Incidence, aetiology and adverse outcomes associated with respiratory distress in term neonates admitted to a tertiary care centre

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Abstract

Introduction: Respiratory distress (RD) is a leading cause of admission of all gestational ages to neonatal intensive care units. RD develops in 7% neonates and causes significant morbidity and mortality. The aetiology of RD could be respiratory and non-respiratory and the presence of some risk factors may predict the development of RD. Newborns with RD are at 2-4 times higher risk of death.

Objectives: To determine the incidence and aetiology of RD and to identify risk factors and adverse outcomes of RD in term neonates.

Method: A descriptive cross-sectional study was conducted at Sri Jayewardenepura General Hospital for a period of eighteen-months, including 105 term newborns with RD, defined by the Silverman score of more than 3. Statistical analysis was done with the SPSS beta version.

Results: The incidence of RD with Silverman score of more than 3 was 2.2%. Aetiologies of RD in decreasing order of frequency were congenital pneumonia, transient tachypnoea of the newborn (TTN), early-onset sepsis (EOS) without pneumonia, respiratory distress syndrome (RDS), meconium aspiration syndrome, persistent pulmonary hypertension of the newborn and critical congenital heart disease. There were significant associations between prolonged rupture of membranes (PROM), 3 or more vaginal examinations, congenital pneumonia and EOS. Caesarean delivery increased the risk of developing TTN and RDS. There were 4 neonatal deaths and 2 babies developed ventilator-associated pneumonia. None had chronic lung disease. Mean duration of hospital stay was 8.8 days and mean duration to establish breastfeeding was 5.1 days.

Conclusions: Incidence of RD with Silverman score more than 3 was 2.2% and the commonest aetiology was congenital pneumonia. PROM and 3 or more vaginal examinations were associated with increased risk of congenital pneumonia and EOS. Caesarean delivery had significant association with TTN. Elective caesarean section and gestational diabetes mellitus were risk factors for RDS. Mean duration of hospital stay and duration to establish breastfeeding were 8.8 and 5.1 days respectively.

(Keywords: Term neonate, Respiratory distress, Pneumonia, Transient tachypnea of newborn, Sepsis)

Introduction

Respiratory distress (RD) affects nearly 7% of neonates during the early neonatal period[1,2]. Incidence of RD is higher in low and middle-income countries accounting for 1.2% to 7.2% among term live born neonates[3]. Newborns with RD are at 2-4 times higher risk of death than babies who are unaffected and RD is a leading cause of morbidity in all gestational ages[2].

RD occurs in a variety of respiratory and non-respiratory disorders[2-6]. A study in 65 hospitals in Italy, involving 17,192 live-born term babies revealed that the incidence of common respiratory aetiologies for RD was 70% for transient tachypnoea of newborn (TTN) and 11% each for respiratory distress syndrome (RDS) and meconium aspiration syndrome (MAS)[7]. In the local setting, Gamhewage NC, *et al*[8] found TTN, congenital pneumonia, and MAS as the common aetiologies. Other respiratory causes such as spontaneous pneumothorax, persistent pulmonary hypertension of newborn (PPHN), congenital structural lung malformations, anomalies of the upper airway, and a variety of non-respiratory aetiologies should be considered as possibilities of RD[2-5].

Irrespective of the aetiology, RD in neonates is defined based on the presence of one or more of the following signs viz. tachypnoea (respiratory rate >60/min), apnoea and chest retractions (intercostal,

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subcostal, suprasternal), nasal flaring, inspiratory stridor, grunting, and cyanosis[2,6,9]. Objective assessment of the severity of RD in the early neonatal period by a scoring method is a useful tool[2,10].

Known risk factors that increase the likelihood of RD are prematurity, meconium-stained amniotic fluid (MSAF), caesarean delivery, gestational diabetes mellitus (GDM), maternal chorioamnionitis and prenatal ultrasonographic findings, such as oligohydramnios and structural lung abnormalities[1]. In term neonates, it is difficult to predict which babies develop RD. Hence, identification of risk factors and having an open mind concerning different respiratory and non-respiratory causes are of utmost importance in early intervention and escalation of the supportive care before the refractory stage to reduce morbidity and mortality[1,2].

Studies on epidemiology and morbidity of RD among term newborns are scarce[3]. Therefore, given early intervention and allocation of available resources to improve the outcome of this condition, data on this entity are of utmost importance.

Objectives

To determine the incidence, aetiology, risk factors and adverse outcomes of RD in term newborn babies admitted to a tertiary care centre.

Method

This descriptive cross-sectional study was conducted at the neonatal intensive care unit (NICU) of Sri Jayewardenepura General Hospital (SJGH) for a period of 18 months from 01/01/2019 to 30/06/2020.

Inclusion criteria: Neonates born at or more than 37 completed weeks of gestation and who presented with RD with the Silverman score of 3 or more before discharge home were included in the study. Babies with antenatally undiagnosed congenital heart diseases and surgical conditions were also included.

Exclusion criteria: Term neonates re-admitted after discharge from the hospital with RD and those who were transferred from other hospitals for ventilator support were excluded.

The severity of RD was objectively assessed using Silverman Anderson Respiratory Severity Score (SMS)[11]. SMS is a non-invasive simple tool designed by Silverman and Anderson to quantify RD in neonates based on 5 clinical signs[11]. Routinely, the severity of RD of all the babies who are admitted to NICU is assessed on admission using SMS by the admission doctor. Babies who scored more than 3 were enrolled in the study.

The aetiology of the RD was established based on the following clinical and laboratory parameters by the consultant.

- *Congenital pneumonia*: RD present within a few hours of birth accompanied by chest x-ray changes such as diffuse parenchymal infiltrates with air bronchograms or lobar consolidation[1,3,12]. This is often accompanied by elevated inflammatory markers [C-reactive protein (CRP) greater than 10mg/dL] and or positive blood culture[1,3].
- *Respiratory distress syndrome (RDS):* Neonates present within the first 4 to 6 hours of age with chest radiograph findings of diffuse fine granular infiltrates with air bronchogram[3]. Inflammatory markers and blood cultures are usually negative[1,3,4,12].
- *Transient tachypnoea of newborn (TTN):* RD occurs within the first 2 hours and usually settles within 3 days[2]. Chest radiograph shows fluid in the interlobar fissures, hyperinflation, and prominent pulmonary vascular markings[1,4,5,12]. Inflammatory markers and blood cultures are negative.
- *Meconium aspiration syndrome (MAS):* RD in a baby who is born through meconium-stained amniotic fluid (MSAF). The typical chest radiograph shows diffuse parenchymal infiltrates with hyperinflation and a flat diaphragm with patchy areas of atelectasis[3].
- *Primary persistent pulmonary hypertension of newborn (PPHN):* Babies present within the first 24 hours of age with RD and echocardiographic findings of right to left shunt, tricuspid regurgitation, and ventricular septal deviation towards the left ventricle without an underlying cause [e.g., pneumonia, RDS, congenital diaphragmatic hernia (CDH)][5].
- *Early onset sepsis:* This is characterized by signs and symptoms of infection, with or without accompanying bacteraemia, which present within the first 72 hours of life[10].
- *Spontaneous pneumothorax:* Newborns with radiological evidence of pneumothorax without any other contributing causes such as pneumonia, MAS, or CDH.

The following details were recorded from the patient's notes in a separate data collection form.

1. *Birth details:* Gestation, birth weight, sex, mode of delivery, Apgar score, birth trauma

2. *Details of hospital stay*
    a) Admission details: Silverman score, age on admission
    b) Investigations: chest x-ray findings, CRP, blood culture, echocardiography
    c) Treatment: mode of respiratory support and duration, treatment (antibiotics), diagnosis, complications, duration of hospital stay and days to establish breastfeeding.
    d) Maternal details (evidence suggestive of chorioamnionitis, parity, GDM, other medical conditions, medication)

We assessed short-term adverse outcome of infants with RD and the parameters assessed were mortality, ventilator associated pneumonia (VAP), chronic lung disease (CLD), prolonged hospital stay (more than two weeks), and delay in establishment of breast feeding.

Ethical issues: Approval for the study was obtained from the Ethics Review Committee of Sri Lanka College of Paediatricians (Ref. No. SLCP/ERC/2019/01). Written informed consent was obtained from the parents of the neonates included in the study.

Statistical analysis: The statistical software (SPSS beta version) was used for the data entering and analysis. Descriptive statistics were used to analyse characteristics of the study group. Odds ratio (OR) was used to analyse risk factors

Results

During the study period, 105 (2.2%) term neonates (total term live births=4742) developed RD with the Silverman score of 3 or more; 88 (1.8%) had moderate to severe respiratory distress (SMS >4) with an incidence of 18.5 per 1000 live births; 71 (68%) were boys and 34 (32%) were girls. Mean birth weight was 3019 ± 0.39g and mean gestational age was 38 ± 0.9 weeks and 3 days. Aetiologies of RD are shown in in Table 1.

Table 1: ***Aetiology of respiratory distress (n=105)***

Aetiology	Number (%)
Congenital pneumonia	41 (39.0)
Transient tachypnoea of newborn (TTN)	22 (20.9)
Early-onset sepsis without pneumonia (EOS)	16 (15.2)
Respiratory distress syndrome (RDS)	12 (11.4)
Meconium aspiration syndrome (MAS)	06 (05.7)
Persistent pulmonary hypertension of newborn (PPHN)	04 (03.8)
Critical congenital heart disease (CCHD)	02 (01.9)
Congenital diaphragmatic hernia (CDH)	01 (01.0)
Spontaneous pneumothorax	01 (01.0)

We assessed risk factors for congenital pneumonia and EOS in the presence of risk factors such as prolonged rupture of membranes (PROM) more than 24 hours, maternal pyrexia more than 38^0C, three or more vaginal examinations, foul smelling liquor and maternal bacteriuria or infection during current pregnancy[13]. None of the mothers had bacteriuria in this cohort. Furthermore, we assessed the association of known risk factors for developing TTN and RDS (Table 2).

Table 2: ***Association of risk factors with early-onset pneumonia / sepsis, TTN and RDS***

Risk factor	Odds ratio	95% confidence interval	p-value
EOS and pneumonia			
PROM	8.625	1.050 – 70.802	0.044
3 or more vaginal examinations	4.300	1.464 - 12.630	0.008
Maternal pyrexia	2.611	0.262 - 25.958	0.412
Foul smelling liquor	6.229	0.313 - 123.676	0.230
TTN			
Born by LSCS	3.238	1.091 – 9.603	0.034
Male sex	1.357	0.478 – 3.851	0.565
RDS			
Male sex	1.573	0.397 – 6.223	0.518
Elective LSCS	37.272	7.205 – 192.818	<0.0001
Maternal diabetes	4.000	1.117 – 14.319	0.033

EOS: early onset pneumonia, TTN: transient tachypnoea of newborn, RDS: respiratory distress syndrome, LSCS: lower segment caesarean section, PROM: prolonged rupture of membranes

PROM and three or more vaginal examinations had significant association with congenital pneumonia and EOS. Among 22 neonates with TTN, 73.9% were born by caesarean section (OR=3.238, p= 0.034). Of neonates with RDS 83.3% were boys (OR= 1.573 and p= 0.518). Furthermore, 83.3% of babies with RDS were born by elective caesarean section (OR=37.272, p<0.0001). Indications for elective caesarean section were previous caesarean section and large for gestational age. All the babies with RDS were born at 37 to 38 weeks of gestation and 2 babies were born to mothers with gestational diabetes mellitus (OR=4, p=0.033).

Eighteen babies had severe RD (SMS of 7 or more) on admission and 17 of them required mechanical ventilation (r= 44, p= 0.001). Three babies died. Figure 1 illustrates the requirement for a different type of respiratory support based on the SMS.

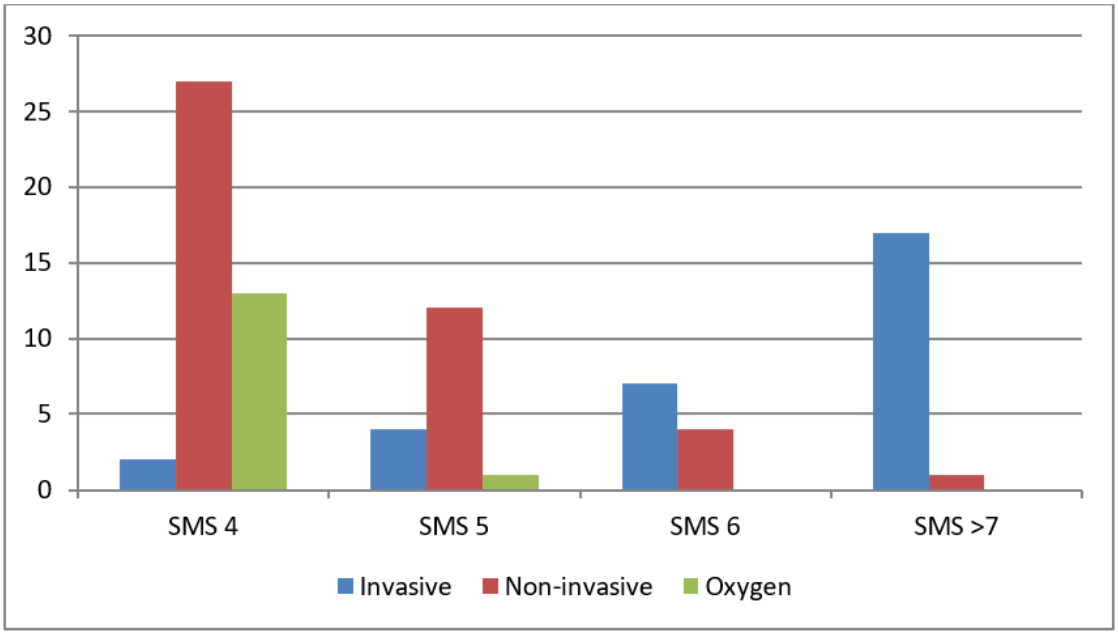

Figure 1: ***Mode of respiratory support based on Silverman score***

There were 4 (3.8%) neonatal deaths. Of the 4 neonates who died, 2 had critical congenital heart diseases (hypoplastic left heart syndrome) and the other two deaths were due to severe pulmonary hypertension and MAS[6]. Two babies were transferred to tertiary care centres and one of them had left sided CDH. The other baby was transferred for mechanical ventilation for underlying congenital pneumonia due to non-availability of mechanical ventilation. Out of 30 babies who required invasive ventilation, only two babies had VAP and none had CLD. The mean duration of hospital stay was 8.86 ± 5.2 days and 19% of them required prolonged hospital stay more than 2 weeks. The mean duration to establish breastfeeding was 5.1 ± 3.7 days.

Discussion

Of the term neonates 2.2% developed RD with the Silverman score of 3 or more and 1.8% had moderate to severe RD which accounted for an incidence of 18.5 per 1000 live births. Kumar A, *et al*[14] revealed an incidence of 4.2% and 20.9% among term and post-term neonates respectively. In a Sri Lankan study, the overall incidence has been reported as 8.2%[8]. However, the inclusion criteria were different from this study as our cohort only included term neonates with SMS greater than 3. Aetiologies of RD among term neonates include a variety of respiratory and non-respiratory causes and in the Sri Lankan context, TTN was the commonest aetiology[8]. MAS and congenital pneumonia were the second and third common aetiologies[8]. In our cohort, the commonest aetiology was congenital pneumonia (39%) and the second common cause was TTN (20.9%). Brahmaiah P, *et al*[15] observed similar findings. Our study included only babies who had Silverman score >3 and TTN commonly presents with mild to moderate respiratory distress which most probably would have been the reason for this difference.

The majority of neonates with sepsis and approximately one-third of neonates with pneumonia had risk factors for sepsis. Brahmaiah *et al*[15] demonstrated a significant association (50%) of PROM with pneumonia. We demonstrated an association between pneumonia / sepsis and the presence of risk factors PROM (p=0.044) and 3 or more vaginal examinations (p=0.008). Caesarean delivery, male sex, maternal diabetes, asthma and

low birth weight are known risk factors for TTN[6,12]. We found caesarean section a risk factor for TTN (p= 0.034) but, there was no significant association with male sex and no mothers had asthma in our cohort. Jing L, *et al*[16] have demonstrated a significant association between male sex, elective caesarean section and maternal GDM with RDS. Even though we could not find a significant association between male sex and RDS (p=0.518), maternal GDM and elective caesarean section had significant associations (p=0.033 and p<0.0001 respectively).

None of the babies with a Silverman score of 3 required invasive ventilation. Requirements for invasive ventilation among babies with moderate to severe RD were 18.5% and 94.4% respectively. The majority (60.8%) of babies with SMS more than 5 required invasive ventilation. In the local setting, Gamhewage NC, *et al*[8] demonstrated a similar result. In our study, we found a significant correlation between SMS greater than 7 and the requirement for invasive ventilation (r=44, p=0.00).

In our study cohort, 4 (3.8%) expired, and 2 (1.9%) were transferred to other tertiary care centres and subsequently, they have been discharged home. Among the 4 neonatal deaths, 3 babies had severe RD and the other baby had an SMS of 3. The causes of death were CCHD (n=2), severe PPHN, and MAS. Inhaled nitric oxide (iNO) was not available and it was not possible to transfer to the only centre where iNO was available as it was occupied at that time. Severe MAS was managed only with conventional ventilation and supportive care due to unavailability of HFOV. A similar result has been demonstrated in a local setting but an increased mortality rate (17 %) has been observed in an Indian study in 2017[8,15].

Conclusions

Incidence of RD with Silverman score of more than 3 was 2.2% and the commonest aetiology was congenital pneumonia. PROM and three or more vaginal examinations had significant associations with EOS and congenital pneumonia. Birth by caesarean section was a risk factor for developing TTN. Elective caesarean section and maternal diabetes increased the risk of developing RDS. Death rate was 3.8% in this cohort and none of the babies had VAP; 19% required prolonged hospital stay and mean duration to establish breast feeding was 5.1 days.

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