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The incidence and factors predicting survival among preterm infants with respiratory distress syndrome admitted to neonatal intensive care unit

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ABSTRACT

Introduction: Respiratory distress syndrome (RDS) or hyaline membrane disease (HMD) is the most common cause of neonatal morbidity and mortality in preterm infants. The aims of the study were to determine the incidence of RDS in preterm infants in Thailand and to identify factors predicting survival of preterm infants with RDS.

Methods: A retrospective cohort study was conducted with 820 preterm infants from January 2016 to December 2019 in the Neonatal Intensive Care Units (NICUs) of a tertiary hospital located in the north of Thailand. Data were collected from hospital medical records. The incidence of RDS was analyzed. Binary logistic regression was used to predict factors related to survival of preterm infants with RDS.

Results: The incidence of RDS in infants born at <37 weeks' gestation was 44.15% of all preterm infants. This study showed that birth weight and length of stay could significantly predict survival of preterm infants with RDS (p<0.05).

Conclusions: The current study found that the incidence remains a problem, while birth weight and length of stay predicted survival of preterm infants with RDS. These findings provide nurses and other healthcare providers with information to anticipate care required in the NICU to improve survival of preterm infants. This information can be used to plan care for the infant and to educate and support parents.

Keywords: incidence, survival, preterm infant, respiratory distress syndrome

Introduction

A primary concern of preterm infants remains a challenge as approximately 15 million are born preterm per year (WHO, 2018). Prematurity can lead to many physical health issues that contribute to morbidity and mortality in preterm infants (WHO, 2017). Around 1 million preterm infants die each year from complications such as pneumonia, sepsis, necrotizing enterocolitis, and respiratory distress syndrome (Liu et al., 2016; WHO, 2017). RDS is the most common cause of morbidity and mortality in preterm infants (Reuter,

Moser and Baack, 2014; Fraser, 2015). Moreover, RDS is the most common cause for preterm infants to be hospitalized in neonatal intensive care units for invasive or non-invasive respiratory support (Moya et al., 2019). Evidence indicates that RDS occurs in approximately 5% of near-term infants, 30% of infants less than 30 weeks of gestational age, and 60% of premature infants less than 28 weeks of gestational age (Pramanik, Rangaswamy and Gates, 2015). In Thailand, evidence indicates that the incidence of RDS occurs in approximately 50 % of preterm infants (Sangpanit et al., 2020).

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┌─────────────────────────────────────────────────────────────┐
│ Medical records of preterm infants from January 1, 2016, to  │
│ December 31, 2019 (N=1021)                                    │
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┌────────────────────────────────────────┐
│ Excluded (n=201)                        │
│  -   Congenital abnormally              │
│  -   Congenital heart disease           │
│  -   Missing data                       │
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┌──────────────────────┐
│ Included (n=820)      │
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┌────────────────────────────────┐    ┌────────────────────────────┐
│  -   TTNB (251 Cases)          │    │ RDS (362 cases)            │
│  -   Birth asphyxia (86 cases) │    │  -   Mild (116 cases)      │
│  -   Sepsis (37 cases)         │    │  -   Moderate (153 cases)  │
│  -   Pneumonia (27 cases)      │    │  -   Severe (93 cases)     │
│  -   Others (57 cases)         │    │                            │
└────────────────────────────────┘    └────────────────────────────┘
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┌──────────────────┐
│ Mortality        │
└──────────────────┘
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┌────────────────────────┐    ┌────────────────────────┐
│ Survival (299 cases)   │    │ Death (63 cases)       │
└────────────────────────┘    └────────────────────────┘
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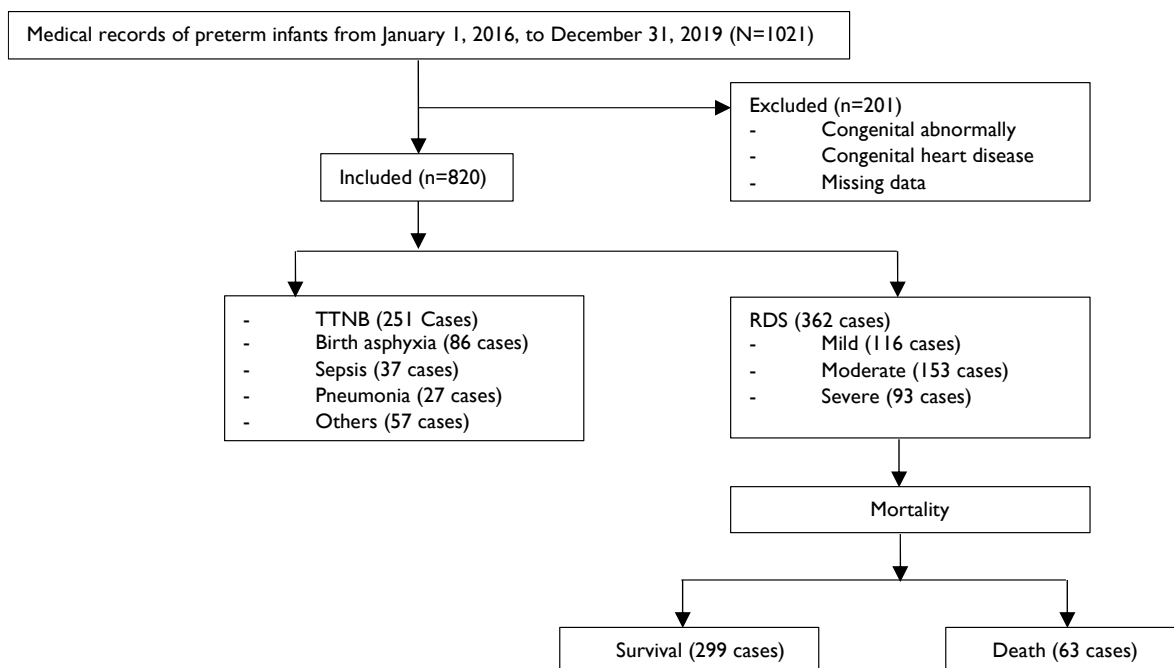
Figure 1 The flow diagram of the study

Respiratory distress syndrome (RDS), also known as hyaline membrane disease (HMD), is the most common respiratory disorder in infants (Fraser, 2015). It is caused by a deficiency of alveolar surfactants, which cover the alveolar surface, leading to atelectasis (Warren and Anderson, 2010), ventilation-perfusion inequality, and hypoventilation (Pramanik, Rangaswamy and Gates, 2015). RDS is divided into three levels; mild, moderate, and severe RDS (Qari et al., 2018). The clinical features of RDS, including dyspnea, tachypnea, nasal flaring, inspiratory stridor, grunting, and cyanosis, appear immediately after birth or within 48-72 hours (Qari et al., 2018). The administration of surfactant, a natural lipoprotein, into the alveoli may relieve an infant's respiratory distress syndrome (Donn and Sinha, 2006; Bahadue and Soll, 2012). Although this treatment improves pulmonary function, a lack of alveolar growth from immaturity can reduce the surface area for gas exchange and lead to mortality (Bahadue and Soll, 2012). According to a literature review, previous studies examined that factors of gestational age (GA), birth weight, mother's age, route of delivery (Mekasha et al., 2020), RDS level, surfactant and length of stay (Saboute et al., 2015), were associated with survival rates of preterm infants with RDS.

Although there are studies regarding prematurity and RDS from other countries, information about infants born in Thailand is scarce. Therefore, the purpose of this study was to: 1) determine the incidence of RDS in preterm infants and 2) examine factors that predict survival of preterm infants with RDS in Thailand.

Materials and Methods

This study was a retrospective cohort study of preterm infants hospitalized in the NICUs of a tertiary hospital located in the north of Thailand because there is the highest rate of preterm births in Thailand. The study was conducted in a tertiary care center which serves as a referral center for hospitals from the seven provinces located in the northern region of Thailand.

Data were collected from electronic health records. The sample consisted of preterm infants < 37 weeks gestational age, both being diagnosed as RDS and not diagnosed as RDS, who were admitted to the NICUs of the tertiary hospital for at least one day from January 1, 2016 to December 31, 2019. Preterm infants who had congenital abnormalities, congenital heart disease, and incomplete data were excluded. For preterm infants who were diagnosed with RDS, they were divided into three groups: mild, moderate, and severe RDS. RDS

Table 1 Diagnoses of all participants (N=820)

Disease	Numbers	Percent
RDS	362	44.15
Mild RDS	116	14.15
Moderate RDS	153	18.65
Severe RDS	93	11.35
TTNB	251	30.61
Birth Asphyxia (BA)	86	10.49
Sepsis	37	4.51
Pneumonia	27	3.29
Others	57	6.95
Total	820	100.00

Table 2 Correlations between factors and survival of preterm infants with RDS

Independent Variables	Survival group	Non-survival group	p - value
	Number (299)	Number (63)	
GA at birth (weeks)	(Mean=30.29, SD=2.70)	(Mean=26.28, SD=3.06)	<0.001
Less than 28	44	42	
28 - <32	149	16	
32- < 37	106	5	
Mother's age (years)	(Mean=28.15, SD=7.89)	(Mean=26.75, SD=8.33)	0.087
<20	101	29	
20 − 35	131	23	
>35	67	11	
Route of delivery			0.160
Vaginal delivery	167	40	
Cesarean section	132	23	
Birth weight (grams)	(Mean=1447.80, SD=521.03)	(Mean=867.06, SD=291.70)	<0.001
<1,000	48	48	
1,000-1,499	142	13	
≥1,500	109	2	
RDS level			<0.001
Mild RDS	113	3	
Moderate RDS	123	30	
Severe RDS	63	30	
Surfactant dose			<0.001
1 dose	268	46	
≥2 doses	31	17	
Length of stay (days)	(Mean=46.76, SD=38.22)	(Mean=20.24, SD=37.71)	<0.001
1-15	58	45	
16-30	52	8	
31-60	111	5	

severity was determined by the neonatal physicians at the target hospital. Mild RDS is defined as partial pressure of oxygen (PO_2) of 50-80 mmHg and fraction of inspired oxygen (FiO_2) of less than 0.3, while moderate RDS is defined as PO_2 of 50-80 mmHg and FiO_2 of 0.4-0.6 and requires Continuous positive airway pressure (CPAP) (Luerti et al., 1987). Severe RDS is defined as PO_2 less than 50 mmHg or PCO_2 higher than 60 mmHg with $FiO2$ at 0.4-1.0 and ventilation (Luerti et al., 1987). Data as predicting factors of this study were collected and recorded from electronic health records (EHR), including survival, gestational age (GA), mother's age, route of delivery, birth weight (BW), RDS level, surfactant dose, and length of hospital stays (LOS) of preterm infants with RDS.

The software package SPSS version 24 was used to perform the statistical analysis. The incidence of RDS in this study was calculated as the number of preterm infants with RDS divided by the total number of admitted preterm infants during the study period. Chi-square test was used to examine correlation between predicting factors and survival of preterm infants with RDS. In addition, probability of factors affecting survival of preterm infants with RDS were analyzed using multivariate logistic regression analyses. P-value less than 0.05 was considered statistically significant.

Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the university (Project No.068/2563) and the hospital (Project No.229/63). After ethical approvals were obtained, a researcher contacted the staff at the HER department of the hospital who were responsible for keeping EHRs in order to explain the objectives, and the procedure for the study, and to seek assistance with obtaining the data. The EHRs of every preterm infant who were admitted to the NICUs of the tertiary hospital for at least one day from January 1, 2016 to December 31, 2019 were reviewed by the researchers. The preterm infants' data, including the demographic data and data related to RDS, were reviewed for study variables. The preterm infants whose EHR were incomplete on study variables and had congenital abnormalities or congenital heart disease were excluded. The researchers recorded the data of all qualifying preterm infants in a specific data collection sheet in Excel program that the researchers developed and rechecked again before analyzing via SPSS program.

Results

Incidence of RDS among preterm infants

For the study, 1,021 preterm infants' charts were reviewed. Of these, 201 preterm infants were excluded from the study due to congenital heart disease, congenital anomalies, and missing data ([Figure 1]). Therefore, 820 preterm infant charts were included ([Figure 1]). Of these, 56.3% were male, 51.46% were moderate to late preterm infants (GA 32 to less than 37 weeks) and 41.22% were born with birth weight greater than 1,500 grams. For the mothers, 62.3% were between the ages of 20 and 35 years old, and 53.90% delivered vaginally.

As many as 362 out of 820 (44.15%) preterm infants were diagnosed with RDS. Other common causes of admission were transient tachypnea of the newborn (TTNB), birth asphyxia, sepsis, apnea and pneumonia ([Table 1]). Moreover, the results revealed that 45.58% of preterm infants with RDS were very preterm (GA 28-32 weeks), 42.82% had birth weight at 1,000-1500 grams. 86.7% received one dose of surfactant and 32.04% were admitted to the hospital between 31-60 days.

Factors predicting survival of preterm infants with RDS

For total number of preterm infants with RDS were 362; 299 cases (82.60%) survived, and 63 cases (17.4%) did not. The study identified significant correlation

between seven factors, including GA at birth, mother's age, route of delivery, birth weight, RDS level, surfactant dose, and length of hospital stay, and survival of preterm infants with RDS. The results showed that GA at birth, birth weight, RDS level, surfactant dose, and length of stay statistically significantly related to survival of preterm infants with RDS between the groups in terms of (p<0.05).

Discussions

In the current study, we have reviewed the incidence of RDS in preterm infants admitted to NICUs in the northern region of Thailand. The results of this study found that 44.15% of the overall preterm infants suffered from RDS, which is quite similar to a study by Caner et al. (2015) who reported an incidence rate of 40.6%. However, the incidence of RDS in this study is lower than some previous studies. Saboute et al. (2015) presented the incidence of RDS to 65.5% of preterm infants while Zhang et al. (2015) reported the incidence of RDS in 50%. Most preterm infants of the current study (45.58%) were very preterm infants (GA 28-32 weeks), which is similar to Saboute et al., (2015) and Zhang et al. (2015). In Saboute et al.'s (2015) study, 52.1% of participants were very preterm (28-32 weeks) while Zhang et al. (2015) reported the incidence of RDS in preterm infants with GA less than 30 weeks at 50%. Prematurity is a major cause of RDS. Infants whose GA is less than 37 weeks have immature lungs and surfactant deficiency, which can lead to RDS (Fraser, 2015). Premature infants who have lower GA have higher rate of RDS than ones who have higher GA (Margoushy, 2017). The findings of this study confirm that RDS can occur in preterm infants, especially those with a lower GA. Therefore, preventing preterm birth is the most important for healthcare providers and necessary approach to prevent RDS in infants.

In addition, this study found that birth weight and length of hospital stay could statistically significantly predict the survival of preterm infants with RDS from Thailand (p<0.001) (Table 3). For birth weight, preterm infants with RDS and low birth weight tend to be 20 times more likely to not survive than preterm infants with RDS and higher weight. This result is similar to a study by Intayote et al. (2019) which indicated that preterm infants with RDS who had low birth weight had a lower survival rate than those who have normal weight. The present research study is also consistent with studies by Wang et al. (2017) and Rojsanga (2018) which reported that birth weight positively affected an infant's survival. Previous studies indicated that survival

Table 3 Multivariate logistic regression of factors for survival of preterm infants with RDS

Predicting factors	Odds ratios	95%CI	p-value
Gestational age at birth	0.080	0.807-1.333	0.788
Birth weight	20.404	1.003-1.007	<0.001
Surfactant	0.182	0.379-1.864	0.669
Mild RDS	3.839	0.268-1.925	0.147
Moderate RDS	3.219	0.051-1.140	0.073
Severe RDS	3.733	0.033-1.025	0.053
Length of stay	35.516	1.031-1.061	<0.001

of infants was very low in infants less than 1000 grams (Vilanova et al., 2019; West, 2021). The findings of the present study found that the majority of the survival group (47.5%) had birth weight at 1,000-1,499 grams whereas those of the non-survival group (76.2%) had birth weight less than 1,000 grams (Table 2). This result confirms that birth weight affects survival of preterm infants. This might be possible because low birth weight preterm infants have low growth and immature organ development. This can increase complications and death (Belay et al., 2022). Therefore, birth weight of preterm infants with RDS could predict survival of preterm infants with RDS.

In addition, the findings of this study suggested that the length of stay could be 35 times more likely to significantly predict survival of preterm infants with RDS (p<0.001). The result is different from a previous study which illustrated that there was no significant relationship between LOS and survival among preterm infants with RDS (Saboute et al., 2015), but it is consistent with a study by Karunarathna (2018). The finding demonstrates that prolonged LOS can influence increased survival of preterm infants with RDS. This is likely to due to the fact that most of the non-survival group of this study died early. The data of the present study (Table 2) demonstrated that most of the non-survival group had shorter length of stays (1-15 days) and more severe RDS than the survival group whereas the majority of the survival group had longer length of stays (31-60 days) and milder and more moderate RDS than the non-survival group. Severe RDS can cause death in preterm infants at an earlier stage, especially within the first two to three weeks of birth (Patel et al., 2017; van Beek et al., 2021). This can influence short length of hospital of non-survival preterm infants. Another reason might be that the survival group might receive appropriate and timely interventions, such as surfactant therapy and continuous respiratory support. Therefore, the length of stay could be a predictor of survival of preterm infants with RDS. However, we do not have detailed data for an in-depth explanation of this result. Further studies about length of stay and

survival of preterm infants with RDS need to be conducted to clearly confirm this relationship.

This study has some limitations. Firstly, it was conducted in a single tertiary hospital. This might limit the generalization of the findings. Therefore, further studies should be conducted in multiple settings with a prospective study. In addition, there might be other factors that affect survival of preterm infants with RDS, such as prenatal factors, that are not considered in this study. Therefore, future research studies should consider these factors.

Conclusions

The results of this study have shown that RDS is frequent in preterm infants and incidence was inversely associated with gestational age. Moreover, factors predicting survival of preterm infants with RDS were birth weight and length of stay. Birth weight and length of stay can increase probability of survival of preterm infants with RDS. The findings of this study about incidence and factors predicting RDS in preterm infants may be important data for healthcare professionals in increasing awareness of RDS in preterm infant and searching appropriate care to prevent RDS in preterm infants or improve survival in preterm infants with RDS. Prevention of preterm birth is a crucial role of maternity nurses by screening, educating, and counselling pregnant women throughout pregnancy. In addition, helping preterm infants with RDS increase body weight and length of stay are roles that nurses in NICUs should consider.

Acknowledgment

Conflict of Interest

No conflict of interest has been declared by the authors.

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