# Factors associated with severe neonatal respiratory distress syndrome

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## Abstract

**Introduction**: Neonatal respiratory distress syndrome is a pathology associated with premature male neonates. At the regional level, no data is associated with severe neonatal respiratory distress syndrome (RDS), so an observational study was developed to measure risk factors.

**Methodology**: The present cross-sectional - retrospective study was carried out in the neonatology service of the "Teodoro Maldonado Carbo" Hospital, in Guayaquil, Ecuador, from January 2017 to December 2020. Neonates with RDS entered the study with a probabilistic sample. . The variables were maternal, neonatal, Silverman scale, and Downes assessment. Based on the Silverman scale, two groups are analyzed: mild and moderate RDS versus Severe RDS; Odds Ratio is presented, and a 95% confidence interval with a P value.

**Results**: 302 cases were analyzed, with a gestational age of 33 ± 4.2 weeks. Silverman scores 5.07 ±2.06. The identified risk factors were cesarean section OR 3.92 (95% CI 2.13-7.21) P<0.0001, pre-eclampsia OR 1.73 (1.05-2.87) P=0.033. Gestational age <28 Weeks 7.626 (2.657-21.89) P=0.0002. Gestational age >36 weeks OR 0.4 (0.273-0.782) P=0.004. Sex male OR 2.19 (1.32-3.63) P=0.002.

**Conclusion**: The risk factors were cesarean section, pre-eclampsia, gestational age less than 28 weeks, and male sex. A protective factor was gestational age greater than 36 weeks.

## Keywords:

**MESH**: Infant, Premature; Risk Factors; Respiratory Distress Syndrome, Newborn; Mortality.

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# Introduction

Respiratory distress syndrome (RDS), also known as hyaline membrane disease, primarily affects the respiratory system and involves the adaptation of the newborn to extrauterine life. It usually presents in preterm infants [ 1 ]. The term RDS was mentioned for the first time in 1821 in the "Treatise on diseases of the chest" described by Laennec Ashbaugh et al., who described the most frequent symptoms of this syndrome associated with tachypnea, hypoxia, and decreased lung compliance in a sample of 11 adults and one child with respiratory failure [ 2, 3 ].

Neonatal RDS is clinically characterized by polypnea, tachypnea, and progressive respiratory distress, which increases the need for oxygen use and can progress from moderate to severe. These signs include nasal flaring, laryngeal grunting, intercostal retractions, cyanosis, and systemic involvement, such as shock, hypotension, acidosis, and asphyxia. The diagnosis is based on a detailed history to identify the risk factors associated with the pathology, clinical data, and laboratory and radiological diagnosis, where it is common to observe bilateral ground glass imaging with an air bronchogram [ 4 ].

The risk factors associated with this pathology can be maternal as well as neonatal; among the most important is preterm delivery; it has also been associated with an increase in cases when the newborn is male [ 5 - 8 ]; however, this appreciation does not have a clear explanation related to sex. Other studies also determine that cesarean section increases the risk of this neonatal pathology, associated with failures in calculating gestational age and hastening the delivery time [ 9 ]. RDS worldwide is 2 to 12.8 per 100,000 neonates, whose mortality has increased from 20 to 30% in recent years [ 10-11 ].

Other studies have determined that the lower-weight twin product is also at risk for RDS [ 15, 16 ]. With these antecedents, the present investigation was proposed to describe the factors associated with the risk of RDS in a regional reference center in neonatology in Guayaquil, Ecuador.

# Population and methods

### Design of the investigation

This research is an observational, cross-sectional, retrospective study.

### Scenery

The study was carried out in the neonatology service of the "Teodoro Maldonado Carbo" Specialty Hospital of the Ecuadorian Institute of Social Security in Guayaquil, Ecuador. The study period was from January 1, 2017, to December 31, 2020.

### Inclusion criteria

Neonates of both sexes with severe respiratory distress syndrome entered the study. Participants with incomplete records were excluded from the analysis.

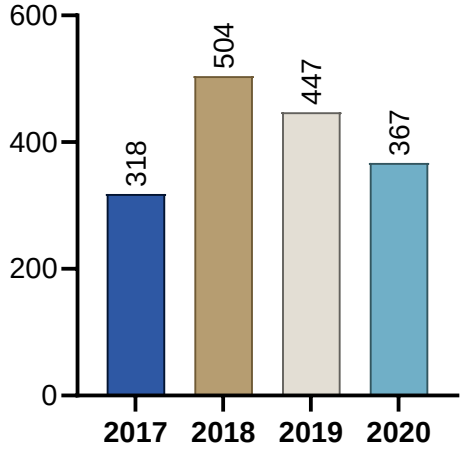


**Figure 1.** Prevalence of RDS in the Teodoro Maldonado Carbo Specialty Hospital.

### Studio size

The sample consisted of patients admitted to the hospital in the institution's neonatology department. The sample calculation was probabilistic. The annual prevalence (Figure 1) of the institution was taken into account with a total number of 1636 cases; the population survey or descriptive study was used through random sampling (not cluster) with a confidence level of 95%, an expected frequency of 59.7%, 5% confidence

limits, and the sample size was 302 cases. The program used for the sample calculation was Epiinfo ™ (CDC, Atlanta, USA).

### Variables

The variables were the type of delivery, maternal age, maternal morbidity, gestational age, sex of the newborn, race, genopathies, fetal morbidity, treatment with surfactant factor, Silverman scale, Downes assessment, pattern, and radiological assessment of the chest X-ray.

### Data sources/measurement

The data were collected from the clinical history in a form designed exclusively for that purpose. The institutional electronic system for case investigation (AS400) was used. The following root codes of the ICD-10 international classification related to inguinal hernias were used:

P22.0 Respiratory distress syndrome of the NB
P22 Respiratory distress of the NB
P22.1 Transient tachypnea of the newborn
P22.8 Other respiratory difficulties of the newborn
P22.9 Respiratory distress of newborn, unspecified
P23 Congenital pneumonia
P24 Neonatal aspiration syndromes
P24.0 Neonatal meconium aspiration
P28 Other respiratory problems of the NB originating in the perinatal period
P28.4 Other apneas of the newborn
P28.5 Respiratory failure of the newborn
P28.8 Other specified respiratory problems of the newborn
P28.9 Unspecified respiratory condition of the newborn.
P29.2 Neonatal hypertension.
P29.3 Persistent fetal circulation

The database was coded with serial numbers, thus protecting the confidentiality of the information and identity of the patients.

### Statistical method

In the initial phase, the data analysis is univariate and descriptive with frequencies and percentages. In one part of the analysis, a bivariate analysis is presented using the Silverman severity scale: Group 1 mild + moderate, versus Group 2 severe. Risk factors are presented with odds ratios; significant differences were considered when the P value was less than 0.05. Proportions are compared with the chi-square test. The statistical package SPSS v.25 (Armonk, NY: IBM Corp.) was used for the analysis.

## Results

A total of 302 patients were analyzed (Figure 2 ).

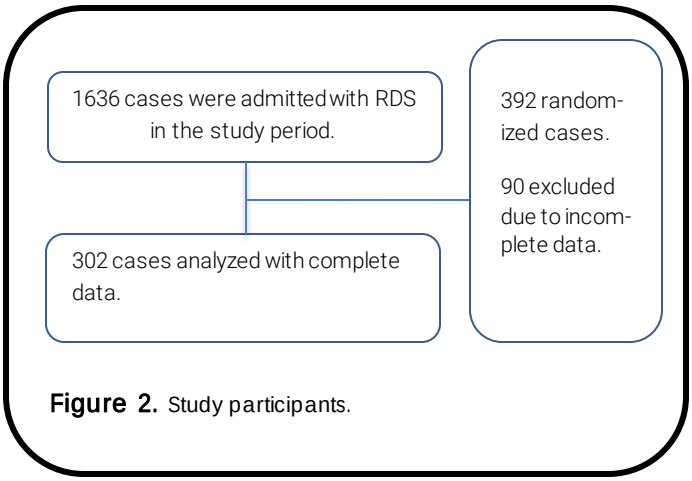


**Figure 2.** Study participants.

### General characteristics of the study sample

Table 1 shows the gestational age of 33.42 ± 4.2 weeks of gestation and the Silverman score of 5.05 ± 2.06.

Table 2 shows the maternal variables of patients with RDS. The most frequent variable was cesarean delivery, with a percentage of 82.1%, and the maternal age group between 20-35 years was 64.9%. Among the comorbidities classified as "others", urinary tract infection and leukorrhea occurred in 43.0% of the cases. The percentage of patients who received prophylactic treatment for RDS based on injectable steroids was 64.6%.

**Table 1.** Central tendency measures of patients with RDS

| | Gestational age (weeks) n = 302 | Silverman Score n=302 |
|---|---|---|
| Average | 33.42 | 5.07 |
| Median | 3. 4 | 5 |
| Fashion | 3. 4 | 3 |
| Standard deviation | 4,239 | 2,056 |
| Minimum | 24 | 1 |
| Maximum | 41 | 8 |

**Table 2.** Maternal variables of patients with RDS.

| Variable | Frequency n=302 | Percentage |
|---|---|---|
| **Type of delivery** | | |
| Cesarean section | 248 | 82.1% |
| eutocic | 54 | 17.9% |
| **maternal age** | | |
| < 20 years | 25 | 8.3% |
| 20-35 years | 196 | 64.9% |
| **> 35 years** | 81 | 26.8% |
| **Maternal morbidity** | | |
| Arterial hypertension | 62 | 20.5% |
| preeclampsia | 110 | 36.4% |
| Others | 130 | 43.0% |
| **Prophylactic treatment*** | | |
| Yes | 195 | 64.6% |
| Nope | 107 | 35.4% |

* Maternal treatment for fetal maturation with steroids.

Among the neonatal variables, gestational age between 28-36 SG was 51.0%, male sex was 53.1%, Mestizo race was 87.1%, there were no genopathies 97.0%, neonatal sepsis was 66.2% and who did not receive surfactant factor (SF) was 70.2%. In the same way, the degree of severity was studied according to clinical assessment and radiological patterns. The severity of neonatal RDS was assessed according to the Silverman scale and showed that most patients presented moderate RDS with a percentage of 39.1%, different from the Downes assessment, which showed a higher frequency of mild RDS at 50.0%. The radiological pattern showed a prevalence of fine reticular infiltrates of 43.0%, which translates into mild respiratory distress of 43.0%.

**Table 3.** Neonatal variables of patients with RDS.

| Variable | Frequency n=302 | % |
|---|---|---|
| **Silverman scale** | | |
| Mild | 94 | 31.1% |
| Moderate | 118 | 39.1% |
| Severe | 90 | 29.8% |
| **Downes Rating *** | | |
| Mild | 151 | 50.0% |
| Moderate | 82 | 27.2% |
| **Serious** | 69 | 22.8% |
| **Radiological pattern** | | |
| Fine reticular infiltrates | 130 | 43.0% |
| Fine reticulo-nodular infil- | 57 | 18.9% |
| ground glass pattern | 57 | 18.9% |
| Not defined/not reported | 43 | 14.2% |
| Reticulonodular opacity | 15 | 5.0% |
| **Radiological assessment** | | |
| Mild | 130 | 43.0% |
| Moderate | 57 | 18.9% |
| Serious | 15 | 5.0% |
| Very serious | 57 | 18.9% |
| Not classified/not referred | 43 | 14.2% |

Downes - Ferrés Scale (Bronchiolitis), based on the presence of wheezing, retractions, respiratory rate, heart rate, air entry, and cyanosis.

### Risk factors.

The study variables for the severe Silverman score outcome are presented in Table 4. The risk factors were cesarean section, preeclampsia, gestational age less than 28 weeks, and male sex, and a protective factor was gestational age greater than 36 weeks.

**Table 4.** Risk factors for the presence of severe RDS.

| Variable | Silverman: Mild + moderate n=212 | Silverman: Severe N=90 | OR | CI 95% | *P* |
|---|---|---|---|---|---|
| **Type of delivery** | | | | | |
| Cesarean section | 188 (88.7%) | 60 (66.7%) | 3.917 | 2127-7211 | <0.0001 |
| Eutotic delivery | 24 (11.3%) | 30 (33.3%) | | | |
| **Comorbidities** | | | | | |
| AHT | 41 (19.3%) | 21 (23.3%) | 0.788 | 0.434-1.429 | 0.4325 |
| preeclampsia | 69 (32.5%) | 41 (45.5%) | 1.734 | 1.0469-2.8723 | 0.0325* |
| **Gestational age (weeks)** | | | | | |
| <28 GW | 5 (2.3%) | 14 (15.5%) | 7.6263 | 2.6569-21.8901 | 0.0002 |
| 28-36 GW | 105 (49.5%) | 49 (54.4%) | 1.2179 | 0.7427-1.9971 | 0.4347 |
| >36 GW | 102 (48.1%) | 27 (30%) | 0.4622 | 0.2734-0.7815 | 0.0040 |
| Sex | | | | | |
| Men | 91 (42.9%) | 56 (62.2%) | 2.1900 | 1.3210-3.6308 | 0.0024 |
| Woman | 121 (57.1%) | 34 (37.8%) | | | |

AHT: Arterial hypertension. GW: gestational weeks.

## Discussion

At the end of this investigation, the results were obtained based on the stated objectives. The sociodemographic characteristics that were analyzed were significant. Based on the Neonatal Respiratory Distress Syndrome, the highest prevalence of cases occurred at 33 weeks of gestation. The RDS was assessed using the Silverman score with a mean of 5. According to the demographic data of the neonates, the male sex was the most frequent, while the age group between 28 and 36 weeks of gestation was the most common, which translates into preterm pregnancies being risk factors for the development of respiratory distress syndrome. These data coincide with previous reports, where RDS affected male neonates more than 66% [ 17, 18 ]. This prevalence is due to delayed fetal lung maturation in men, which is associated with epidermal growth factor.

The risk factors identified in this study are summarized in neonates with a gestational age of 33 GS on average (preterm deliveries), males, and with a history of neonatal sepsis, to which maternal factors are added where it was more prevalent. During a cesarean delivery, 21% had gestational hypertension and were women between 20 and 35 years old. Having genopathies was not significant for the development of RDS; in addition, most of the pregnant women were of the Hispanic race due to the region in which the research was carried out; therefore, it is not considered significant either. At least 30% of the neonates with RDS presented asphyxia before the Silverman test. These data are related to those of Chowdhury Naema et al. [8 ], who reported in their study that only 5% of patients with RDS delivered at term, that is, premature infants have a high incidence of developing the syndrome, and agreed that the presence of neonatal sepsis also increased the risk.

Armas and López also [9 ] agreed that newborns with RDS are primarily male. Additionally, among their objectives was to determine the risk factors where cesarean section and preterm delivery increased morbidity and mortality. Pulmonary involvement Likewise, Jin Hyeon Kim [ 6 ] and Tefera [ 7 ] concluded in their investigations that cesarean section increases the risk of RDS since adequate absorption of fetal lung fluid is not entirely achieved through this delivery route. There is not enough surfactant, and Tefera agreed that neonates delivered by cesarean section develop respiratory morbidities.

The severity of RDS was evaluated using the Silverman, Downes Rating, and image scales. According to the Silverman Scale, most neonates with RDS were moderate, with a mild Downes assessment, and the most frequent radiological pattern was fine reticular infiltrates; it was also mild according to the radiological data. Through this analysis, it was found that the degree of lethality was low. These scales to assess severity allow for determining the prognosis and the efficacy of adequate therapeutic management.

## Conclusions

The risk factors were cesarean section, preeclampsia, gestational age less than 28 weeks, and male sex. A protective factor was gestational age greater than 36 weeks.

### Abbreviations

RDS: respiratory distress syndrome.

## Supplementary information

Supplementary materials are not declared.

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### Author contributions

Stefanía Loor Zambrano: Conceptualization, Data Retention, Fundraising, Research, Resources, Software, Writing - original draft.
Marilyn Urrutia Garcés: Conceptualization, Data Conservation, Supervision, Fundraising, Research, Resources, Writing: review and editing.
Johanna Huacón Mazón: Conceptualization, Data Conservation, Supervision, Acquisition of Funds, Research, Resources.
Fátima Ramírez Carillo: Data curation, research, fundraising, Supervision, Methodology.
Cindy Lara Morales: conceptualization, data retention, supervision, supervision, methodology.
All authors read and approved the final version of the manuscript.

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### Availability of data and materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality but are available through the corresponding author upon reasonable academic request.

## Statements

### Ethics committee approval and consent to participate

It was not required for a retrospective database study.

### Publication consent

It does not apply to studies that do not publish MRI/CT/Rx images or physical examination photographs.

### Conflicts of interest

The authors declare no conflicts of interest.


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