Risk factors of neonatal respiratory distress syndrome in Mukalla city hospital - Yemen

العوامل الخطرة للرضع المصابين بمتلازمة الضائقة التنفسية في مستشفى مدينة المكلا- اليمن

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Abstract :

Respiratory distress syndrome (RDS) is a common critical disease in neonates.

Objectives:*The aim of this study was to find the main risk factors of neonatal respiratory distress syndrome.*

Methods: *This is a case-control study enrolled 150 cases with RDS and 150 controls without RDS with gestation age 23 to 41 weeks, who attended and admitted to department of neonatology in Mukalla city hospital, Mukalla, Yemen, from January 2015 to December 2015.*

Results: *We found that the significant risk factors associated with RDS were male (odds ratio (OR) 2.35; 95% confidence interval (CI) 1.46 to 3.80; p-value=0.0004), Prematurity whether very preterm (OR 115; 95% CI 35.22 to 375.49; p-value < 0.0001), or moderate preterm (OR 40; 95% CI 13.98 to 114.41; p-value < 0.0001), or late preterm (OR 6.25; 95% CI 2.16 to 18.01; p-value 0.0007) and low birth weight(OR 8.33; 95% CI 4.88 to 14.22; p-value < 0.0001), cesarean section (OR 1.81; 95% CI 1.03 to 3.188; p-value 0. 0.03), premature rupture of membranes (PROM)(OR 3.79; 95% CI 1.79 to 8.04; p-value 0.0005), maternal fetal infection (OR 3.91; 95% CI 1.78 to 8.57; p-value 0.0006), and birth asphyxia(OR 27.16; 95% CI 1.59 to 463.18; p-value 0. 0.02).*

Conclusions: *Several high-risk factors, such as prematurity, male sex, low birth weight, cesarean section, PROM, maternal fetal infection, and birth asphyxia are closely correlated with neonatal RDS. These could provide a significant reference for the diagnosis and treatment of neonatal RDS.*

Keywords: *Neonatal respiratory distress syndrome, risk factors.*

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الملخص :

المقدمة : إن متلازمة الضائقة التنفسية الوليدية هي متلازمة تصيب الخدج والذين يولدون ولادة مبكرة وسببها قصور نمائي في إنتاج الفاعل بالسطح الرئوي وعدم نضوج في تكوين الرئتين.

هدف الدراسة: هذه الدراسة قيمت العوامل الخطرة بمتلازمة الضائقة التنفسية الوليدية بمستشفى مدينة المكلا في الفترة ما بين يناير وديسمبر٢٠١٥.

طريقة الدراسة : أجريت دراسة حالات وشواهد على ١٥٠ حالة مصابة بمتلازمة الضائقة التنفسية الوليدية وتم تأكيد التشخيص من خلال الصورة السريرية والتصوير السيني للصدر، وتم أملاء استبيان معياري للأسئلة عن العوامل الديموجرافيه والعوامل الخطرة بالإضافة إلى ١٥٠ خدج غير مصاب بمتلازمة الضائقة التنفسية الوليدية متوافقين في العمر والجنس كمجموعه ضابطة.

وقد تم جمع البيانات، وتم تحليلها إحصائيا باستخدام برنامج الحزمة الإحصائية للعلوم الاجتماعية.

النتائج : لوحظ بأن نسبة إصابة الذكور(٧١,٣ ٪) أعلى من الإناث(٢٨,٧٪) في الوليد المصاب بمتلازمة الضائقة التنفسية الوليدية وإن معدل الولادة المبكرة (٨٨ ٪) ، نقص الوزن (٨٢٪)، الولادة القيصرية (٢٦,٧ ٪)، التمزق المبكر للأغشية الجنينية (٢١,٣٪)، عدوى الام الجنيني(٢٠٪) والاختناق اثناء الولادة (٨٪) في حالات متلازمة الضائقة التنفسية الوليدية أعلى مقارنة بالمجموعة الضابطة (٢٨ ٪) ، (٣٥,٣)، (١٦,٧٪)، (٦,٧ ٪)، (٦ ٪) (٠٪)على التوالي.

الخلاصة : اهم العوامل الخطرة لحدوث متلازمة الضائقة التنفسية الوليدية هي الذكورة، الولادة المبكرة، نقص الوزن، الولادة القيصرية، التمزق المبكر للأغشية الجنينية، عدوى الام الجنيني والاختناق اثناء الولادة.

الكلمات المفتاحية: متلازمة الضائقة التنفسية الوليدية - العوامل الخطرة.

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Introduction :

Respiratory distress syndrome (RDS) or hyaline membrane disease (HMD) is a main cause of morbidity and mortality in the early neonatal period. Related to the degree of prematurity, it occurs in 7% - 50% of neonates. It is also responsible for 30% - 40% of newborns' hospital admission (1,2). Classically, RDS is observed in preterm infants, however, 6.4% of cases with RDS are diagnosed in infants born at ⩾37 weeks' gestation (3). The risk for development of RDS increases with maternal diabetes, multiple births, cesarean delivery, precipitous delivery, asphyxia, cold stress, and a maternal history of previously affected infants. The incidence is highest in preterm male or white infants (4).The significant cause of RDS is deficiency of alveolar surfactants due to immaturity of Type II pneumocyte, resulting low compliance of lungs, alveolar surface tension, decreased gas exchange and a demand for high ventilatory pressures (5). Signs of RDS are usually present soon after birth. The chest radiograph demonstrates poorly inflated lungs with a "ground glass" appearance of reticular nodular shadowing throughout the lung fields and air bronchograms (6).

The aim of this study is to determine the possible risk factors for RDS.

Subjects and Methods:

This is a case-control study enrolled 150 cases with RDS and 150 controls without RDS with gestation age 23 to 41 weeks, who attended and admitted to department of neonatology in Mukalla city hospital, Mukalla, Yemen, from January 2015 to December 2015. Informed consent from relatives of patients were taken.

Inclusion criteria were all neonate attended and admitted to department of neonatology in Mukalla city hospital with a diagnosis of RDS.

Excluded from the study, neonates patients with congenital heart disease, meconium aspiration syndrome or neonatal sepsis. and other major congenital defects.

The following information's were recorded: maternal age at pregnancy, sex, gestational age (weeks),birth weight, mode of

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delivery, Multiple gestation, gestation diabetic, premature rupture of membranes, maternal fetal infection, birth asphyxia, pregnancy hypertension disease and placental abruption.

We divided gestational age at birth into very preterm (23-31weeks), moderate preterm (32-33 weeks), late preterm (34-36 weeks), early term (37-38 weeks), and full term (39-41 weeks) (7).

Diagnostic criteria for RDS were considered by the presence of clinical sign, such as grunting, flaring, tachypnea, retractions, requiring a respiratory support (supplemental oxygen requirement and/or non-invasive or invasive ventilation). Typical radiological findings were reticulogranular patterns, air bronchograms and ground glass appearance (8).

Statistical methods :

The collected data were coded, tabulated, and statistically analyzed using SPSS program and version 17. Data were presented in frequency, percentage, mean, standard deviation and odd ratio. We compared demographic characteristics of infants with and without RDS using 2χ - *test* and the Mann-Whitney test, when appropriate. Multivariate logistic regression test was used to analyze risk factors. $P< 0.05$ was considered significant.

Results :

During the study period, a total of 150 patients with neonatal RDS were identified and 150 neonates without RDS were assigned to the control group, who attended and admitted to department of neonatology in Mukalla city hospital during the same period of time.

Table (1): Demographic data of studied groups:

Out Of 150 cases, 107(71.3%) were male and 43(28.7%) female (P= 0.0006). The mean gestation age of neonatal RDS (34.3±2.9) was significantly lower compared to mean age of control (38.1±2.3) (P<0.0001). The percentage frequency of low birth weight was significantly higher in cases 123(82%) compared to control 53(35.3%)(< 0.0001).The percentage of delivery with Cesarean delivery were significantly higher in cases 40(26.7%) compared to control 25(16.7%) (P= 0.04).The percentage frequency of neonates

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with history of PROM, Maternal fetal infection and birth asphyxia were significant higher in cases 32(21.3%),30(20%) and12(8%), respectively compared to control 10(6.7%), 9(6%) and 0(0%)respectively (P<0.05). No significant difference between cases and control regarding maternal age, multiple gestation, gestation diabetic, pregnancy hypertension disease and Placental abruption.

Table (2): Logistic regression analysis of risk factors for RD :

Our study found that male (OR 2.35; 95% CI 1.46 to 3.80; p-value=0.0004), Prematurity whether very preterm (OR 115; 95% CI 35.22 to 375.49; p-value < 0.0001), or moderate preterm (OR 40; 95% CI 13.98 to 114.41; p-value < 0.0001), or late preterm (OR 6.25; 95% CI 2.16 to 18.01; p-value 0.0007) and low birth weight(OR 8.33; 95% CI 4.88 to 14.22; p-value < 0.0001), cesarean section (OR 1.81; 95% CI 1.03 to 3.188; p-value 0. 0.03), PROM (OR 3.79; 95% CI 1.79 to 8.04; p-value 0.0005), maternal fetal infection (OR 3.91; 95% CI 1.78 to 8.57; p-value 0.0006), birth asphyxia(OR 27.16; 95% CI 1.59 to 463.18; p-value 0.02), were the main risk factors of RDS in neonates.

Table (3): The influence of some risk factors on outcomes of RDS infants:

It was found that prematurity, PROM, maternal-fetal infection and birth asphyxia and maternal-fetal infection were most associated with death in RDS patients (p<0.05).

Figure(1): The percentage of cases with respiratory distress syndrome according to gestation age:

Our study found that the percentage of cases with respiratory distress syndrome were 69(46 %) 48(32%),15(10%),12(8%),6(4%) in very preterm, moderate preterm, late preterm, early term and full term respectively.

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Table (1): Demographic data of studied groups

Variable	Cases N= 150	Control N= 150	P. value
Maternal age			
<24	48(32%)	45(30%)	
25-29	39(26%)	42(28%)	
30-34	30(20%)	33(22%)	0.80
35-39	18(12%)	20(13.3%)	
40+	15(10%)	10(6.7%)	
Sex			
Male	107(71.3%)	77(51.3%)	0.0006
Female	43(28.7%)	73(48.7%)	
Gestational age	34.3±2.9	38.1±2.3	< 0.0001
Birth weight			
≤2500g	123(82%)	53(35.3%)	< 0.0001
>2500g	27(18%)	97(64.7%)	
Mode of delivery			
Vaginal delivery	110(73.3%)	125(83.3%)	0.04
Cesarean delivery	40(26.7%)	25(16.7%)	
Multiple gestation			
Yes	5(3.3%)	3(2%)	0.72
No	145(96.7%)	147(98%)	
Gestation diabetic			
Yes	2(1.3%)	4(2.7%)	
No	148(98.7%)	146(97.3%)	0.68
PROF			
With	32(21.3%)	10 (6.7%)	0.0004
Without	118(78.7%)	140 (93.3%)	
Maternal fetal infection			
Yes	30(20%)	9(6%)	0.0005
No	120(80%)	141(94%)	
Birth asphyxia			
Yes	12(8%)	0 (0%)	0.0004
No	138(92%)	150(100%)	
Pregnancy hypertension disease	7(4.7%)	3(2%)	0.33
Yes	143(95.3%)	147(98%)	
No			
Placental abruption			
Yes	5(3.3%)	1(0.7%)	0.21
No	145(96.7%)	149(99.3%)	

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Table (2):Logistic regression analysis of risk factors for RDS

Variable	Cases N= 150	Control N= 150	OR	95% CI	P. value
Maternal age					
<24	48(32%)	45(30%)	1	Reference group	0.70
25-29	39(26%)	42(28%)	1.14	0.63 to 2.08	0.64
30-34	30(20%)	33(22%)	1.17	0.61 to 2.22	0.62
35-39	18(12%)	20(13.3)	1.18	0.55 to 2.52	0.65
40+	15(10%)	10(6.7%)	0.71	0.28 to 1.74	0.45
Sex					
Male	107(71.3)	77(51.3%)	1	Reference group	0.0004
Female	43(28.7%)	73(48.7%)	2.35	1.46 to 3.80	
Gestational age					
Full term	6 (4%)	60 (40%)	1	Reference group	< 0.0001
Early term	12 (8 %)	48 (32%)	2.50	0.87 to 7.15	0.08
Late preterm	15(10 %)	24 (16%)	6.25	2.16 to 18.01	0.0007
Moderate preterm	48(32 %)	12 (8%)	40	13.98 to 114.41	< 0.0001
Very preterm	69 (46%)	6 (4%)	115	35.22 to 375.49	< 0.0001
Birth weight					
≤2500g	123(82%	53(35.3%)	1	Reference group	< 0.0001
>2500g	27(18%)	97(64.7%)	8.33	4.88 to 14.22	
Mode of delivery					
Cesarean delivery	40(26.7%)	25(16.7%)	1	Reference group	0.03
Vaginal delivery	110(73.3%)	125(83.3%)	1.81	1.03 to 3.188	
Multiple gestation					
Yes	5(3.3%)	3(2%)	1	0.39 to 7.200	0.47
No	145(96.7%)	147(98%)	1.68		
Gestation diabetic					
Yes	2(1.3%)	4(2.7%)	1	Reference group	0.41
No	148(98.7)	146(97.3)	0.49	0.08 to 2.73	
PROF					
With	32(21.3%)	10 (6.7%)	1	Reference group	0.0005
Without	118(78.7%)	140 (93.3%)	3.79	1.79 to 8.04	
Maternal fetal infection					
Yes	30(20%)	9(6%)	1	Reference group	0.0006
No	120(80%)	141(94%)	3.91	1.78 to 8.57	
Birth asphyxia					
Yes	12(8%)	0	1	Reference group	0.02
No	138(92%)	150(100%)	27.16	1.59 to 463.18	
Pregnancy hypertension disease					
Yes	7(4.7%)	3(2%)	1	Reference group	0.21
No	143(95.3%)	147(98%)	2.39	0.60 to 9.45	
Placental abruption					
Yes	5(3.3%)	1(0.7%)	1	Reference group	0.13
No	145(96.7%)	149(99.3%)	5.13	0.59 to 44.51	

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Table (3): The influence of some risk factors on outcomes of RDS

Variable	Dead N= 70	Alive N=80	P. value
Sex			
Male	47(67.1%)	60(75%)	0.36
Female	23(32.9%)	20(25%)	
Gestation age			
Very preterm	45 (64.3%)	24 (30%)	
Moderate preterm	17 (24.3%)	31 (38.8%)	
Late preterm	3 (4.3%)	12 (15%)	<0.0001
Early term	4(5.7%)	8 (10%)	
Full term	1 (1.4%)	5 (6.2%)	
Birth weight			
≤2500g	58(82.9%)	65(81.2%)	0.83
>2500g	12(17.1%)	15(18.8%)	
Mode of delivery			
Vaginal delivery	53(75.7%)	57(71.3%)	0.58
Cesarean delivery	17(24.3%)	23(28.7%)	
Prolonged rupture of Membranes			
With	24(34.3%)	8(10%)	0.0005
Without	46(65.7%)	72(90%)	
Maternal fetal infection			
Yes	20(28.6%)	10(12.5%)	0.02
No	50(71.4%)	70(87.5%)	
Birth asphyxia			
Yes	10(14.3%)	2(2.5%)	0.01
No	60(85.7%)	78(97.5%)	

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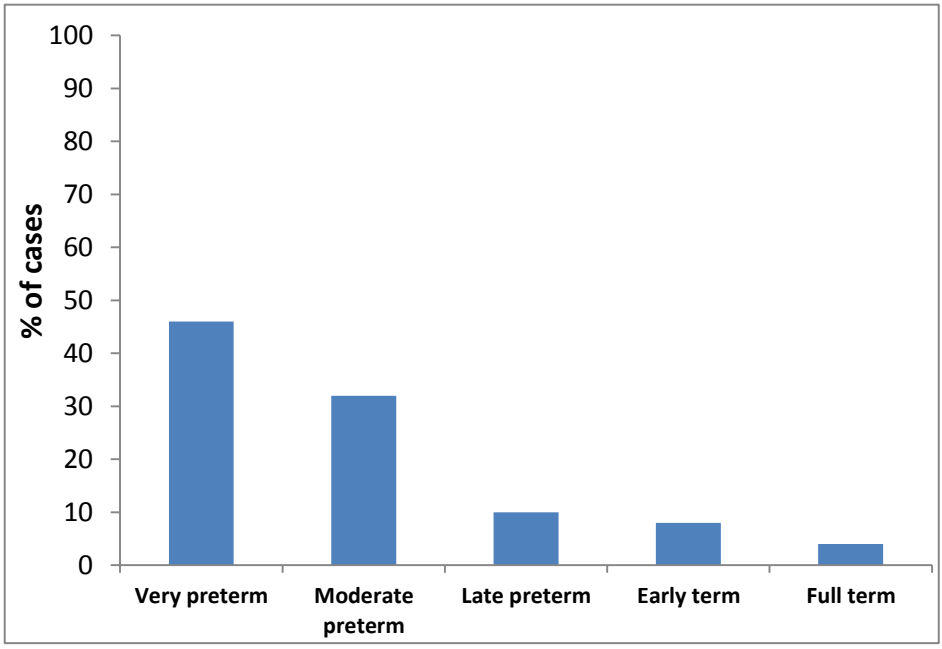
Figure(1): The percentage of cases with respiratory distress syndrome according to gestation age



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Discussion :

Respiratory distress syndrome (RDS) is one of the most common causes of neonatal respiratory failure and neonatal death (9). It was observed that the male patients was significantly higher in RDS compared to female. This study also showed male an important risk factor for neonatal RDS (Tables 1 and 2).This is consistent with several studies (8,10,11). Differences in hormonal regulation of lung development provide candidate mechanisms to account for an increased risk of RDS associated with male sex (12,13). Androgens delay lung fibroblast secretion of fibroblast pneumocyte factor, which can delay the development of alveolar type II cells; furthermore, they reduce the release of surfactant. Androgens slow fetal lung development by adjusting the signaling pathways of epidermal growth factor and transforming growth factor-beta. On the contrary, estrogens promote the synthesis of surfactant, including phospholipids, lecithin and surfactant proteins A and B, and improve fetal lung development by increasing the number of alveolar type II cells and the synthesis of lamellar bodies (13,14). The percentage of cases with respiratory distress syndrome were 69(46%), 48(32%), 15(10 %), 12(8%), 6(4%) in very preterm, moderate preterm, late preterm, early term and full term respectively (Figure1). This is in agreement with the results of other studies (8,10,15). Respiratory distress syndrome occurs primarily in premature infants; it occurs in 60-80% of infants <28 wk of gestational age, in 15-30% of those between 32 and 36 wk of gestational age, and rarely in those >37 wk of gestational age(4). This study also showed that prematurity was the main risk factor associated with RDS(Tables 1 and 2), which is similar to other studies (8,15,16,17,18,19). In preterm the immature lung structure may be functionally associated with delayed intrapulmonary fluid absorption, surfactant inefficiency and inefficient gas exchange (20).

It was observed that cesarean delivery was significantly higher in RDS compared to control. This study also showed cesarean delivery

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was risk of RDS (Tables 1 and 2). This is in agreement with the results of other studies (8,10,15). Neonates born by cesarean section have a larger residual volume of lung fluid, secrete less surfactant to the alveolar surface and have a delayed clearance of lung fluid (21); thus, they are at higher risk of developing RDS.

It was also found that low-birth weight was significantly higher in RDS compared to control. This study also showed low birth weight an important risk factor for neonatal RDS (Tables 1 and 2),which is similar to other studies(8,15,17,18,22).This can be explained by the fact that a bigger proportion of neonates in our study were premature. Lack of surfactant in the alveoli of the lungs causes respiratory distress syndrome and this is common among premature neonates(22). It was observed that PROM was significantly higher in RDS compared to control. This study also showed PROM was associated with RDS (Tables 1 and 2). This is consistent with several studies (10,15 23).It was also observed that maternal fetal infection was higher in RDS compared to group control. This study also showed maternal fetal infection was associated with RDS (Tables 1 and 2). These data are in accordance with those reported in other studies(10,15,23). PROM leads to maternal fetal infection; this occurs in nearly 1/3 of patients with PROM (24). Intrauterine infection and chorioamnionitis caused by PROM can result in direct injury to the fetal lungs and alveolar type II cells, decreasing the synthesis or release of surfactant (23).

It was found that birth asphyxia was higher in RDS. This study also showed that birth asphyxia is also an important risk factor for neonatal RDS(Tables 1 and 2). This is consistent with several studies (9,23,25). Acute lung injury caused by severe birth asphyxia or maternal-fetal infection decreases the synthesis and secretion of pulmonary surfactant; and the hypoxia or maternal fetal infection inhibits the activity of pulmonary surfactant and even leads to its inactivation (23).

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Among the 150 neonates formally diagnosed with the RDS, 70(46.7) died (Table 3), which is higher than that of Qian et al, (5.4%) (26) and Abdelrahman et al, (15%) (27).

It was also found that prematurity, PROM, severe asphyxia and maternal-fetal infection were significantly associated with death in RDS ($p<0.05$). This is in agreement with the results of other studies(23,25). The higher percentage of death and associated risk factors in RDS can be explained by inadequate antenatal care, less use of steroid in prematurity antenataly, less meticulous management of high risk pregnancies beside unavailability of synthetic surfactant and mechanical ventilation.

Conclusion:

The majority of RDS cases occur in preterm infants, obstetric and neonatal strategies are needed to prevent premature delivery. Future studies to elucidate mechanisms that account for this differential risk will inform obstetrical counseling and decision-making.

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