Original Article

Incidence, Presentation, Risk Factors and Causes of Respiratory Distress in Term Newborns at Thammasat University Hospital

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Abstract

Background: Respiratory distress (RD) is the most common problem in term newborn infants and it is the main cause of neonatal morbidity and mortality. Early recognition and initiation of appropriate management are critical to ensure optimal outcomes.

Objectives: To assess incidence, presentation, risk factors and causes of RD in term newborns at Thammasat University Hospital.

Methods: This cross-sectional study enrolled 625 term newborns born between March 1st, 2017 to May 7th, 2017. Their clinical information, chest X-ray findings, and outcomes were collected from medical records.

Results: Fifty-nine (9.4%) term newborns developed RD, and 92% had RD symptoms within 4 hours of life. Transient tachypnea of the newborn (TTNB) was the most common cause (7.5 %). The significant RD risk factors in term newborns were maternal pregnancy induced hypertension (adjusted odd ratio [OR] 5.45, 95% confidence interval [CI] 1.3 - 23, *P* = 0.02), no antenatal care (adjusted OR 5.23, 95%CI 1.2 - 22.5, *P* = 0.02), meconium-stained amniotic fluid (adjusted OR 2.85, 95% CI 1.1 - 7.6, *P* = 0.03), and large for gestational age (adjusted OR 2.54, 95%CI 1.1 - 6, *P* = 0.03).

Conclusions: Our rate of RD in term neonates was 9.4%. We recommend that all term newborns be closely observed after birth for at least 4 hours as this is the most critical time in which RD may manifest. Health care practitioners must promptly recognize RD signs and symptoms and give appropriate treatment quickly.

Key words: Respiratory distress, Transient tachypnea of the newborn, Term newborn

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Introduction

Respiratory distress (RD) is a common problem in term newborn infants; 15% of them develop significant respiratory morbidity.[1] However, RD incidence can vary. For example, Italian, Indian and Thai studies (the latter set in a Chiangmai primary care center) showed 2.2%[2], 6.7%[3] and 18.9%[4], respectively. RD is defined as any signs of breathing difficulty in term newborns such as tachypnea, flaring alar nasi, chest wall retraction, grunting, apnea, or cyanosis.[5 - 7] One of the most helpful investigation in making a diagnosis of RD is chest radiographic which reveals abnormal finding in 70% of the cases.[8]

There are many possible risk factors associated with developing neonatal RD: maternal risks including tobacco use during pregnancy, gestational diabetes mellitus, asthma, drug use during pregnancy[5, 9], previous cesarean section[8 - 10], cesarean sections especially during gestational age (GA) of 37 to 38-6/7 weeks without labor pain or appropriate indications for operation[11 - 16], as well as fetal risk factors like small or large for gestational age, and abnormal vasculogenesis of pulmonary blood vessels.[5, 7, 9, 17]

RD may result from cardiopulmonary and non-pulmonary causes.[18] Common causes include transient tachypnea of the newborn (TTNB), neonatal pneumonia, respiratory distress syndrome (RDS), and meconium aspiration syndrome (MAS).[17, 19]

Neonates with RD have mortality rate 2-4 times higher when compared to neonates with no RD. Regardless of the cause and the outcomes, delays in detection and management of neonatal RD can cause respiratory failure and cardiopulmonary arrest.

In our study, it was important to assess incidence, presentation, risk factors and causes of RD in term newborns at Thammasat University Hospital.

Methods

A cross sectional study was conducted between March 1st, 2017 to May 7th, 2017, at Thammasat University Hospital. This was approved by the Institutional Review Board, Faculty of Medicine, Thammasat University. All neonates who were born after 37 weeks of gestational age (GA) and did not have major congenital anomaly or chromosomal abnormalities, were enrolled to this study. Their clinical information, short term outcomes and chest X-ray finding were collected from their medical records.

Based on the 7% incidence rate of neonatal RD in full term newborns in a previous study[5], 625 term newborns were needed for a level of significance of 0.05 and power of 0.8. Analysis was done by using Fisher's exact test, Chi-squared test. Risk factors are analyzed by multiple logistic regression method. The final logistic model included 7 risk factors; gestational age < 38 weeks, large for gestational age, no antenatal care, meconium stained amniotic fluid, maternal gestational diabetes mellitus, maternal pregnancy induced hypertension and requiring positive pressure ventilation and was presented with adjusted odd ratio (OR) and 95% confidence interval (CI) with $P < 0.05$ being statistically significant.

Results

Fifty-nine (9.4%) neonates developed RD with the median age of onset at 2 hours after birth (range: at birth -66 hours of age). Fifty-four of them (92%) developed RD within 4 hours of age. The most common manifestation were tachypnea (89.8%), followed by desaturation (33.9%), accessory respiratory muscle use or chest retraction (11.9%), nasal flaring (8.5%) and grunting (6.8%).

The top four most common causes of RD were transient tachypnea of the newborn (TTNB) (79.6%), early onset neonatal sepsis (6.8%), persistent pulmonary hypertension of the newborn (PPHN) (3.4 %), and birth depression (3.4 %) (Table 1)

Table 1 Causes of respiratory distress in term newborns

Diagnosis	N (%)
Transient tachypnea of the newborn (TTNB)	47 (79.6)
Early onset neonatal sepsis	4 (6.8)
Persistent pulmonary hypertension of the newborn (PPHN)	2 (3.4)
Birth depression	2 (3.4)
Transient pulmonary hypertension	1 (1.7)
Birth asphyxia	1 (1.7)
Meconium aspiration syndrome	1 (1.7)
Spontaneous pneumothorax	1 (1.7)

The most commonly appeared chest radiography results were related to TTNB, showed fluid retention in interlobar spaces (49.1%) followed by hyperinflation (40.6%) and diffuse parenchymal infiltrates (5.1%).

Initially, all infants with RD were admitted to either the neonatal intensive care unit or high risk unit. They were given respiratory support which included invasive respiratory support (3.4%) (one newborn received high frequency oscillatory ventilation, whilst another conventional ventilation), continuous positive airway pressure (CPAP) (3.4%), heated humidified high flow nasal cannula (5%), nasal oxygen cannula (10.2%), and oxygen hood (78%). Their median duration of hospital stay was 5 days (range: 3 - 26 days), and the need for respiratory support was 2 days (range 1 - 19 days). The mortality rate of neonatal RD was one case (1.6%) who was diagnosed with PPHN.

The baseline characteristics of term newborns with RD and non-RD groups were shown in Table 2. There were significant differences between both regarding appropriate weight for gestational age, born before 38 weeks of gestational age, no antenatal care, maternal pregnancy induced hypertension (PIH), requiring positive pressure ventilation at birth, and infants who had an Apgar score equal to or less than 3 at first minute of life.

Table 2 Baseline characteristics of term newborns: respiratory distress (RD) and non-RD groups

Characteristics	RD (N = 59)	Non RD (N = 618)	*P*-value
Body weight (g) (mean±SD)	3202.2 ± 580.7	3147.1 ± 383.4	0.32
Appropriate for gestational age (%)			0.04
•Appropriate for gestational age	49 (83)	517 (91.3)	
•Small for gestational age	1 (1.7)	15 (2.7)	
•Large for gestational age	9 (15.3)	34 (6)	
Gestational age (weeks) (mean±SD)	38.6 ± 0.9	38.8 ± 0.9	0.09
Gestational age < 38 weeks (n,%)	16 (27.1)	90 (15.9)	0.04
Male gender (n,%)	37 (62.7)	282 (49.8)	0.07
Route of delivery (n, %)			0.36
• Vaginal delivery	33 (55.9)	310 (54.8)	
• Elective cesarean section	10 (17)	139 (24.5)	
• Medically indicated cesarean section	15 (25.4)	100 (17.7)	
• Failed induction cesarean section	1 (1.7)	17 (3)	
Maternal age (years) (mean±SD)	29.8 ± 6.4	29.1 ± 5.9	0.38
No antenatal care (n, %)	3 (5.1)	7 (1.2)	0.05
Premature rupture of membrane > 18 hours (n, %)	0 (0)	3 (0.5)	1
Duration ruptured of membrane (hours) (mean±SD)	2 ± 3	2.2 ± 4.8	0.74
Meconium stained amniotic fluid (n, %)	6 (10.2)	27 (4.8)	0.11
Maternal gestational diabetes mellitus (n, %)	9 (15.5)	45 (8)	0.08
Maternal pregnancy induced hypertension (n, %)	5 (8.5)	6 (1.1)	< 0.01
Requiring positive pressure ventilation (n, %)	4 (6.8)	2 (0.3)	< 0.01
Requiring endotracheal tube intubation (n, %)	1 (1.7)	0	0.09
Requiring chest compression (n, %)	1 (1.7)	1 (0.2)	0.18
Apgar at 1 mins ≤ 3 (n, %)	3 (5.3)	1 (0.2)	< 0.01

In multivariate analyses, the significant risk factors associated with neonatal RD were infants with a large for gestational age (adjusted OR 2.54, 95% CI 1.1 - 6, *P*= 0.03), no antenatal care (adjusted OR 5.23, 95%CI 1.2 - 22.5, *P*= 0.02), meconium stained amniotic fluid (adjusted OR 2.85, 95%CI 1.1 - 7.6, *P*= 0.03) and maternal PIH (adjusted OR 5.45, 95%CI 1.3 - 23, *P*= 0.02), (Table 3).

Table 3 Risk factors of respiratory distress in term newborns by multiple logistic regression analysis

Risk factors	Adjusted OR	95% confidence interval	*P*-value
Gestational age < 38 weeks	1.97	0.8 - 5.0	0.15
Large for gestational age	2.54	1.1 - 6	0.03
No antenatal care	5.23	1.2 - 22.5	0.02
Meconium stained amniotic fluid	2.85	1.1 - 7.6	0.03
Maternal gestational diabetes mellitus	0.75	0.3 - 1.8	0.53
Maternal pregnancy induced hypertension	5.45	1.3 - 23	0.02
Requiring positive pressure ventilation	8.58	0.5 - 148.5	0.13

Discussion

During our two-month study period, the neonatal RD incidence was 9.4%, which was almost equal to Edwards, et al. (7%)[5] but less than Chaosin P. (18.9%). The latter study was at a primary care hospital center in Thailand.[4] These differences might be due to the setting of our hospital, which is a tertiary care center, and most of our patients had good antenatal care.

Tachypnea, chest retractions, and desaturation below 95% or cyanosis were the most common clinical presentations of RD in our study, corresponding to previous studies[5-7]

Our study showed that the most common cause of neonatal RD in full term newborns was TTNB followed by early onset sepsis, PPHN, and birth depression. Less common causes were transient pulmonary hypertension, birth asphyxia, pneumothorax and MAS, as described in the studies of Parikh, et al[17] and Dani, et al.[19]

Salemi JL, et al[11] and Doan E, et al[20], found additional statistically significant risk factors associated with neonatal RD in term newborns which were cesarean section delivery without previous labor pain and without appropriate indications for the operation, compared with normal vaginal delivery. Many studies showed that newborns with gestational age of 37 to 38-6/7 weeks born by cesarean section without previous labor pain and without appropriate indications showed a statistically significant increased risk of neonatal RD than newborns with gestational age of 39 to 41-6/7 weeks.[11-16]

We found that the following conditions, including large for gestational age, not receiving antenatal care, meconium stained amniotic fluid, and maternal PIH increased the risk of neonatal RD in full term newborns. On the contrary, we could not demonstrate an association between risk of neonatal RD, gestational age or cesarean section delivery; this might be due to the limited population in our study.

Not all causes of RD were addressed in our research. Due to the short period of our study, we were unable to address RD from congenital heart disease and most of them develop RD at 2-4 weeks of age.

Incidence of neonatal RD in full-term newborns was 9.4%; ninety two percent of our newborns developed RD within 4 hours of age. It is important to closely observe full term newborns continuously after birth for at least 4 hours. Healthcare personnel should be aware of full-term newborns who have large size for gestational age, meconium stained amniotic fluid, maternal PIH and no antenatal care. Early recognition and treatment of common neonatal RD will improve outcomes.

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Conflicts of interest

All authors report no conflicts of interest relevant to this article.

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บทคัดย่อ

อุบัติการณ์ ลักษณะอาการทางคลินิก ปัจจัยเสี่ยง และสาเหตุของการหายใจลำบากในทารกแรกเกิดครบกำหนดและเกินกำหนด ในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

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บทนำ: ภาวะหายใจลำบากในทารกแรกเกิดครบกำหนดพบได้บ่อย ภาวะหายใจลำบากเป็นสาเหตุสำคัญของการเกิดภาวะทุพพลภาพและเป็นสาเหตุการเสียชีวิตในทารกแรกเกิด ดังนั้นการให้การวินิจฉัยตั้งแต่ระยะเริ่มต้นและให้การรักษาที่เหมาะสมจึงมีความสำคัญในให้การดูแลรักษาทารกแรกเกิดที่มีภาวะหายใจลำบากให้ได้ผลดีที่สุด

วัตถุประสงค์: เพื่อหาอุบัติการณ์ ลักษณะอาการทางคลินิก ปัจจัยเสี่ยง และสาเหตุของการหายใจลำบาก ในทารกแรกเกิดครบกำหนด ในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

วิธีการศึกษา: การวิจัยในครั้งนี้ใช้ระเบียบวิธีวิจัยแบบ cross-sectional study มีผู้เข้าร่วมวิจัย 625 คน เป็นทารกแรกเกิดครบกำหนดที่เกิดใน รพ.ธรรมศาสตร์เฉลิมพระเกียรติ ระหว่างวันที่ 1 มีนาคม พ.ศ. 2560 ถึง วันที่ 7 พฤษภาคม พ.ศ. 2560 โดยเก็บข้อมูลอาการทางคลินิก ภาพถ่ายรังสีทรวงอก และผลการรักษาจากแฟ้มเวชระเบียน

ผลการศึกษา: พบทารกที่มีภาวะหายใจลำบาก 59 คน คิดเป็นร้อยละ 9.4 โดยร้อยละ 92 ของทารกมีอาการภายในอายุ 4 ชั่วโมง สาเหตุภาวะหายใจลำบากที่พบมากที่สุดคือ ภาวะหายใจเร็วชั่วคราว 47 คนคิดเป็นร้อยละ 7.5 จากการศึกษานี้พบว่าปัจจัยเสี่ยงของภาวะหายใจลำบากในทารกแรกเกิดครบกำหนดคือ มารดามีภาวะความดันโลหิตสูงขณะตั้งครรภ์ มารดาไม่ได้ฝากครรภ์ มีขี้เทาปนในน้ำคร่ำ และทารกที่มีน้ำหนักตัวมากกว่าอายุครรภ์

สรุปผลการศึกษา: ภาวะหายใจลำบากในทารกแรกเกิดครบกำหนดพบได้บ่อยคิดเป็นร้อยละ 9.4 โดยมีภาวะหายใจเร็วชั่วคราวเป็นสาเหตุที่พบมากที่สุด ทารกแรกเกิดครบกำหนดทุกคนควรได้รับการสังเกตอาการอย่างใกล้ชิดเป็นเวลาอย่างน้อย 4 ชั่วโมงหลังเกิด เนื่องจากเป็นช่วงเวลาที่ทารกมักจะเริ่มมีอาการหายใจลำบาก บุคลากรที่ให้การดูแลควรจะต้องรู้ถึงอาการและอาการแสดงของภาวะหายใจลำบาก และให้การรักษาที่เหมาะสมอย่างรวดเร็วเพื่อให้ได้ผลลัพธ์ที่ดีขึ้น

คำสำคัญ: ทารกแรกเกิดครบกำหนด, ภาวะหายใจลำบาก, ภาวะหายใจเร็วชั่วคราว