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Regional pulmonary oxygen saturations in late preterm and term infants with respiratory distress at birth

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Abstract

Background: Measurement of regional pulmonary oxygen saturation by near-infrared spectroscopy is a novel monitorization method. This study aimed to determine the early regional pulmonary oxygen saturations in neonates with respiratory distress.

Methods: This observational study was conducted at the delivery room in infants above 35 weeks of gestation who developed respiratory distress immediately after birth. Preductal oxygen saturation (Covidien Nellcor®) and regional oxygen saturations of both apical ($raSO_2$) and basal regions ($rbSO_2$) of right lung were measured (Covidien INVOS®) within the first 15 min of life and compared to those of healthy neonates.

Results: Of the 165 infants included to the study, 15 were late preterm and 55 developed respiratory distress. Infants with respiratory distress had significantly lower gestational age and birth weight. Regional pulmonary oxygenations at both apex and basal lung areas were positively correlated with SpO_2 in all infants. The $rbSO_2$ was significantly lower than $raSO_2$ until 10th minute of life regardless of respiratory distress. The fractionized tissue oxygen extraction of both apical and basal lung areas was significantly higher in infants with respiratory distress until 5th minute of life.

Conclusion: This study is one of the pioneer studies evaluating the early pulmonary oxygenation values of infants with respiratory distress. Oxygenation of apical lung regions are better than basal areas. Higher fractionized tissue oxygen extraction showed the impaired pulmonary perfusion in infants with respiratory distress.

KEYWORDS

neonate, near-infrared spectroscopy, pulmonary oxygenation, respiratory distress

1 | INTRODUCTION

Transition period after birth consists of many complex physiological processes in both respiratory and cardiovascular systems.[1] Immediately after birth, neonatal oxygen saturations rise within few minutes by the expansion of the lungs.[2] Studies reported that slow rise in peripheral oxygen saturation (SpO_2) needs more than 5 min to reach $SpO_2 > 80\%$ and nearly 10 min to attain SpO_2 value > 90%.[3] The neonates are more vulnerable to hypoxia. Especially preterm infants are at high risk of hypoxic injury due to respiratory insufficiency on one hand and organ injury due to biochemical oxidative stress on the other.[4,5] Therefore, SpO_2 targeting is under debate in infants with respiratory distress.[6]

American Heart Association Neonatal Resuscitation Guideline recently recommends titrating the oxygen use based upon the

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targeted oxygen saturation of newborn infants and starting resuscitation with 21% oxygen in newborns born at 35 weeks' gestation or late.[7] However, monitorization of SpO_2 and heart rate via pulse oximetry may not provide adequate information about oxygen supply of tissues as oxygen delivery depends on organ perfusion and hemoglobin levels especially during the transition period and early hours of life.[6,8] Therefore, monitorization of regional tissue oxygen saturations are important in neonates.

Near-infrared spectroscopy (NIRS) is a common and standard method for measurement of regional oxygen saturation (rSO_2). NIRS is easy to apply, noninvasive and painless tool and monitors tissue oxygenation continuously.[9] NIRS monitorization may allow early recognition of abnormalities in tissue perfusion. Cerebral and mesenteric NIRS have been increasingly and more widely used for monitorization of critically ill neonates. However, pulmonary NIRS is a novel method and there is very limited data about the use of pulmonary NIRS in neonates.[9–11] Although cerebral oxygenation changes in the transitional period has been well defined, only one study reported reference pulmonary NIRS values during transition period in neonates.[10] There exists scarce data about the use of pulmonary NIRS monitorization in neonates with respiratory distress.

Therefore, this study is aimed to define the early pulmonary regional oxygen saturations in infants with respiratory distress just after birth and compare these values with those of healthy newborns without respiratory distress.

2 | MATERIALS AND METHODS

This prospective observational study was conducted at two training and research hospitals between June 2020 and April 2021 after local ethics committee approval (2020.06.90) and obtaining the informed consent. The study was conducted following the principals of the Declaration of Helsinki.

A total of 165 neonates with gestational age >35 weeks were included to the study. The infants with respiratory distress immediately after birth consisted the study group and infants without respiratory distress were defined as the control group. The Silverman-Andersen Score (SAS) was used to assess the severity of respiratory distress. The SAS includes five clinical categories as upper chest movement, lower chest retractions, xiphoid retractions, nares dilatation and expiratory grunting. Each category was scored from 0 to 2, with an infant breathing comfortably receiving a score of "0" and an infant in severe respiratory distress receiving a score of "10" point.[12,13] For the SAS, 0-2 points were accepted as no/mild respiratory distress, 3 points as moderate respiratory distress and SAS ≥ 4 points as significant respiratory distress as it has been reported by Nussbaum et al.[14] All infants with a SAS score ≥3 points received standardized noninvasive ventilatory support as nasal continuous positive airway pressure (n-CPAP) with a positive end-expiratory pressure (PEEP) of 6 cmH_2O. Infants <35 weeks of gestational age, infants with congenital malformations and whose parents disagreed to participate were all excluded. Pulmonary rSO_2 was monitored by NIRS at the apex and base of right lung during the transition period, within first 15 min of life at the delivery room. Right lung had been chosen to prevent the artifact effect of cardiac pulses. The earliest monitorization could be performed at third minute of life.

Antepartum history, perinatal data including gestational age, birth weight, gender, delivery mode, umbilical cord blood gases, cord hemoglobin levels, Apgar scores were all recorded. The same NIRS monitor (INVOS 5100c monitor, Medtronic) with neonatal probs, was used for monitoring the study population for the first 15 min of life for evaluation of pulmonary rSO_2. Also the same pulse oximetry (Nellcor™ Bedside SpO_2 Patient Monitoring System; Medtronic) was used to measure simultaneous preductal arterial oxygen saturation at right wrist. NIRS monitorization probes were located at right lung apex (second intercostal space) and right basal lung areas (seventh intercostal space). Infants who needed resuscitation were managed according to the Neonatal Resuscitation Program Guidelines.[7] Fractional tissue oxygen extraction (FTOE) was calculated from SpO_2 and rSO_2 values.

Statistical analysis was performed by IBM SPSS 22.0 (IBM SPSS for Windows version 22; Armonk). The consistency of continuous variables to normal distribution was tested using the Shapiro Wilk test and histogram plots. Descriptive statistics are given as mean ± standard deviation, median (min–max) for continuous variables and *n* (%) for categorical variables. Mean values were compared by using Mann Whitney U test, categorical values were compared by using Fischer's exact tests, *p*-value of less than 0.05 was considered statistically significant. NIRS values at different time points were compared by using One-way ANOVA test.

3 | RESULTS

During the study period a total of 165 infants were evaluated. Pulmonary rSO_2 of infants who developed respiratory distress immediately after birth ($n = 55$) and healthy controls ($n = 110$) were assessed. Fifteen (9%) of infants were late preterm and 91% were term infants. The mean gestational age and birth weight of infants at birth were 38.4 ± 1.4 weeks and 3324 ± 501 g, respectively. Of these infants, 63% were delivered by cesarean section and 54.5% were male. The mean gestational age and birth weight of infants with respiratory distress were significantly lower than the infants without respiratory distress ($p < .05$). Apgar scores at first and fifth minutes of life and cord blood hemoglobin levels were similar between the groups. Cord blood gases pH values were significantly lower in the study group ($p < .05$). Neonatal resuscitation requirement was significantly higher in infants with respiratory distress ($p < .05$). A total of 21 (38.1%) infants with respiratory distress required oxygen support and 19 (34.5%) of them required more than 30% fractionated oxygen (FiO_2). The mean FiO_2 levels of these infants was 24.4% ± 4.9%. Sixteen (29%) infants needed positive pressure ventilation following the initial steps of resuscitation in the study group, none of those needed intubation nor advanced resuscitation. Positive pressure ventilation was initiated with 21% FiO_2, in infants

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who needed resuscitation and titrated according to the targeted SpO_2 levels. Demographical data about the study and control groups are shown in Table 1.

Earliest preductal SpO_2 measurement and NIRS monitorization could be performed at third minute of life. The median (5%–95%) preductal SpO_2 at 3rd, 4th, and 5th minutes of life was 86% (68%–99%), 90% (74%–100%) and 93% (80%–100%) respectively in the study group and 80% (67%–95%), 85% (73%–97%) and 89% (82–98) respectively in the control group as shown in Table 2. Both median FiO_2 requirement (24.4% vs. 21%, $p < .01$) and the preductal SpO_2 (94% vs. 86%, $p < .01$) of infants with respiratory distress within the first 5 min of life were significantly higher than those without respiratory distress. The preductal SpO_2 after 5 min of life were similar between groups (96% vs. 95%, $p > .05$). The preductal SpO_2 rose to 95.5% (90%–100%) at 10 min and 95.9% (92%–100%) at 15 min of life in the study group; 97.3% (92%–100%) at 10 min and 97.8% (94%–100%) at 15 min of life in the control group ($p > .05$).

Regional pulmonary oxygenation at right lung apex ($raSO_2$) and right basal lung area ($rbSO_2$) were similar between two groups. The median (5%–95%) $rbSO_2$ was significantly lower than $raSO_2$ in both groups until 10 min of life. The FTOE of both apical and basal lung areas was significantly higher in infants with respiratory distress until 5 min of life. The median (5%–95%) $raSO_2$, rbSO2 and FTOE for both groups during transitional period are shown in Table 2. Regional pulmonary oxygenations at both apex and basal lung areas are positively correlated with SpO_2 in all infants with or without having respiratory distress. There was a moderate correlation in infants with respiratory distress for the first 5 min of life in terms of SpO_2 and regional pulmonary saturations ($r > 0.06$). The correlation coefficient in healthy infants without respiratory distress at any time and beyond 5 min of life in infants having respiratory distress was weaker ($r < 0.04$). The SpO_2, regional apical/basal pulmonary saturations and correlation between them are shown in Table 3 minute by minute.

In the study group, 23 infants had respiratory distress beyond the first hour of life despite appropriate noninvasive ventilatory support. Ten (18.2%) of them were hospitalized and 13 (23.6%) were transported to another neonatal intensive care unit. The remaining 32 (58.2%) of the study group recovered from respiratory distress. No significant difference in terms of regional pulmonary oxygenation levels during transition period was detected between infants whose respiratory distress improved or persisted.

4 | DISCUSSION

To the best of our knowledge, this is the first prospective observational study that evaluates early regional pulmonary oxygenation in infants with respiratory distress. Lung tissue extracts more oxygen in infants with respiratory distress until the first 5 min of life but tissue oxygen extraction was found to be similar to healthy infants after 5min. The regional oxygenation of basal lung areas was lower compared to the apical lung areas throughout the transitional period, regardless of having respiratory distress or not.

Regional oxygenation monitorization by NIRS is easy to apply and can be currently used in delivery rooms.[15] NIRS measures oxygenation of a tissue vasculature that mostly contains venous blood. As it reflects the oxygenation of venous blood, NIRS values result from the balance between arterial oxygen supply and tissue

TABLE 1 Demographical data of the infants.

	All infants ($n = 165$)	Study Group ($n = 55$)	Control Group ($n = 110$)
Sex (male) (%)	54.5	54.5	54.5
Delivery mode (C/S) (%)	63	69	60
Gestational age (week)	38.4 ± 1.4	37.9 ± 1.3[a]	38.6 ± 1.4
Birth weight (g)	3 324 ± 501	3 246 ± 508[a]	3 363 ± 483
Apgar 1 min (median)	8	7	9
Apgar 5 min (median)	9	9	10
Neonatal resuscitation need (n) (%)	16 (9.7)	16 (29)[b]	0
Positive pressure ventilation	16 (9.7)	16 (29)	0
Intubation	0	0	0
Oxygen requirement n (%)	21 (12.7)	21 (38.2)	0
Mean FiO_2 (%)	22.1	24.4	21
pH	7.33 ± 0.07	7.29 ± 0.07[a]	7.34 ± 0.07
Base excess	-2.2 ± 3.2	−3.6 ± 3.1[a]	−1.3 ± 2.9
Cord hemoglobin (g/dL)	16.6 ± 1.97	16.3 ± 2.4	0.3 ± 1.6

[a]Mann Whitney U test, $p < .05$.

[b]Fischer's exact test, $p < .05$.

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TABLE 2 Arterial oxygenation and regional oxygenation of lung apex and basal lung areas at transitional period.

	Third minute	Fourth minute	Fifth minute	Tenth minute	Fifteenth minute
Preductal SpO_2, study group	86	90	93	95	95
Median (5–95)	(68–99)[a]	(74–100)[a]	(80–100)[a]	(90–100)	(92–100)
Preductal SpO_2, control group	80	85	89	97	97
Median (5–95)	(67–95)	(73–97)	(82–98)	(92–100)	(94–100)
$raSO_2$, study group	82	89	88	93	93
Median (5–95)	(40–95)	(40–95)	(54–95)	(72–95)	(70–95)
$raSO_2$, control group	79	83	85	85	94
Median (5–95)	(58–95)	(63–95)	(67–95)	(67–95)	(81–95)
$rbSO_2$, study group	79	84	86	89	91
Median (5–95)	(39–94)	(45–95)	(45–95)	(68–95)	(67–95)
$rbSO_2$, control group	78	79	84	87	90
Median (5–95)	(46–95)	(49–95)	(56–95)	(66–95)	(72–95)
FTOE apex, study group	0.12[a]	0.07[a]	0.05	0.05	0.05
Median (5–95)	(−0.14 – 0.56)	(−0.06–0.44)	(−0.09–0.35)	(−0.04–0.23)	(−0.03–0.29)
FTOE apex, control group	0.02[a]	0.03[a]	0.05	0.08	0.05
Median (5–95)	(−0.28–0.27)	(−0.18–0.26)	(−0.09–0.27)	(0.01–0.26)	(0.01–0.18)
FTOE basal lung, study group	0.10[a]	0.08[a]	0.09	0.08	0.06
Median (5–95)	(−0.14–0.44)	(−0.07–0.44)	(−0.0–0.35)	(−0.03–0.28)	(−0.01–0.30)
FTOE basal lung, control group	0.03[a]	0.04[a]	0.09	0.11	0.09
Median (5–95)	(−0.24–0.38)	(−0.16–0.41)	(−0.09–0.35)	(0.01–0.34)	(0.02–0.27)

[a]One-way ANOVA.

TABLE 3 The correlation between SpO_2 and regional pulmonary saturations.

Time after birth (minute)	SpO_2 (%), $raSO_2$ (%), correlation coefficient in infants with respiratory distress	SpO_2 (%), $rbSO_2$ (%), correlation coefficient in infants with respiratory distress	SpO_2 (%), $raSO_2$ (%), correlation coefficient in healthy infants	SpO_2 (%), $rbSO_2$ (%), correlation coefficient in healthy infants
3	86, 82; $r = 0.71$	86, 79; $r = 0.65$	80, 79; $r = 0.35$	80, 78; $r = 0.44$
4	90, 89; $r = 0.68$	90, 84; $r = 0.65$	85, 83; $r = 0.34$	85, 79; $r = 0.34$
5	93, 88; $r = 0.47$	93, 86; $r = 0.53$	89, 85; $r = 0.25$	89, 84; $r = 0.27$
10	95, 93; $r = 0.25$	95, 89; $r = 0.20$	97, 87; $r = 0.04$	97, 85; $r = 0.18$
15	95, 93; $r = 0.14$	95, 91; $r = 0.07$	97, 94; $r = 0.11$	97, 90; $r = 0.07$

oxygen use.[16] Brain oxygenation is most commonly investigated via NIRS in neonates and followed by mesenteric/splanchnic and renal oxygenation.[17,18] Somatic NIRS measurements sought to be more realistic in neonates due to fewer fat and muscle layers in newborn infants compared to adults.[19] Recently, as our group defined the reference ranges and centile charts of pulmonary rSO_2 for healthy neonates, pulmonary NIRS monitoring can also be used in neonates.[10]

Even most of the studies up to date assessed the somatic oxygenation at splanchnic, renal or skeletal muscle areas, the oxygenation of lung tissue is still obscure. Although the penetration depth of 1.0–1.5 cm of NIRS light is appropriate to assess the oxygenation of lung parenchyma, there is a concern about whether NIRS can measure oxygenation of a non-solid air filled tissue accurately.[11] The first study that reveals the oxygenation of lung parenchyma showed that NIRS is technically able to assess quantitatively tissue oxygenation of lung tissue both in vivo and in vitro medium.[20] One of the pioneer clinical study evaluating the regional oxygenation of lung areas was performed by Yang et al. They evaluated regional pulmonary oxygenation in 26 preterm infants and reported that NIRS objectively reflected the changes in oxygenation in the lung tissue.[9] They aimed to define the correlation between

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regional pulmonary oxygenation (pulmonary rSO_2) and SpO_2, arterial partial pressure of oxygen (PaO_2), arterial oxygen saturation (SaO_2). Although pulmonary rSO_2 was found to be positively correlated with both PaO_2 and SaO_2, no significant correlation was detected between rSO_2 and SpO_2.[9] In our study, we found a positive correlation with regional pulmonary oxygenation and SpO_2 in infants both with or without respiratory distress. The correlation in infants with respiratory distress was stronger within the first 5min of life.

The data about lung oxygenation during transitional period is lacking. A recent study described the reference regional pulmonary NIRS values and established the pulmonary oxygenation percentiles for the first 15min of life.[10] We obtained lower $raSO_2$ and $rbSO_2$ levels in infants with respiratory distress when compared to healthy infant percentiles defined by our group.[10] The comparison of $raSO_2$ and $rbSO_2$ values of infants with respiratory distress to normal percentile values, are shown as Figures 1 and 2.

A recent study evaluated postnatal pulmonary oxygenation in 20 preterm infants within the first 24 h of life and demonstrated that regional pulmonary oxygenation was correlated with other oxygenation indices such as SpO_2/FiO_2, arterial/alveolar oxygen tension ratio (a/AO_2) and oxygenation index (O.I). The authors concluded that continuous monitoring of rSO_2 of lung in preterm infants was feasible and correlated with other reliable indices of oxygenation and RDS severity.[11] Apart from this study, there exists no data about the early pulmonary oxygenation in late preterm and term newborn infants with respiratory distress. Our study was performed to clarify the

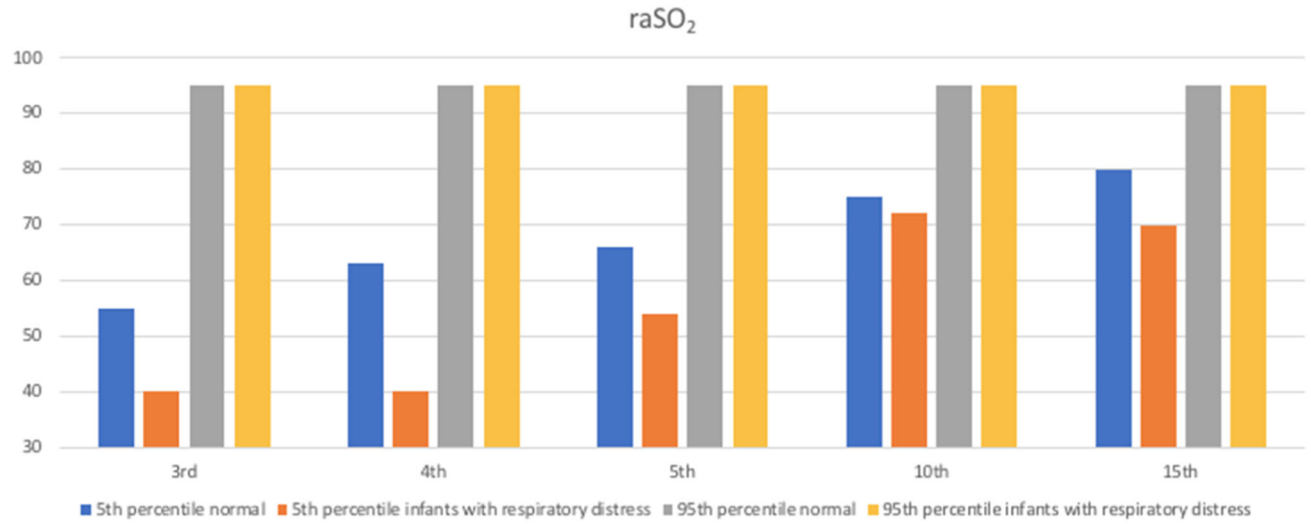


FIGURE 1 The comparison of normal percentile values of $raSO_2$ measurements with that of infants having respiratory distress.

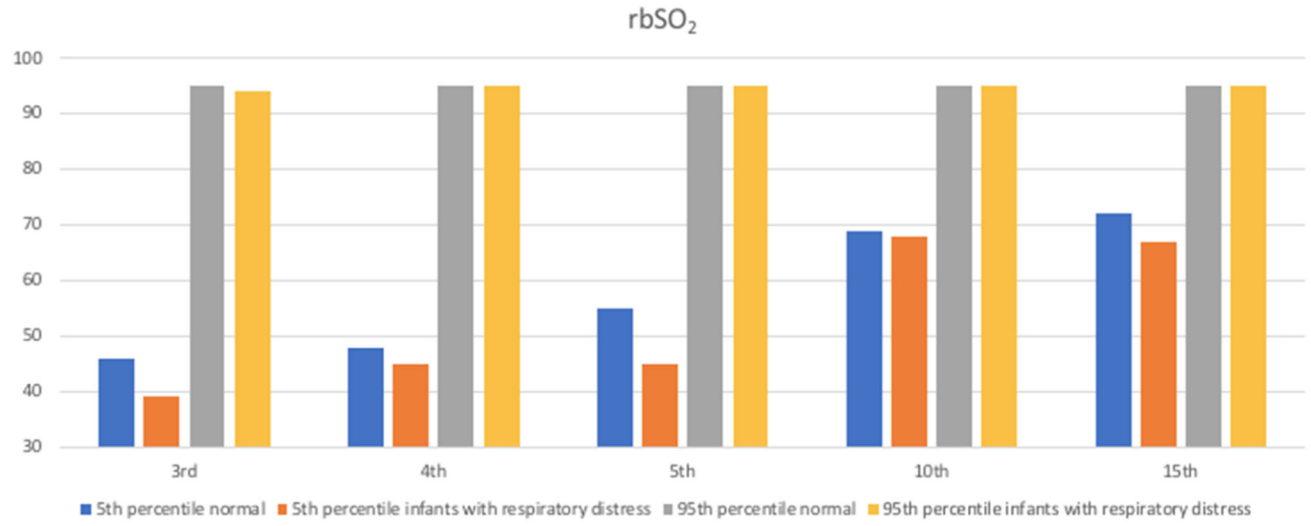


FIGURE 2 The comparison of normal percentile values of $rbSO_2$ measurements with that of infants having respiratory distress.

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regional pulmonary oxygenation in cases of respiratory distress. None of the previous studies evaluating peripheral tissue oxygenation in newborn infants with respiratory distress described the pulmonary rSO_2. We suggest that higher regional pulmonary oxygenation in cases of respiratory distress may be associated with early postnatal oxygen supplementation to these infants.

As no other studies evaluated the pulmonary rSO_2 levels in newborn infants with respiratory distress, we are not able to compare our data with previous studies. However, the oxygenation of basal lung areas was lower than the apical lung areas and this thought to be associated with better aeration of apical lung tissues. In infants with respiratory distress lung tissue needs and extracts more oxygen within the first 5 min of life, which became similar in both groups beyond the 5 minute.

The small sample size and being unable to compare with any data available at the literature are the limitations of our study. In addition, the short duration of early monitorization, evaluation of only late preterm and term infants can also be defined as the other limitations of this study. Therefore, larger clinical studies including especially preterm infants with longer monitorization periods are required to elucidate the role of pulmonary NIRS in neonates with respiratory distress.

As a conclusion, to our best of knowledge, this is the first study evaluated the early pulmonary oxygenation values of late preterm and term neonates with respiratory distress during the transitional period. Even the higher pulmonary rSO_2 during the first 5 min of life in infants with respiratory distress can be associated with early postnatal oxygen supplementation and higher preductal SpO_2, the higher fractionized tissue oxygen extraction showed the impaired pulmonary perfusion in infants with respiratory distress during the transitional period. Further prospective studies are needed to clarify the role of early and late pulmonary rSO_2 evaluation for prediction of hospitalization, invasive or noninvasive ventilation requirement and severity of respiratory distress in neonates. It can be suggested that pulmonary NIRS can be a promising monitorization technique in the delivery room for neonates with respiratory distress.

AUTHOR CONTRIBUTIONS

Beril Yasa: Conceptualization; data curation; writing—original draft; methodology; formal analysis; writing—review and editing; investigation. **Sinem Gülcan Kersin**: Data curation; formal analysis; methodology. **Merih Cetinkaya**: Conceptualization; data curation; formal analysis; visualization; supervision; methodology; writing—review and editing. **Eren Ozek**: Conceptualization; methodology; investigation; supervision; writing—review and editing. **Hulya Bilgen**: Conceptualization; methodology; investigation; supervision.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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