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Prediction of neonatal respiratory distress outcomes: a multicenter retrospective observational study

Прогнозирование исходов респираторного дистресса у новорожденных: многоцентровое ретроспективное наблюдательное исследование

D.O. Ivanov[1], Yu.S. Aleksandrovich[1,*], D.A. Temirova[1], N.N. Artemev[1], L.V. Kolotilov[1], I.V. Boronina[2], E.V. Dubova[1]

[1] Saint Petersburg State Pediatric Medical University, St. Petersburg, Russia
[2] Voronezh State Medical University, Voronezh, Russia

Д.О. Иванов[1], Ю.С. Александрович[1,*], Д.А. Темирова[1], Н.Н. Артемьев[1], Л.В. Колотилов[1], И.В. Боронина[2], Е.В. Дубова[1]

[1] ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет», Санкт-Петербург, Россия
[2] ФГБОУ ВО «Воронежский государственный медицинский университет им. Н.Н. Бурденко», Воронеж, Россия

Abstract

INTRODUCTION: Respiratory distress (RD) is the most common cause of the development of critical neonatal conditions requiring treatment in the intensive care unit, while the identification of early predictors of an unfavorable outcome of RD is one of the most important tasks of modern neonatology. **OBJECTIVES:** To develop a prediction model for respiratory distress outcomes in newborns requiring treatment in the neonatal intensive care unit (NICU). **MATERIALS AND METHODS:** Design — retrospective observational study. 180 newborns were examined, among which there were 109 (61 %) boys and 71 (39 %) girls. The average weight of children was 1620 (1075–2197.5) g, and the gestational age was 31.8 (29–34.5) weeks. The Apgar score in the first minute was 5 (4–7), in the fifth — 7 (6–7) points. The duration of mechanical ventilation was 52 (12.5–242) hours, the duration of treatment in the NICU was 10 (6–19) days. Deaths occurred in 6 (3 %) cases, nine (5 %) children were transferred for further treatment to other hospitals. **RESULTS:** The maximum prognostic significance with respect to outcome was birth weight and gestational age (AUC ROC = 0.80); Apgar score at 1st minute (AUC ROC = 0.71); Silverman-Andersen scores (AUC ROC = 0.73) and nSOFA scores (AUC ROC = 0.74). A mathematical model was developed to assess the probability of an unfavorable outcome of respiratory distress in newborns, including birth weight, Apgar scores at 1st minute and nSOFA organ dysfunction on the first day of life. The model has high predictive power (AUC ROC was 0.865 (p = 0.0001); sensitivity — 84.5 %, specificity — 82 %, accuracy — 86 %).

Реферат

АКТУАЛЬНОСТЬ: Респираторный дистресс (РД) — наиболее частая причина развития критических состояний неонатального периода, требующая лечения в отделении реанимации и интенсивной терапии новорожденных (ОРИТН), при этом выявление ранних предикторов неблагоприятного исхода РД является одной из наиболее важных задач современной неонатологии, решение которой позволит снизить развитие тяжелых осложнений и летальных исходов. **ЦЕЛЬ ИССЛЕДОВАНИЯ:** Разработать модель прогнозирования исходов РД у новорожденных, нуждающихся в лечении в отделении реанимации и интенсивной терапии. **МАТЕРИАЛЫ И МЕТОДЫ:** Дизайн — ретроспективное обсервационное исследование. Обследовано 180 новорожденных, среди которых было 109 (61 %) мальчиков и 71 (39 %) девочек. Средний вес детей составил 1620 (1075–2197,5) г, а гестационный возраст — 31,8 (29–34,5) недель. Оценка по шкале Апгар на первой минуте была 5 (4–7), на пятой — 7 (6–7) баллов. Продолжительность искусственной вентиляции легких была равна 52 (12,5–242) ч, длительность лечения в ОРИТН составила 10 (6–19) сут. Летальные исходы имели место в 6 (3 %) случаях, девять (5 %) детей были переведены для дальнейшего лечения в другие стационары. **РЕЗУЛЬТАТЫ:** Максимальной прогностической значимостью в отношении исхода обладали масса тела при рождении и срок гестации (AUC ROC = 0,80); оценка по шкале Апгар на 1-й мин (AUC ROC = 0,71); оценки по шкале Сильвермана—Андерсен (AUC ROC = 0,73) и шкале

CONCLUSIONS: Independent predictors of an unfavorable outcome of respiratory distress in newborns are birth weight less than 1475 g, Apgar score at 1st minute less than 5 points and nSOFA organ dysfunction on the first day of life more than three points.

Neonatal Sequential Organ Failure Assessment (nSOFA) (AUC ROC = 0,74). Разработана математическая модель для оценки вероятности неблагоприятного исхода РД у новорожденных, включающая массу тела при рождении, оценку по шкале Апгар на первой минуте и по шкале органной дисфункции nSOFA в первые сутки жизни. Модель обладает высокой прогностической мощностью (AUC ROC = 0,865 (p = 0,0001); чувствительность составила 84,5 %, специфичность — 82 %, точность — 86 %). **ВЫВОДЫ:** Независимыми предикторами неблагоприятного исхода РД у новорожденных являются масса тела при рождении менее 1475 г, оценка по шкале Апгар на первой минуте менее 5 балов и по шкале органной дисфункции nSOFA в первые сутки жизни более 3 баллов.

KEYWORDS: infant, newborn, respiratory distress syndrome, critical care outcomes, infant mortality, prognosis

КЛЮЧЕВЫЕ СЛОВА: респираторный дистресс, новорожденные, предикторы, осложнения, неблагоприятный исход

* *For correspondence:* Yuri S. Aleksandrovich — MD, professor, honored scientist of the Russian Federation, head of the department of anesthesiology and intensive care and emergency pediatrics postgraduate education Saint Petersburg State Pediatric Medical University, St. Petersburg, Russia; e-mail: yus.aleksandrovich@gpmu.org

* *Для корреспонденции:* Александрович Юрий Станиславович — заслуженный деятель науки Российской Федерации, доктор медицинских наук, профессор, заведующий кафедрой анестезиологии, реаниматологии и неотложной педиатрии факультета послевузовского и дополнительного профессионального образования ФГБОУ ВО «Санкт-Петербургский государственный педиатрический медицинский университет» Минздрава России, Санкт-Петербург, Россия; e-mail: yus.aleksandrovich@gpmu.org

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Introduction

Respiratory failure or respiratory distress (RD) is the leading cause of admission to neonatal intensive care units (NICUs) [1].

Between 2012 and 2022, 71 studies reported the incidence of neonatal respiratory failure, which ranged from 0.9 % to 84.8 % depending on gestational age [2]. The decline in prevalence with advancing gestational age reflects the morphological and functional immaturity of preterm infants [3].

Respiratory distress in newborns is a pathological syndrome characterized by respiratory disorders of pulmonary and extrapulmonary origin, diagnosed when one or more clinical signs indicate increased work of breathing. When an elevated respiratory rate is insufficient to meet the ventilatory demands of the child, severe respiratory failure develops, characterized by impaired oxygenation (hypoxemia) and/or ventilation (respiratory acidosis).

In the neonatal period, respiratory distress most often results from transient tachypnea of the newborn, neonatal pneumonia, respiratory distress syndrome, intra-amniotic infection, sepsis, asphyxia, or meconium aspiration syndrome [1, 4].

Prematurity, meconium stained amniotic fluid, cesarean delivery, gestational diabetes mellitus, chorioamnionitis, and low Apgar scores are known to significantly increase the risk of respiratory distress in newborns [5–7].

However, the current literature lacks studies evaluating clinical and laboratory parameters and intensive care interventions that may predict the likelihood of an unfavorable course and outcome of respiratory distress. Addressing this gap served as the rationale for conducting the present study.

Objective

This study aimed to develop a predictive model for outcomes of respiratory distress in newborns requiring intensive care.

Materials and methods

Study design: a retrospective, observational, multicenter study was conducted at the neonatal intensive care units of the Perinatal Center of the Leningrad Regional Clinical Hospital and the Perinatal Center of the Voronezh Regional Clinical Hospital No. 1.

Ethical approval was granted by the Local Ethics Committee of Saint Petersburg State Pediatric Medical University, Ministry of Health of the Russian Federation (Protocol No. 1/3, January 21, 2019).

The study involved a retrospective analysis of neonatal medical histories and inpatient records of newborns admitted between January 2019 and February 2021.

Primary stabilization of the condition in the delivery room was performed for all newborns with respiratory disorders manifested by ineffective spontaneous breathing [8, 9].

Non-invasive respiratory support was initiated when the Silverman Andersen Respiratory Severity Score exceeded 4 points. If severe oxygen dependence ($FiO_2 > 0.4$) and symptoms of respiratory failure persisted within 30 minutes after birth, exogenous surfactant («Curosurf», Chiesi, Italy) was administered endotracheally at a dose of 200 mg/kg.

The newborn was transported from the delivery room to the NICU in a transport incubator (ITN-01 incubator by JSC “Production Association Ural Optical and Mechanical Plant named after E.S. Yalamov”, Russia) while continuing non-invasive ventilation with the Stephan Reanimator F120 Mobile (Stephan, Germany).

Non-invasive respiratory support was maintained upon admission to the NICU. If oxygen dependence persisted ($FiO_2 > 0.4$) to maintain target transcutaneous saturation levels (SpO_2 = 90–94 %) and respiratory acidosis persisted (pH ≤ 7.20), infants were transitioned to mechanical ventilation. Appropriate supportive therapy was provided concurrently.

Administered fluid volume, fluid balance, and the vasoactive-inotropic score were evaluated to determine the extent of infusion therapy and hemodynamic support required to maintain optimal cardiac output [10].

$$\text{Vasoactive — inotropic score} = \text{Dopamine}\left(\frac{mcg}{\frac{kg}{min}}\right) + \text{Dobutamine}\left(\frac{mcg}{\frac{kg}{min}}\right) + \text{Epinephrine}\left(\frac{mcg}{\frac{kg}{min}}\right) \times 100 + \text{Norepinephrine}\left(\frac{mcg}{\frac{kg}{min}}\right) \times 100.$$

The mechanical ventilation invasiveness index was calculated using the formula:

$$3800 \,/\, (\text{PIP} - \text{PEEP}) \times f \times pCO_2.$$

The primary outcome assessed in this study was 28-day mortality.

Duration of mechanical ventilation and length of NICU stay served as surrogate endpoints.

A favorable outcome was defined as full recovery without any complications. Unfavorable outcomes included death, occurrence of complications, extended mechanical ventilation, or prolonged NICU care.

A total of 143 parameters were analysed using information from the newborn’s medical history and inpatient records, including anamnesis, clinical-laboratory and instrumental examinations, intensive care interventions, and disease outcomes.

Statistical analysis

Statistical data processing was performed using nonparametric statistics methods. The quantitative characteristics are presented as median and interquartile range (25th and 75th percentiles). The statistical significance of squared deviations between observed and theoretical frequencies was evaluated using the Pearson chi-square test, with the χ^2 concordance coefficient value reported. Differences in ordinal and scale variables were assessed using the Wilcoxon test, with the Z coefficient reported. The diagnostic significance of risk factors was assessed using binary classification with receiver operating characteristic (ROC) curve analysis. Quantitative interpretation was performed by calculating the area under the ROC curve (AUC). Parametric ROC analysis results were reported with standard error, significance level, and 95 % confidence interval (95 % CI). For statistically significant models with an AUC greater than 0.6, the optimal cut-point was determined using the Youden method (Youden index), corresponding to the optimal ratio of sensitivity and specificity. The odds ratio of a factor's effect on the event was calculated using Cochran's test, with significance level, χ^2 statistic, sensitivity, and specificity reported. The level of statistical significance in the study was defined as $p < 0.05$. Mathematical models for outcome prediction were developed using multiple logistic regression.

Results

An analysis was performed on clinical, laboratory, and instrumental examination data from 180 newborns, including 109 boys (61 %) and 71 girls (39 %). The median birth weight was 1620 g (1075–2197.5 g), and the median gestational age was 31.8 weeks (29–34.5). The Apgar score was 5 (4–7) points at 1st minute and 7 (6–7) points at 5th minute. The duration of mechanical ventilation was 52 hours (12.5–242), and the length of NICU stay was 10 days (6–19). Mortality occurred in 6 cases (3 %), and 9 children (5 %) were transferred to other hospitals for further treatment.

Complete recovery was achieved in 83 newborns (47 %), while unfavorable outcomes were observed in 97 (53 %), including 6 fatal cases (3.3 %).

The most frequent complications were intraventricular hemorrhage (12 %), bronchopulmonary dysplasia (5 %), hemodynamically significant patent ductus arteriosus (4 %), retinopathy of prematurity (2 %), and air leak syndrome (2 %). Two or more complications (e.g., bronchopulmonary dysplasia and intraventricular hemorrhage) were diagnosed in 20 % of newborns. Necrotizing enterocolitis was identified in a single case (1 %) associated with intra-amniotic infection.

Statistically significant adverse outcomes of RD were more frequent in neonates with low birth weight of 1160 g (IQR: 890–1750 g), gestational age of 30 (27–32) weeks, and low Apgar scores at both 1st and 5th minutes (5 and 6, respectively) (Table 1).

Poor RD outcomes were associated with longer respiratory support (162.7 hours vs 18 hours) and extended NICU treatment, with a median of 15 days (range 8–36) which was more than double that of infants without complications. Delivery room stabilization was more commonly performed in neonates with RD complications, 93.8 % compared with 86.7 % in the control group, $p < 0.05$. The Neonatal Sequential Organ Failure Assessment (nSOFA) scores demonstrated a moderate positive correlation with adverse outcomes of respiratory distress ($r = 0.436$; $p = 0.001$).

Assessment of clinical and laboratory status revealed that newborns with adverse outcomes of respiratory distress exhibited significantly higher heart rates and lower systolic and mean arterial pressures in the delivery room and during the first day of NICU care compared with those who experienced favorable outcomes.

In infants with complicated respiratory distress, C-reactive protein levels were significantly elevated (1.5 mg/L vs 0.67 mg/L; $p = 0.004$), more than twice the levels observed in the favorable outcome group, and total plasma protein levels were reduced (44 g/L vs 50.3 g/L), both reaching statistical significance (Table 2). A weak positive correlation was observed between the Silverman—Andersen score and venous carbon dioxide tension ($r = 0.35$, $p = 0.045$).

A comparative analysis of intensive care interventions during the first day of NICU treatment revealed that newborns with adverse respiratory distress outcomes required

Table 1. Characteristics of newborns included in the study

Parameters	The value of indicators in groups		*p*
	favorable outcome, *n* = 83	unfavorable outcomes, *n* = 97	
Birth weight, g	1930 (1660–2530)	1160 (890–1750)	**< 0.001**
Body length, cm	45 (42–28)	39 (35–44)	**< 0.001**
Apgar score at 1st minute, points	6 (5–7)	5 (4–6)	**< 0.001**
Apgar score at 5th minute, points	7 (6–7)	6 (5–7)	**< 0.001**
Age gestation, weeks	34 (32–35)	30 (27–32)	**< 0.001**
Silverman—Andersen score, points	3 (2–5)	5.5 (4–7)	**< 0.001**
nSOFA, points	0 (0–2)	4 (2–6)	**< 0.001**
Duration of mechanical ventilation, hours	18 (0–55.3)	162.7 (40.8–540)	**< 0.001**
Duration of treatment in NICU, days	6 (5–10)	15 (8–36)	**< 0.001**
Duration of anhydrous period, hours	0 (0–0.1)	0 (0–1.845)	0.355
Multiple pregnancy, *n* (%)	26 (31.3 %)	13 (13.4 %)	0.04
The need for therapeutic interventions in the delivery room, *n* (%)	72 (86.7 %)	91 (93.8 %)	0.001

Table 2. Clinical and laboratory status on the first day of treatment in NICU

Parameters	The value of indicators in groups		*p*
	favorable outcome, *n* = 83	unfavorable outcomes, *n* = 97	
SpO_2 on the 1st day of life, %	95 (93–97)	94 (92–96)	0.3
Heart rate, on the 1st day of life, bpm	141 (128–150)	148 (139–159)	**< 0.001**
Systolic blood pressure, on the 1st day of life, mm Hg	58 (52–67)	53 (48–59)	**< 0.001**
Diastolic blood pressure, on the 1st day of life, mm Hg	30 (27–36)	30 (24–35)	0.135
Mean blood pressure, on the 1st day of life, mm Hg	40 (36–45)	38 (30.5–43)	0.002
Venous blood pH, in the delivery room	7.259 (7.185–7.332)	7.26 (7.209–7.306)	0.8
Venous blood pH, on the 1st day of life	7.357 (7.31–7.39)	7.35 (7.29–7.39)	0.66
pvO_2, in the delivery room, mm Hg	52.2 (42.5–70)	50.8 (39.6–61.1)	0.228
pvO_2, on the 1st day of life, mm Hg	53.1 (42.5–69.9)	51.45 (43.8–60.5)	0.24
$pvCO_2$, in the delivery room, mm Hg	40.75 (31.8–52.5)	40.4 (33–50.9)	0.94
$pvCO_2$, on the 1st day of life	32.8 (26.7–36.1)	33.1 (28.3–38.9)	0.216
Venous blood HCO_3 in the delivery room, mmol/l	18.3 (16–20.6)	18.5 (16.6–20.2)	0.698
Venous blood HCO_3, on the 1st day of life, mmol/l	18.2 (16.7–19.9)	18.6 (17.1–20.1)	0.354
Venous BE in the delivery room, mmol/l	8.7 (6.1–10.7)	7.3 (5.9–10.2)	0.137
Venous BE, on the 1st day of life, mmol/l	7.0 (4.9–8.7)	7.45 (5.3–9.6)	0.176
Lactate, mmol/l	3.9 (2.41–6.3)	3.7 (2.75–5.05)	0.647
Lactate, on the 1st day of life, mmol/l	2.9 (2.2–4.4)	3.145 (2.2–4.4)	0.675
Hemoglobin, on the 1st day of life, g/l	174 (155–194)	173 (149–190)	0.284
White blood cells, $\times 10^9$/l	12.6 (9.7–18.3)	12.0 (8.7–16.7)	0.26
Platelets, on the 1st day of life $\times 10^9$/l	243 (190–311)	224 (180–287)	0.158
C-reactive protein, on the 1st day of life, mg/l	0.67 (0.1–1.82)	1.5 (0.26–3.7)	0.004
Procalcitonin test, on the 1st day of life, ng/ml	0.215 (0.16–0.405)	0.39 (0.121–7.43)	0.372
Total protein, on the 1st day of life, g/l	50.3 (44–56.4)	44 (39–52.7)	0.001
Alanine aminotransferase, on the 1st day of life, IU/l	10.9 (5.9–21)	10.9 (6.6–22.6)	0.519
Aspartate aminotransferase, on the 1st day of life, IU/l	51.8 (36.4–74.9)	49.7 (34.1–85.7)	0.732

Table 3. Intensive care in the first day

Parameters	The value of indicators in groups		*p*
	favorable outcome, *n* = 83	unfavorable outcomes, *n* = 97	
Intravenous fluid administration, ml/kg/day	73 (69–80)	90 (80–100)	**< 0.001**
Day 1 diuresis, mL/kg	3.17 (2.0–4.3)	3.1 (2.0–4.4)	0.894
Fluid balance on the 1st day of life, %	75 (36–98)	44 (11–100)	0.075
Vasoactive-inotropic score, points	0 (0–0)	0 (0–7)	**< 0.001**
FiO_2, %	0.3 (0.21–0.34)	0.3 (0.25–0.4)	0.07
Positive inspiration pressure, sm H_2O	19 (12–21)	20 (18–22)	0.012
Positive end-expiratory pressure, sm H_2O	6 (6–6)	6 (5–6)	0.753
Energy on the 1st day of life, kcal/kg/day	29 (27–50)	37.7 (28–50)	0.4
SpO_2/FiO_2	193 (133.7–288)	166.7 (130.5–202.4)	0.02
Ventilator invasiveness index	320 (277–438)	317 (243–368)	0.074

more aggressive fluid therapy (90 mL/kg vs 73 mL/kg; $p = 0.000$), greater inotropic-vasopressor support, and higher inspiratory pressures, while their SpO_2/FiO_2 ratios were significantly lower than those in the favorable outcome group (166.7 vs 193; $p = 0.02$) (Table 3).

ROC analysis demonstrated that the most prognostically significant indicators of neonatal outcomes were birth weight and gestational age (AUC ROC = 0.80), Apgar score at 1st minute (AUC ROC = 0.71), Silverman—Andersen score (AUC ROC = 0.73), and nSOFA score (AUC ROC = 0.74) (Table 4).

Univariate models based on intensive care interventions showed similar overall accuracy; however, the need for mechanical ventilation (AUC = 0.81, sensitivity 63.5 %)

Table 4. Prognostic significance of indicators of clinical and laboratory status and intensive care measures in assessing the likelihood of an unfavorable outcome of respiratory distress in newborns

Parameters	Predictive value of indicators					
	AUC ROC	*p*	J index	cut off	sensitivity	specificity
Birth weight, g	0.80	**< 0.001**	0.550	< 1475.00	88.0	66.0
Apgar score at 1st minute, points	0.71	**< 0.001**	0.413	< 5	66.3	75.0
Apgar score at 5th minute, points	0.68	**< 0.001**	0.369	< 6	72.3	64.6
Age gestation, weeks	0.80	**< 0.001**	0.498	< 31	87.9	61.8
Silverman—Andersen score, points	0.73	**< 0.001**	0.408	> 4	79.4	61.4
nSOFA, points	0.74	**< 0.001**	0.379	> 3	58.3	79.5
Heart rate, per/min	0.66	**< 0.001**	0.262	> 136	80.4	45.8
Mean blood pressure, mm Hg	0.68	**< 0.001**	0.249	< 54	65.1	59.8
Total protein, g/l	0.64	0.001	0.252	< 43.4	76.8	48.4
Intravenous fluid administration, 1st day of life, ml/kg	0.77	**< 0.001**	0.531	> 80.5	68.7	84.3
Vasoactive-inotropic score, points	0.67	**< 0.001**	0.331	> 1.5	44.2	88.9
SpO_2/FiO_2, 1st day of life	0.60	0.020	0.204	< 179.57	56.6	63.8
SpO_2/FiO_2, 2nd day of life	0.73	**< 0.001**	0.368	< 186.38	70.6	66.2
The need for invasive ventilation	0.81	**< 0.001**	0.48	> 109.75	63.5	84.3

Table 5. Odds ratio (OR) of adverse outcome

Indicator	OR	95 % CI
Birth weight < 1475 g	14.2	6.4:30.9
Apgar score at 1st minute < 5 points	5.9	3.1:11.3
Apgar score at 5th minute < 6 points	4.7	2.5: 8.9
Age gestation, < 31 weeks	11.8	5.4:25.7
Silverman—Andersen score > 4 points	6.1	3.2:11.9
nSOFA score > 3 points	5.4	2.8:10.6
Heart rate > 136 per/minute	3.5	1.8:6.8
Mean blood pressure < 54 mmHg	2.7	1.5:5.1
Venous blood pH, in the delivery room < 7.2	1.2	0.54:2.8
Total protein, on the 1st day of life, < 43.4 g/l	3.1	1.6:5.9
Intravenous fluid administration on the 1st day of life > 80.5 ml/kg	11.8	5.7:24.6
Vasoactive-inotropic score > 1.5	6.3	2.8:14.1
SpO_2/FiO_2 on the 1st day of life < 179.57	2.2	1.2:4.1
The need for invasive ventilation	9.4	4.5:19.3
Absence of enteral nutrition on the 1st day of life	6.5	3.3:12.8

Table 6. Independent predictors of adverse neonatal respiratory distress outcome

Variables	Regression coefficient B	Standard error	Wald test	*p*
Birth weight	–0.001	0.000	27.842	< 0.001
Apgar score at 1st minute, points	–0.288	0.110	6.892	0.009
nSOFA	0.332	0.082	16.335	**< 0.001**
Constant	3.284	0.785	17.504	**< 0.001**

was less sensitive than the volume of fluid support during the first day in the NICU (AUC = 0.77, sensitivity 68.7 %).

The risk of an adverse outcome in neonatal respiratory distress was increased by the following factors: birth weight < 1475 g (odds ratio [OR] = 14.2, 95 % confidence interval [CI]: 6.4–30.9), gestational age < 31 weeks (OR 11.8, 95 % CI: 5.4–25.7), fluid therapy during the first day > 80.5 mL/kg (OR 11.8, 95 % CI: 5.7–24.6), requirement for mechanical ventilation (OR 9.4, 95 % CI: 4.5–19.3), catecholamine index > 1.5 (OR 6.3, 95 % CI: 2.8–14.1), and Silverman—Andersen score > 4 (OR 6.1, 95 % CI: 3.2–11.9) (Table 5).

Several mathematical models based on patient condition indicators were developed using multivariable logistic regression to help predicting adverse outcomes of neonatal respiratory distress. From a practical standpoint, the model of primary interest comprises three parameters: birth weight, Apgar score at 1st minute, and nSOFA organ dysfunction score (Table 6).

$$\text{Probability of unfavorable outcome of RD} = 1/[1 + e\hat{\ }(-(3.284 + 0.332 \times \text{nSOFA} - 0.001 \times \text{WT} - 0.288) \times \text{Apgar 1})],$$

where: Apgar 1 — Apgar score at 1st minute; nSOFA — Neonatal sequential organ failure assessment score; WT — birth weight.

Model performance assessment revealed high prognostic accuracy for predicting adverse outcomes in neonatal respiratory distress, with an AUC of 0.865 ($p = 0.0001$), sensitivity 84.5 %, specificity 82 %, and overall accuracy 86 % (Figure 1).

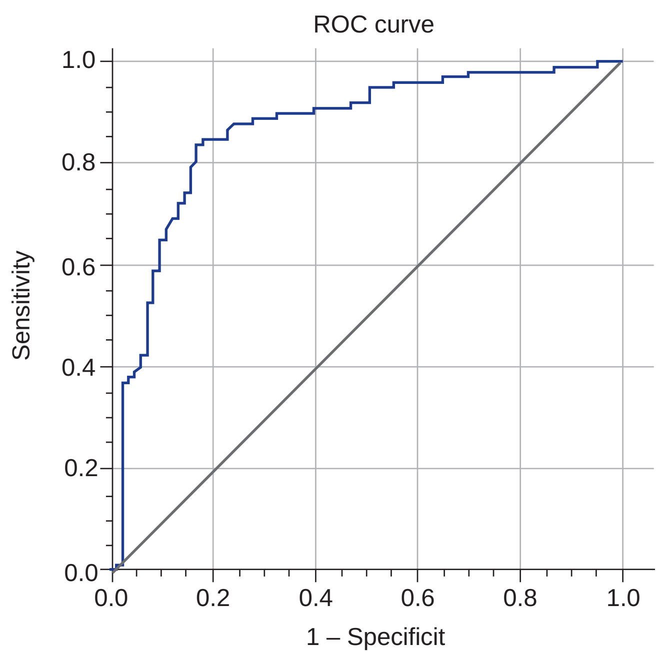

Fig. 1. Discriminatory ability to assess the likelihood of an adverse outcome of neonatal respiratory distress

Diagonal segments generated by links.

Discussion

The diagnosis and assessment of the severity of respiratory distress (respiratory failure) in both adults and newborns are based on clinical symptoms and blood gas analysis.

According to Tochie J.N. et al., there are more than 40 different definitions of neonatal respiratory distress. The most widely cited definition, referenced by ten authors, includes at least two of the following: respiratory rate ≥ 60/min (tachypnea), chest retractions (subcostal, xiphoid, suprasternal, intercostal, or jugular), nasal flaring, expiratory grunting, and cyanosis [2].

Our study showed that the risk of severe neonatal respiratory distress was highest in infants with birth weight < 1475 g, gestational age < 31 weeks, Apgar score at 1st minute < 5, and elevated Silverman—Andersen (> 4) and nSOFA (> 3) scores, consistent with findings reported by other authors [6, 11].

It should be noted that two of the five Apgar score parameters (skin color and respiration) are indirect indicators of respiratory status; therefore, low Apgar scores consistently serve as reliable diagnostic criteria for respiratory distress of various etiologies.

The Silverman—Andersen Respiratory Severity Score is widely used to assess the severity of respiratory distress during the first hours of life [2]. In our study, scores > 4 correlated with increased venous carbon dioxide tension, complications, and prolonged invasive respiratory support, consistent with Hedstrom A.B. et al., who reported that scores ≥ 5 predicted the need for respiratory support [12].

One notable finding of this study is that an nSOFA score greater than 3 within the first day of NICU treatment serves as a reliable marker of adverse neonatal respiratory distress progression. Similar results were reported by Mironov P.I. et al. [13], showing that an nSOFA score greater than 3 raised the risk of adverse outcome in critically ill neonates by 2.5 times (95 % CI: 1.39–4.64, $p = 0.002$).

Meanwhile, the SNAPPE-II (Score for Neonatal Acute Physiology, Perinatal Extension II) remains the most commonly used tool for evaluating illness severity in neonates with respiratory failure, as it also incorporates measures of the infant's respiratory status. Ding S. et al. (2022) demonstrated that median SNAPPE-II scores were strongly correlated with neonatal mortality due to respiratory failure ($r = 0.895$, $p < 0.001$) [14]. In the neonates included in our study, a similar trend was observed, with significantly higher nSOFA scores in patients with severe respiratory distress.

Unlike other authors, we did not observe significant differences between the study groups in hemoglobin oxygen saturation measured by pulse oximetry, regardless of the severity of the course or the outcome of respiratory distress. This likely reflects the lack of severe perfusion or metabolic disturbances due to aggressive respiratory support [15].

We also found that neonates with severe respiratory distress had significantly higher heart rates and lower systolic and mean arterial pressures, accompanied by elevated C-reactive protein levels and reduced total plasma protein. This pattern likely reflects the fact that adverse courses and outcomes of respiratory distress were more common in preterm infants with clinical and laboratory signs of perinatal infections, in whom arterial hypotension occurs in 15–50 % of cases, according to Dempsey E.M. [16]. Similar results have been reported by other authors, demonstrating the clinical and prognostic value of C-reactive protein measurements for early identification of infection in neonates with respiratory insufficiency [17, 18].

Following Cao C. et al. (2024), we consider C-reactive protein may serve as a useful marker for evaluating disease severity, yet it must be interpreted in conjunction with comprehensive clinical and laboratory data and the patient's individual course [19–21].

In our study, low total plasma protein was found to be a prognostically relevant marker of adverse RD course, albeit specificity remained relatively modest (sensitivity 76.8 %; specificity 48.4 %). While we did not assess serum albumin concentration in this study, it can be assumed that neonates with hypoproteinemia also had hypoalbuminemia, which is independently associated with the development of neonatal respiratory distress syndrome. These effects can be attributed to the role of albumin in supporting optimal intravascular volume, fluid balance, and its antioxidant capacity [22].

ROC analysis demonstrated that unfavorable RD progression with complications was associated with prolonged mechanical ventilation, a known risk factor for bronchopulmonary dysplasia or chronic nonspecific lung disorders in the long term [23].

Intravenous fluid therapy is among the aggressive intensive care interventions known to affect patient outcomes. Our study showed that a volume load greater than 80.5 ml/kg on the first day of life, independent of gestational age, raised the risk of adverse RD progression by 11.8 times, attributable to congestive heart failure caused by volume overload [24, 25].

It has been previously shown that in preterm neonates in critical condition, infusion therapy volume should be guided not only by gestational and postconceptional age but also by mean right ventricular pressure and the Neonatal Sequential Organ Failure Assessment score [5].

Study limitations

The principal limitation of the research is the relatively small number of participants and the absence of a control group in which the predictive accuracy of the proposed model could be tested, indicating the necessity for additional investigations.

Conclusion

Newborns experiencing a complicated course of respiratory distress with a high probability of adverse outcomes typically present with birth weight below 1475 g, gestational age under 31 weeks, low 1st minute Apgar scores (< 5 points), and elevated Silverman—Andersen scores (exceeding four points) and nSOFA scores (exceeding three), reflecting the severity of respiratory distress and multi-organ involvement.

Low SpO_2/FiO_2 ratios below 180 within the first day after birth, requiring invasive mechanical ventilation together with aggressive fluid administration and inotropic-vasopressor therapy serves as early predictors of poor respiratory distress outcomes in newborns.

The mathematical model developed to estimate the probability of adverse outcome of respiratory distress in newborns demonstrated strong performance, with sensitivity of 84.5 %, specificity of 82 %, and accuracy of 86 %.

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Author contribution. All authors according to the ICMJE criteria participated in the development of the concept of the article, obtaining and analyzing factual data, writing and editing the text of the article, checking and approving the text of the article.

Ethics approval. This study was approved by the local Ethical Committee of Saint Petersburg State Pediatric Medical University (reference number: 1/3-21.01.2019).

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Data Availability Statement. The data that support the findings of this study are openly available in repository Mendeley Data at https://data.mendeley.com/datasets/yf856mhh5d/1

Author's ORCID:

Ivanov D.O. — 0000-0002-0060-4168
Aleksandrovich Yu.S. — 0000-0002-2131-4813
Temirova D.A. — 0009-0003-2854-8473
Artemev N.N. — 0009-0001-3235-2612
Kolotilov L.V. — 0000-0003-1231-8051
Boronina I.V. — 0000-0003-2266-3297
Dubova E.V. — 0009-0006-3870-9367

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