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RISK FACTORS FOR NEONATAL RESPIRATORY DISTRESS SYNDROME – CASE CONTROL STUDY CONDUCTED IN MOSUL-IRAQ

[*1]Muthana Ahmed Azeez, [2]Mohammed Ali Hazim Mohammed Ali and [3]Ziad Khalid Majeed Al Bazzaz

[1]M.B.Ch.B./F.A.B.H.S (Ped.), Department of Pediatric, Ibin Al Atheer Teaching Hospital.
[2]M.B.Ch.B./F.I.B.M.S (Ped.), Department of Pediatric, Ibin Al Atheer Teaching Hospital.
[3]M.B.Ch.B./D.C.H/F.A.B.H.S, Department of Pediatric (Ped.), Al Salam Teaching Hospital.

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***Corresponding Author: Muthana Ahmed Azeez**

M.B.Ch.B./F.A.B.H.S (Ped.), Department of Pediatric, Ibin Al Atheer Teaching Hospital.

ABSTRACT

Background: Neonatal respiratory distress syndrome is the most common cause of morbidity and mortality in preterm newborns. It is diagnosed by grunting, nasal flaring, chest wall retractions, and increased breathing effort, either during delivery or later. Prematurity is the main risk factor for respiratory distress syndrome, however other variables, such as twin pregnancies, cesarean sections, male gender, and others, may also contribute to the development of the illness. Antenatal steroids have emerged as a significant obstacle to lung maturation and the prevention of respiratory distress syndrome in premature infants. **Objectives:** Is to evaluate various risk factors for the development of respiratory distress syndrome among newborns attending Neonatal units of Ibin Al Atheer and Al Salam Teaching hospitals in Mosul city. **Methods:** A case-control study was conducted, from January 2023 to the end of December 2023. The study included 60 neonates who were admitted to the neonatal department, diagnosed with respiratory distress disorder (cases) and 60 neonates which collected from the same hospitals provided that they had no respiratory manifestations (controls). The questionnaire includes Three parts; part one for socio-demographic data such as patients' age, sex, birth weight, gestational age at birth (<37 weeks considered premature), Apgar score at 5 min, and mode of delivery. Part two for maternal obstetric history including maternal smoking and multiple pregnancy. Part three for severity of respiratory distress syndrome. **Results:** The mean gestational age of the study participants was 35.89 ± 3.14 weeks. Of them 77 neonates are males (64.16%) and 43 (35.84%) are females, with male to female ratio of 1.79:1. It's evident that patients of less than 32 weeks gestational age, male gender, born by cesarean section, having low or high birth weight, having maternal history of smoking, and multiple pregnancy found to have risky association with respiratory distress syndrome. **Conclusion:** According to the study findings; preterm and post-term delivery, male gender, selective cesarean section, neonates with low 5- minutes Apgar score, low and high birth weight, maternal smoking and multiple pregnancy were risk factors for RDS. These findings have important clinical implications for the diagnosis and treatment of neonates with RDS.

KEYWORDS: Prematurity, Cesarean section, Low Birth weight, Mosul, Iraq.

1- INTRODUCTION

Neonatal respiratory distress syndrome is the most common cause of morbidity and mortality in preterm newborns.[1-2] RDS, commonly referred to as hyaline membrane disease, is characterized by surfactant insufficiency.[3] RDS is characterized by grunting, nasal flaring, chest wall retractions, and increased breathing effort either at delivery or later.[4] These newborns usually exhibit early warning indicators and require further oxygen assistance.[5] The arterial blood gas analysis results are initially characterized by fluctuating metabolic and respiratory acidosis, hypoxemia, and hypercapnia.[5-6]

The chest radiograph shows air bronchograms and ground-glass opacification in both sided lung fields, indicating decreased lung volume. In more severely affected infants, a complete "white-out" of the lung fields is often observed.[7] Interpreting the pathophysiology and treating RDS has advanced significantly over the past

three decades. The incidence of RDS decreases steadily as gestational age increases, going from 60–80% in newborns delivered between 26 and 28 weeks GA to 15–30% in those born between 32 and 36 weeks GA.[8]

Since managing these infants is challenging, a multidisciplinary approach is essential to achieving the best results. Temperature control, feeding, cardiovascular maintenance, and the management of early newborn sepsis are the key objectives of treatment.[9-10] Mechanical ventilation (MV), continuous positive airway pressure (CPAP), and surfactant therapy are obviously the main respiratory supports for RDS newborns.[10-11] RDS may occasionally occur in infants born after 36 weeks or at term, and additional diagnostic testing needs to be considered.[12]

Prematurity is the main risk factor for respiratory distress syndrome, however other variables, such as twin pregnancies, cesarean sections, male gender, and others, may also contribute to the development of the illness.[13-14] Antenatal steroids have emerged as a significant obstacle to lung maturation and the prevention of respiratory distress syndrome in premature infants.[15]

This study aimed to evaluate various risk factors for the development of respiratory distress syndrome among newborns attending Neonatal units of Ibin Al Atheer and Al Salam Teaching hospitals in Mosul city.

2-PATIENTS AND METHODS

After obtaining ethical approval from the ethical committee of Nineveh Health directorate. A case-control study was conducted, from January 2023 to the end of December 2023.

The study included 60 neonates who were admitted to the neonatal department, diagnosed with respiratory distress disorder (cases) and 60 neonates which collected from the same hospitals provided that they had no respiratory manifestations (controls).

The questionnaire includes Three parts; part one for socio-demographic data such as patients' age, sex, birth weight, gestational age at birth (<37 weeks considered premature), Apgar score at 5 min, and mode of delivery. Part two for maternal obstetric history including maternal smoking and multiple pregnancy. Part three for severity of RDS.

Statistically analysis done by using SPSS 30.0 software application. To compare the means, the Student's t-test was employed. The p-value was considered statistically significant if it was less than 0.05 at 95% CI. The odds ratio was calculated using risk estimate analysis using these variables.

3. RESULTS

The mean gestational age of the study participants was 35.89 ± 3.14 weeks. Of them 77 neonates are males (64.16%) and 43 (35.84%) are females, with male to female ratio of 1.79:1. It's evident that statistically significant differences were found between cases and controls regarding gestational age of < 32 weeks and Gestational age of 32-36 weeks. From the other hand; those of less than 32 weeks found to have risky association with RDS. As shown in table 3.1.

Table 3.1: Distribution of the study participants according to their gestational ages.

Gestational age	Case		Control		OR	p-value
	No.	%	No.	%		
< 32	10	16.7	1	1.67	2.206	< 0.001
32-36	35	58.3	5	8.33	0.280	
37-42+	12	20	50	83.3	Referent	
> 42	3	5	4	6.67	0.01	
Total	60	100	60	100		

Table 3.2 illustrate distribution of the study participants according to their gender. Statistically significant difference was found between cases and controls regarding gender. Moreover; male gender shows risky association with RDS.

Table 3.2: Distribution of the study participants according to their gender.

Sex	Case		Control		OR	p-value
	No.	%	No.	%		
♂	44	73.33	33	55	2.749	0.002
♀	16	26.67	27	45	0.285	
Total	60	100	60	100		

Table 3.3 illustrates distribution of the study participants according to their mode of delivery. Statistically no significant difference found between cases and controls regarding mode of delivery but C/S shows risky association with RDS.

Table 3.3: Distribution of the study participants according to their Mode of delivery.

Mode of delivery	Case		Control		OR	p-value
	No.	%	No.	%		
C/S	21	35	10	16.67	2.691	0.002
NVD	39	65	50	83.33	Referent	
Total	60	100	60	100		

Table 3.4 explores that 5-minutes Apgar score of less than 7 was in risky association and the cases had statistically significant different lower Apgar score in comparison to controls.

Table 3.4: Distribution of the study participants according to their 5-minutes Apgar score.

Apgar score	Case		Control		OR	p-value
	No.	%	No.	%		
< 7	27	45	2	4.33	15.2	< 0.001
7-10	33	65	58	95.67	Referent	
Total	60	100	60	100		

Table 3.5 shows distribution of the study participants according to their birth weight, risky association and statically significant difference regarding less than 1 Kg, 1-less than 1.5 Kg, 1.5-2.5 Kg and more than 4 Kgs birth weight.

Table 3.5: Distribution of the study participants according to their Apgar score.

Birth weight (kg)	Case		Control		OR	p-value
	No.	%	No.	%		
< 1	2	6.67	0	0	---	< 0.001
1-<1.5	12	20	1	3.33	2.667	
1.5-<2.5	30	50	17	36.67	6.060	
2.5-4	9	15	40	66.67	Referent	
> 4	1	3.33	2	6.67	2.21	
Total	60	100	60	100		

Regarding maternal smoking. It's evident that maternal smoking of more than 20 cigarette per day is in risk association but the difference is statistically not significant. As shown in table 3.6.

Table 3.6: Distribution of the study participants according to maternal smoking.

No.of cigarette per day	Case		Control		OR	p-value
	No.	%	No.	%		
> 20	2	3.33	0	0.0	---	0.058
< 20	4	6.67	3	5	1.408	0.359
Non	54	90	57	95	Referent	0.589
Total	60	100	60	100		

Table 3.7 shows the distribution of the study participants according to their number of fetuses. Twin and triple pregnancies shows risky associations and statistically significant differences found between cases and controls regarding this issue.

Table 3.7: Distribution of the study participants according to their number of fetuses.

No.of fetuses	Case		Control		OR	p-value
	No.	%	No.	%		
Twin	11	18.33	3	5	4.46	0.011
Triple	3	5	1	1.67	3.64	
Single	46	76.67	56	93.33	Reference	
Total	60	100	60	100		

Figure 3.1 compares the severity of RDS according to neonate age. It's clear that in the first 24 hours of life the percent of sever cases is slightly higher than that of mild to moderate cases (51.7% and 48.3% respectively), the reverse is true for the next three days.

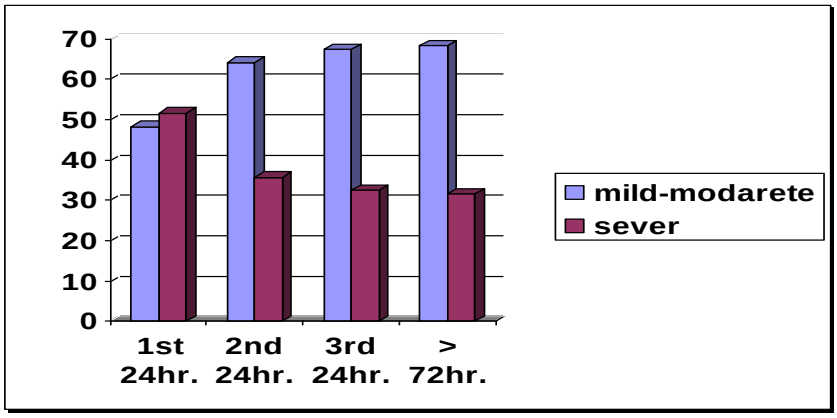

Figure 3.1: Severity of RDS according to the age of neonates.

Figure 3.2 compares the severity of RDS according to neonate gestational ages. It's clear that the higher the gestational age at birth the less the percent of severe cases and the more the percent of mild to moderate cases.

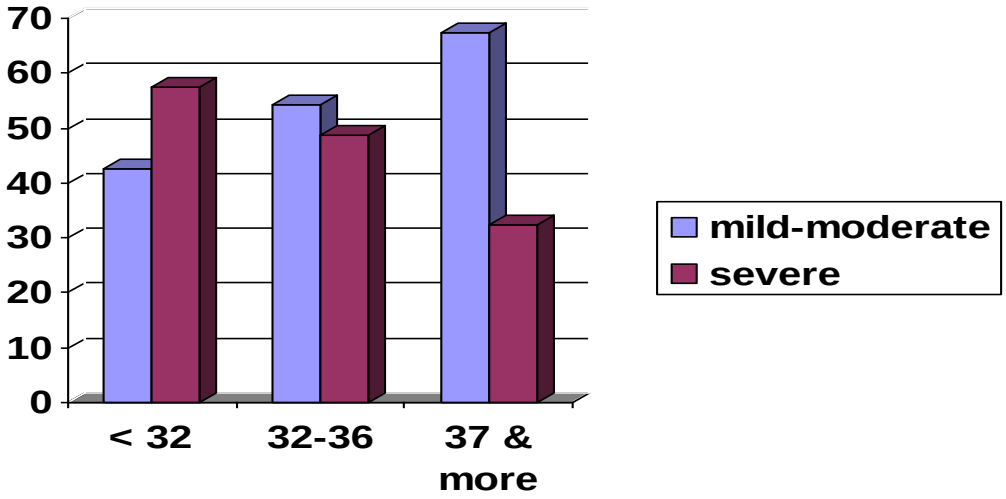

Figure 3.2: Severity of RDS according to the gestational age of neonates.

4. DISCUSSION

This study found that both preterm and post-term delivery were risky for RDS. The fact that these conditions can interfere with the synthesis or release of surfactant.[16] Furthermore, preterm may alter the alveolar-capillary membrane's permeability for fluid and solutes, allowing plasma proteins to enter the alveolar hypophase and further impairing surfactant function.[17] comparable results obtained from Sudeep Yadav et al[18] and Alexander J. Gould et al.[19]

Male gender found to have risk for RDS 2.7 times than female, this is due many facts. First, compared to the male fetal lung, the female fetal lung is believed to develop surfactant earlier in pregnancy.[20] Second, androgens can prevent lung fibroblasts from secreting fibroblast-pneumocyte factor, which can delay the formation of alveolar type II cells and decrease the release of pulmonary surfactants. Furthermore, by changing growth factor-beta and epidermal growth factor signaling pathways, androgens hinder the development of the embryonic lung.[20-21] Third, pulmonary surfactants, such as phospholipids, lecithin, and surfactant proteins A and B, are produced in response to estrogen. Furthermore, estrogen increases the number of alveolar type II cells and lamellated bodies, which aids in the development of the embryonic lung.[22] This finding is consistent with Keren Fang et al study findings.[23]

Regarding the mode of delivery; cesarean section is found to be risky for RDS, as it can reduce the amiloride-sensitive sodium channel activity in alveolar epithelial cells, resulting in decreased fluid clearance and premature birth. Stefanía Loor Zambrano et al had comparable results.[24] Furthermore; unsurprisingly patients with low 5-minutes Apgar score, both low and birth weight found to be risky for having RDS, which goes with Jeongmin Shin et al[25], Mansoor Aslamzai et al[26] and Candra Kusuma Negara et al study findings.[27]

This study found that maternal smoking of less than 20 cigarette was a risky for RDS, in contrast to Mario Alberto Arrieta-Mendoza et al how found that maternal smoking can produce an inflammatory condition which

mature the fetus respiratory system.[28] However; this difference was occurred due to depending on different inclusion and exclusion criteria. From the other hand; multiple pregnancies found to be risky for RDS, with is in the same line of Ivana Bevanda et al study findings.[29]

Regarding the RDS severity, the study found that the incidence of mild to moderate RDS increase as the neonatal ages and gestational ages increased and vice versa for severe RDS. Which is comparable to Stefanía Loor Zambrano et al study results.[24]

This study has certain limitations because it is retrospective in nature which might affect the clinical evaluations of the patients. Additionally, small sample size and depending on only two hospitals can affect the study findings.

5. CONCLUSION

According to the study findings; preterm and post-term delivery, male gender, selective cesarean section, neonates with low 5- minutes Apgar score, low and high birth weight, maternal smoking and multiple pregnancy were risk factors for RDS. These findings have important clinical implications for the diagnosis and treatment of neonates with RDS.

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Conflict of intertest

About this study, the authors disclose no conflicts of interest.

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