) This study is created primarily to ascertain the incidence of RDS across three groups of preterm infants and the link with preterm infant-related factors.

Materials and Method

A cross-sectional, descriptive-analytical study was taken at the NICU ward of Hasan Sadikin Hospital. The research protocol was approved by the Research Ethics Board of University Pajajaran Prior to recruitment, written informed consent was obtained, and previous research has described the recruiting process. (Judistiani *et al*., 2018; Richard *et al*.,2017) The study included infants with a gestational age of 34 weeks who were admitted to the NICU due to RDS between February 1, 2018 and September 31, 2018. Exclusion criteria were missing data, congenital malformation, and RDS accompanied by other complications. All infants' charts were examined using hospital medical records, and newborn data was collected. Some checklists gathered and recorded basic information such as gender, weight, height, head circumference, and RDS history. RDS was diagnosed based on clinical symptoms and chest X-ray findings. We simultaneously examined maternal obstetric medical records to see if there was a link between RDS and preeclampsia. Based on WHO identification (Arit *et al*., 2015), all preterm subjects were divided into three groups: extremely preterm (28 weeks), very preterm (28 to 32 weeks), and moderate preterm (33 to 36 weeks). Finally, we analyzed the frequency of RDS across three groups and looked at correlations between several associated parameters. The statistical analysis was completed using SPSS version 25 software. The Chi Square and Mann-Whitney analysis were applied where applicable. The study had a power of 90% with a suggested sample size of 142. The level of significance was set at p value < 0.05.

Results

Eight preterm neonates (34 weeks) were removed from the study because of missing data, severe cardiac congenital abnormalities, RDS followed by sepsis, and meconium aspiration syndrome. Three groups of 142 preterm neonates made up the target population (extremely preterm, very preterm, and moderate preterm). Thirty-three of neonatal mothers (23.2%) had preeclampsia. All demographic data are shown in Table 1.

Discussion

Significant respiratory morbidity such as RDS affects 15% of term infants and 29% of late preterm infants admitted to the neonatal intensive care unit; this figure is even higher for infants born before 34 weeks (Arit *et al.,* 2015). It affects 0.96 to 12% of live births and accounts for approximately 20% of neonatal mortality (Raha Arit *et al.*, 2015). Respiratory distress syndrome commonly affects preterm infants, particularly those born before 34 weeks. Up to 80% of preterm infants with gestational age within 28 weeks are prone to have RDS (Kommawar Arit *et al.,* 2017).

A study by Imkerson *et al.,*. showed that infants with 34 weeks gestation age has higher incidence rate of RDS than infants with 35-36 weeks and 37-40 weeks gestation age (15.0%, 4.0%, and 0.9% respectively) (Imkerson, *et al.*, 2015) Mehrabadi *et al.,* also reported 42.7% cases of RDS occurred between 32 and 36 weeks of gestation, whereas 26.6% occurred <32 week, 15.3% occurred between 37 and 38 weeks, and 15.3% occurred ≥39 weeks (Mehrabadi *et al.,* 2016). In this study, between the three groups, there is a significant relation between RDS and gestational age statistically. It is shown that RDS is more common in infants within 28-32 weeks of gestation (81%) while infants with <28 weeks of gestation and 33-36 weeks of gestation have lower rates (50% and 52%).

Premature infants are born at the late saccular stage of development, when the surfactant and antioxidant systems are still developing. Immature lung with surfactant deficiency, poor defense mechanism against infections and poor respiratory center maturity are some of the reasons to develop various complications of prematurity like RDS, sepsis and birth asphyxia amongst the preterm babies (Chalsei *et al.,* 2015). Immature lung structure may be associated with delayed intrapulmonary fluid absorption, inefficient surfactant absorption, and gas exchange. Moreover, the fetus begins to develop synchrony and control over breathing during the last six weeks of gestation, so that preterm delivery increases the risk of apnea, as well as RDS.This study suggests that infants within 28-32 weeks are more likely to get RDS (Mahoney *et al.*, 2013).

Table 1. Demographic Characteristic

Variables	n (%)
Sex	
Male	75 (52.8)
Female	67 (47.2)
Weight	
<1000	5 (3.5)
1000-1500	50 (35.2)
>1500	87 (61.3)
G/age	
<28 week	2 (1.4)
28-32 week	63 (44.4)
33-36 week	77 (54.2)
Complications during Pregnancy and Delivery	
No Complication	46 (32.4)
Antepartum/Intrapartum Hemorrhage	15 (10.6)
Preeclampsia	33 (23.2)
Eclampsia	9 (6.3)
Fetal distress	15 (10.6)
Others	24 (16.9)
Antenatal Corticosteroid intake	
No antenatal corticosteroid intake	100 (70.4)
Incomplete corticosteroid intake (<4x)	38 (26.8)
Complete corticosteroid intake (>4x)	4 (2.8)

Table 2. Comparison of factors between 3 gestational age group

Age	Weight mean ± SD (g)	HC mean ± SD (cm)	Length mean ± SD (cm)	RDS n (%)	Duration of hospitalization mean ± SD (day)
<28 week	1600 ± 424.64	28.50 ± 0.71	41.50 ± 4.95	1/2 (50)	13.50 ± 2.12
28-32 week	1377 ± 258.75	28.79 ± 2.08	40.56 ± 3.58	17/21 (81)	21.25 ± 15.62
33-36 week	1854 ± 291.61	29.71 ± 3.14	41.79 ± 3.41	40/77 (52)	13.05 ± 11.84
P value	0.003*	0.168	0.065	0.001*	0.010*

HC: head circumference

Table 3. Correlation of RDS related factors

RDS	Sex	Birth weight	Antenatal corticosteroid Intake	Preeclampsia
P-value	0.015*	0.003*	0.286	0.641

Our study shows a positive correlation between birthweight and gestational age as well as between birthweight and RDS. Preterm infants with 28-32 weeks gestation have lower birth weight than the other groups. Small gestational age causes infants to have low birth weight. In addition, both factors cause immaturity in a lot of the organs (Cutland et al., 2017). Since preterm infants have links

to low birth weight infants, low birth weight infants may also correlate with a high risk of RDS. All infants with RDS have lower birth weight than infants without RDS (64.8%). A study by Nam *et al.,*. showed that infants with low birth weight (< 2500 gram) are more likely to get respiratory failure (Nam *et al.,* 2020).

Very preterm neonates had a longer significant difference in hospitalization period in comparison to those in other groups. Previous research has shown that preterm and late preterm babies have a higher risk ratio for acute morbidities, and these complications affect the length of NICU stay if compared with term infants (Sengupta *et al.,* 2023). Another study revealed that neonates with RDS had the longest mean length in NICU stay, and there was an association between neonatal mortality and RDS. Further to that, RDS is the leading cause of neonatal mortality. Twenty eight percent of infants born between 30-34 weeks had an acute lung disorder (Afrasiabi *et al.,* 2013).

Another intriguing topic is the role of gender in the risk of RDS. Our finding shows that sex is positively correlated with RDS. Some studies have suggested that male gender is associated with a higher risk of RDS, but it is unknown whether gender affects RDS risk consistently across gestational ages (GA) Condo *et al.,* 2017) Female fetal lung is thought to produce pulmonary surfactant earlier in gestation than male lung, most likely due to male infants' different hormonal profile. Androgens inhibit lung fibroblast secretion of fibroblast pneumocyte factor, which can delay the development of alveolar type II cells; they also inhibit surfactant release. Androgens slow fetal lung development by altering epidermal growth factor and transforming growth factor-beta signaling pathways. On the contrary, estrogens promote surfactant synthesis, such as phospholipids, lecithin, and surfactant proteins A and B, and improve fetal lung development by increasing the number of alveolar type II cells and lamellar body synthesis (Mahoney *et al.,* 2013).

Antenatal corticosteroid (ACS) is one of therapy that can be used to accelerate lung development. Additionally, after a complete course of ACS, the incidence of RDS will decrease (Gyamfi-Bannerman *et al.,* 2016) Treatment with antenatal corticosteroids is associated with a reduction in the incidence of RDS in the first 48 hours of life, as well as a reduction in the need for respiratory support and NICU admission. Gyamfi-Bannerman *et al.,* 2016. The gestational age range at which antenatal corticosteroids provide benefit has been subject to debate. Previous reviews have had difficulty demonstrating benefit at gestations less than 26 weeks and beyond 36 weeks. Previous study demonstrated a clear statistical and clinical benefit of corticosteroids on RDS from 34 weeks + 0 days gestation, but not with other primary outcomes. Thus, in very late preterm gestation women (from 35 weeks + 0 days) the use of antenatal corticosteroids needs to be considered in light of the balance of risks and benefits (Liu *et al.,* 2014; Li *et al.,* 2022).

A population-based study by Liu *et al.,* showed the benefit for completing two doses or more of ACS for preventing RDS in very low birth weight infants at gestational age between 26 and 33 weeks.[32] However, in this study, it is shown that there is no significant correlation between RDS and ACS. It is probably because many infants didn’t get a complete course of ACS.

In this cross-sectional, retrospective study, the incidence of RDS has no correlation with preeclampsia. We infer that preeclampsia mothers may have more protective factors towards RDS. The findings of the multivariate analysis confirmed this assumption, showing that maternal preeclampsia increased the risk of severe RDS but not RDS after adjustment for confounding factors (Wen *et al.,*2019). Previous studies promoted the belief that maternal preeclampsia accelerates fetal lung maturation. Some trial results also supported the enhancement of biochemical lung maturation profile by chronic in utero stress, possibly via increased fetal cortisol production (Jelin *et al.,*2010).

Several research has looked at the incidence of RDS in preterm infants, but our findings suggest that respiratory distress

from any cause may affect more than half of preterm infants with gestational age of 36 weeks. Furthermore, this report provides evidence that RDS may be associated with other important factors such as mortality, mechanical ventilation, apgar score, and mode of delivery. However, we believe that this topic should be researched further in the future. Our study has some limitations. First, the reliability of our data depends on the accuracy of the pediatrician's records. Several relevant clinical data were not available in the neonates hospital records that certainly affected our results. Second, RDS diagnoses were based on physicians' subjective interpretations of clinical and chest X-ray data, which may cause bias. For future studies, we suggest to include surfactant usage as an objective indicator of severe RDS.

Conclusion

Respiratory distress syndrome incidence rate is higher in infants with 28 to 32 gestational age. Some risk factors have an effect on RDS rate as well such as birth weight and sex. Low birth weight and male infants are more likely to have RDS. Better obstetrical care and increased awareness of RDS risk factors among mothers and fetuses, as well as adequate pregnancy and labor follow-up for early detection of risk factors and timely intervention, may improve the outcome of neonatal respiratory distress.

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