Original Article

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Paediatrics Section

Saturation Oxygenation Pressure Index: A Novel Non-invasive Approach for Evaluating Pulmonary Disease Severity in Neonates on Non Invasive Ventilation

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ABSTRACT

Introduction: Pulmonary disease poses a significant health challenge for neonates, necessitating precise assessment for effective management. Continuous distending pressure is crucial for achieving adequate Functional Residual Capacity (FRC) in these patients. Changes in distending pressure requirements, Fraction of Inspired Oxygen (FiO_2), or both, indicate variations in disease severity. An integrated tool that incorporates these parameters would facilitate an objective evaluation of disease severity. The Saturation Oxygenation Pressure Index (SOPI) tool effectively scores and quantifies severity based on factors relevant to neonates receiving Non Invasive Positive Pressure Ventilation (NIPPV) or Continuous Positive Airway Pressure (CPAP).

Aim: To determine the correlation between SOPI and the Alveolar-Arterial Oxygen Gradient ($AaDO_2$). Additionally, it seeks to establish the cut-off values of SOPI that correspond to $AaDO_2$ values of 70 (mild), 85 (moderate), and 100 (severe) respiratory diseases, respectively.

Materials and Methods: This cross-sectional study took place at MVJ Medical College and Research Hospital in Bengaluru, Karnataka, India from July 2022 to July 2024. It included a cohort of 125 neonates, all with a gestational age of 28 weeks or older, who were admitted to the Neonatal Intensive Care Unit (NICU) due to pulmonary disease and met the defined inclusion and exclusion criteria. The severity of the condition was assessed using SOPI and $AaDO_2$ values. Spearman's correlation was used to analyse the relationship between SOPI and $AaDO_2$ values.

Results: In the present study, the median age of neonates was one day, with an Interquartile Range (IQR) from 1 to 5 days, and there were 86 males and 39 female babies. The study revealed a strong positive correlation between SOPI and $AaDO_2$, with a correlation coefficient of 0.903 (p-value <0.001). Cut-off values for SOPI were established at 1.33 (sensitivity: 99%, specificity: 96.7%), 1.59 (sensitivity: 99%, specificity: 89.8%), and 1.77 (sensitivity: 97.7%, specificity: 67.6%). These thresholds correspond to $AaDO_2$ levels indicative of mild, moderate, and severe respiratory diseases, respectively, and were statistically significant.

Conclusion: A positive correlation exists between SOPI and $AaDO_2$, with a Spearman's correlation coefficient of 0.903 and p-value <0.001, making it a vital non invasive tool for assessing the severity of respiratory distress in neonates and eliminating the need for Arterial Blood Gas (ABG) analysis.

Keywords: Arterial blood gas, Distending pressure, Mechanical ventilation, Respiratory distress

INTRODUCTION

Newborns are considered a vulnerable population due to the abrupt transition from intrauterine to extrauterine life. To facilitate this transition, several changes occur in the lungs, which develop as the primary organ for gas exchange. At birth, five key events take place: the clearance of foetal lung fluid, the establishment of spontaneous breathing, the reduction in pulmonary vascular resistance, the release of surfactant, and the cessation of right-to-left shunting of venous blood returning to the heart [1].

During foetal life, fluid is secreted into the alveoli to support normal growth and function, and this fluid must be cleared before the onset of air breathing [2,3]. A delay in clearance or inadequate resorption can lead to ineffective gas exchange, resulting in respiratory distress and transient tachypnoea in newborns. Assessing the severity of respiratory distress in newborns is essential, and several metrics are commonly utilised, including the PaO_2/FiO_2 ratio, the $AaDO_2$, and the Oxygenation Index (OI). However, the OI has resource implications and cannot be accurately estimated for neonates receiving Non invasive Positive Pressure Ventilation (NIPPV) or Continuous Positive Airway Pressure (CPAP) [4]. Furthermore, non invasive measurements such as the oxygen saturation index and respiratory severity score are not applicable to infants on CPAP or NIV [5,6].

Neonates experiencing respiratory distress require continuous distending pressure to sustain adequate FRC. Changes in the severity of their pulmonary condition are often reflected in the adjustments made to distending pressure, FiO_2, or both [4]. An assessment tool that combines these parameters could offer a more objective evaluation of pulmonary disease severity.

The SOPI uses metrics accessible to neonates receiving NIV or CPAP to objectively assess respiratory illness [4]. It incorporates the relationship between the newborn's respiratory support and the severity of the condition, allowing for near-continuous evaluation of lung disease [7]. Additionally, SOPI reduces the need for invasive blood gas measurements, thereby lowering costs and minimising workload stress [8].

The $AaDO_2$ serves as an objective indicator of lung disease severity [7]. Invasive blood gas analyses and $AaDO_2$ estimates are periodically conducted to assess the condition and inform critical treatment decisions [9]. The integration of SOPI into routine practice

would be significantly enhanced by evidence of its correlation with a disease severity index such as $AaDO_2$ [7].

In 2017, Krishnegowda S et al., evaluated 75 neonates in the Neonatal Intensive Care Unit (NICU) who required CPAP. They found a positive correlation between $AaDO_2$ and SOPI (r=0.847; p<0.0001), with a determination coefficient (R^2) of 0.71. A SOPI value of 1.6 predicted an $AaDO_2$ of 70, indicating severe disease, with 80% sensitivity and 90% specificity. The study concluded that SOPI demonstrated a strong correlation of 84.7% with $AaDO_2$ for assessing the severity of respiratory disease in neonates receiving CPAP. However, present study involved a small sample size and was limited to patients on CPAP, and it did not determine the cut-off values for SOPI corresponding to $AaDO_2$ levels [7].

Hence, the present study was conducted to determine the correlation between SOPI and the Alveolar-arterial Oxygen Gradient ($AaDO_2$). Additionally, it aims to establish the cut-off values of SOPI that correspond to $AaDO_2$ values of 70 (mild), 85 (moderate), and 100 (severe) respiratory diseases, respectively.

MATERIALS AND METHODS

The present cross-sectional study was conducted at MVJ Medical College and Research Hospital, Hoskote, Bangalore, Karnataka, India, from July 2022 to July 2024. Before commencing data collection, the study was approved by the Institutional Ethics Committee (IEC) of MVJ Medical College and Research Hospital (Approval no. MVJMC&RH/IEC-97/2022).

Inclusion criteria: The study included all neonates with a gestational age of 28 weeks or more who were admitted to the NICU with respiratory distress and required Nasal-CPAP or NIPPV support, provided that an ABG analysis was performed. Respiratory distress is characterised by increased Work of Breathing (WOB) manifested through tachypnoea, grunting, chest retractions, and is often associated with reduced air entry and cyanosis. Clinical severity was assessed using the Downes and Silverman Anderson score; however, all subjects were included in the study regardless of their score [10].

Exclusion criteria: Neonates who required mechanical ventilation within half an hour of starting CPAP/NIPPV support were excluded from the study.

Sample size calculation: The sample size was calculated considering a sensitivity of 80% for the SOPI value of 1.52 taken from the article by Doreswamy SM et al., using the formula [4]:

Estimate a sensitivity: $N \geq Z^2_{1-\alpha/2} \times Sens\ (1-Sens)/d^2 \times Prev$

Where Z is the statistical constant (1.96), sensitivity is 80%, d is the allowable error (10%), prevalence is 50% at the 5% level of significance, and for a precision of 90%, we estimated the sample size to be 122. Therefore, we included a minimum of 125 cases (samples) for the study.

Study Procedure

Neonates meeting the eligibility criteria were included in the study after obtaining informed consent. Neonates admitted to the NICU with respiratory distress were managed according to the unit's protocol.

The CPAP/NIPPV (Stephen Sophie, Germany) was the initial mode of respiratory support. The maximum tolerated FiO_2 and CPAP pressure before escalation to mechanical ventilation were 40% and 7 cm H2O, respectively. SpO_2 monitoring was conducted using a Mediana monitor, and SOPI was calculated using the formula ($FiO_2 \times PEEP/SpO_2$). Blood gas analysis was performed one hour after the initiation of NIV, and $AaDO_2$ was calculated using the formula {[(FiO2×(Patm-PH2O)-$PaCO_2$/R)]-PaO_2} [8]. A single SOPI value and its corresponding $AaDO_2$ value were determined for each subject one hour after NIV initiation. The cut-off values for SOPI, which represent the $AaDO_2$ values for mild (70-85), moderate (86-100), and severe (>100) respiratory distress, were based on the previous study by Thandaveshwara D et al., [8].

Baseline demographic characteristics: These included age, sex, birth weight, mode of delivery, the type of respiratory support the baby was on, and the presence or absence of the need for ventilation, along with other parameters (Spearman's correlation and association between SOPI and $AaDO_2$) which were recorded in a predesigned proforma.

STATISTICAL ANALYSIS

The data were collected and compiled in MS Excel. Descriptive statistics were used to present the data. The Statistical Package for Social Sciences (SPSS) version 22.0 software was utilised to analyse the data. The significance level was set at 5% (p-value <0.05). Qualitative variables were presented as proportions, while quantitative data were summarised using either the mean and standard deviation or the median and interquartile range, depending on the distribution. The correlation between SOPI and $AaDO_2$ was assessed using Spearman's correlation (rho), and Receiver Operating Characteristic (ROC) curves were generated through ROC analysis.

RESULTS

In the present study, the majority of the subjects were one day old (88.8%), although their ages ranged from one to five days. The birth weight of the subjects varied from 900 gm to 4100 gm, with most of them weighing 2480 gm. Of the total 125 cases, 86 were male babies, constituting 68.8%, while the rest were female babies [Table/Fig-1].

Characteristics		Values n (%)
Age (days) Median (IQR)		1 (1-5)
Birth weight in (gm) Median (IQR)		2480 (900-4100)
Gender	Male	86 (68.8)
	Female	39 (31.2)
Gestational age	Preterm	53 (42.4)
	Term	60 (48)
	Postdated	12 (9.6)
Mode of delivery	LSCS	86 (68.8)
	NVD	39 (31.2)
Support	CPAP	40 (32)
	NIPPV	85 (68)
Diagnosis	TTN	52 (41.6%)
	RDS	30 (24.0%)
Need of Mechanical Ventilation (MV)- (failure of NIV)	No	94 (75.2)
	yes	31 (24.8)

[Table/Fig-1]: Baseline demographic characteristics of neonates.
RDS: Respiratory distress syndrome; TTN: Transient tachypnoea of the newborn; LSCS: Lower segment cesarean section

A statistically significant correlation was found between SOPI and $AaDO_2$, with a Spearman's correlation coefficient of 0.903 and p-value <0.001 [Table/Fig-2]. The mean SOPI values for mild, moderate, and severe respiratory distress were found to be 2.10±0.381, 2.29±0.236, and 3.34±2.519, respectively. This association was found to be statistically significant [Table/Fig-3].

There exists a statistically significant relation (p-value <0.001) for severe distress cases, with a 94% prediction accuracy. Hence,

Variables	Values
Correlation of SOPI with $AaDO_2$	
Spearman's correlation	0.903
95% Confidence interval	0.863-0.931
p-value	<0.001*

[Table/Fig-2]: Correlation of SOPI with $AaDO_2$.

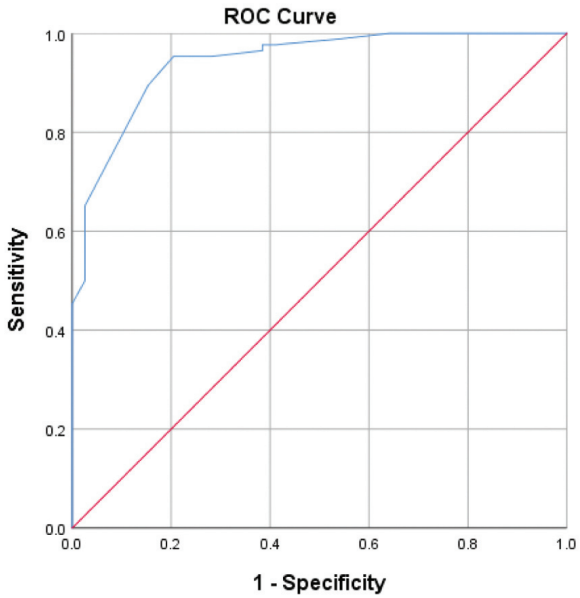
$AaDo_2$ values	n (%)	SOPI Mean±SD		p-value
Normal/No distress (<70)	25	1.845	0.429	0.014*
Mild distress (70-85)	5	2.10	0.381	
Moderate distress (86-100)	7	2.29	0.236	
Severe distress (>100)	88	3.34	2.519	

[Table/Fig-3]: Association of SOPI values with $AaDO_2$ values.

SOPI values have a higher chance of predicting severe cases of respiratory distress according to the $AaDO_2$ values [Table/Fig-4,5].

$AaDO_2$	Area Under the Curve (AUC)	p-value	95% CI Lower bound	95% CI Upper bound
Mild distress (70-85)	0.231	0.042*	0.111	0.351
Moderate distress (86-100)	0.282	0.053	0.180	0.385
Severe distress (>100)	0.942	<0.001*	0.902	0.983

[Table/Fig-4]: Area under the curve of SOPI in predicting $AaDO_2$ value.



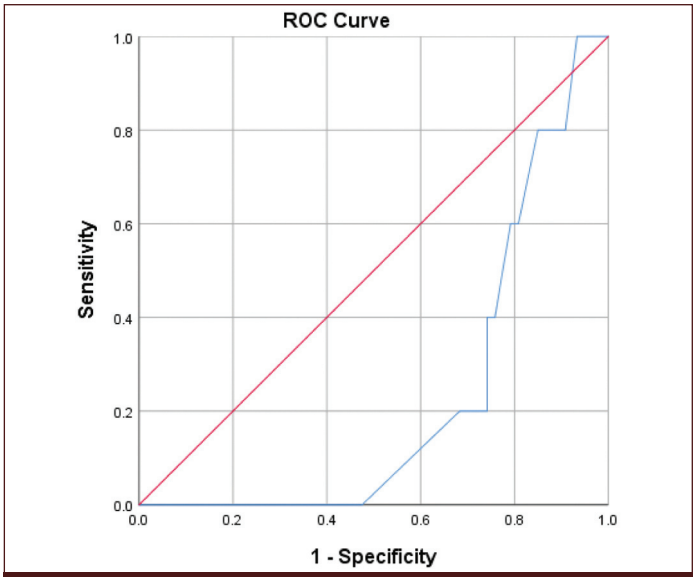
[Table/Fig-5]: ROC curve of SOPI in predicting severe cases respiratory disease ($AaDO_2$).

The cut-off value of 1.33 for SOPI was found to have high sensitivity (99.0%) and high specificity (96.7%) for predicting mild cases. The cut-off value for moderate cases was 1.59, which had high sensitivity (99%) and specificity (89.8%), albeit slightly lower than that for mild cases. For severe cases, the cut-off value was 1.77, exhibiting high sensitivity (97.7%) but lower specificity (67.6%) [Table/Fig-6-8].

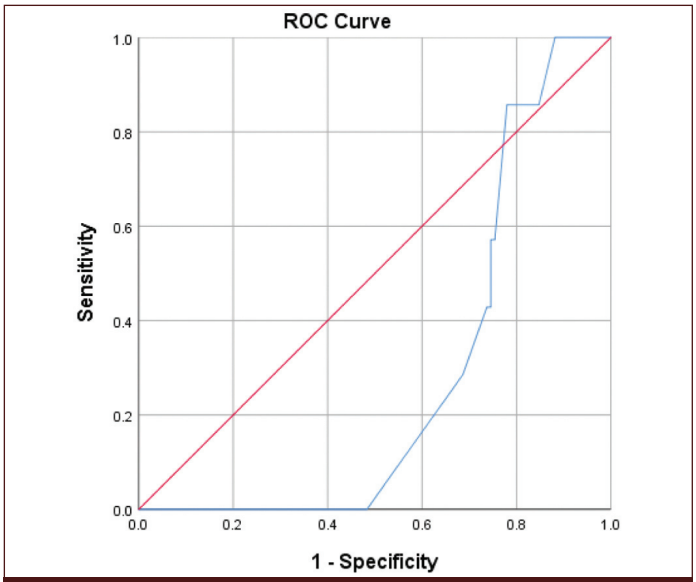
DISCUSSION

The present study was conducted among 125 neonates to evaluate the effectiveness of SOPI as a non invasive tool for measuring the severity of respiratory distress among neonates on NIV, thereby reducing the need for invasive blood gas analysis.

In present study, the majority of the cases were one day old (88.8%), which is consistent with the findings of Krishnegowda S et al., where one-day-old babies constituted the majority [7]. In the study conducted by Thandaveshwara D et al., 80.0% of the subjects were less than 24 hours old [8].



[Table/Fig-6]: ROC curve of SOPI in predicting mild cases respiratory disease ($AaDO_2$).



[Table/Fig-7]: ROC curve of SOPI in predicting moderate cases respiratory disease ($AaDO_2$).

$AaDo_2$ value	Cut-off of SOPI	Sensitivity	Specificity
Mild distress (70-85)	1.33	99%	96.7%
Moderate distress (86-100)	1.59	99%	89.8%
Severe distress (>100)	1.77	97.7%	67.6%

[Table/Fig-8]: Cut-off value of SOPI in predicting $AaDO_2$ value.

In the study by Thandaveshwara D et al., 69.6% of the subjects were male, which is similar to present study, where males accounted for 68.8% [8]. In the study by Krishnegowda S et al., 74% of the cases were males [7].

Approximately 42.4% of subjects in present study were preterm, while 48.0% were term, and 9.6% were post-dated at delivery. In the study conducted by Thandaveshwara D et al., 68.7% were preterm births, and 31.3% were term births [8]. In Krishnegowda S et al., research, 56% were preterm and 44% were term deliveries [7].

In present study, the majority of cases were of normal birth weight (52.8%), with a median birth weight of 2480 gm, ranging from 900 to

4100 gm. This is higher compared to Krishnegowda S et al., where the median birth weight was 2240 gm, ranging between 1485 and 2630 gm [7]. In the study conducted by Thandaveshwara D et al., the median birth weight was 1.650 kg for preterm infants and 2.850 kg for term babies [8].

In present study, normal vaginal delivery was less common (31.2%) compared to LSCS (68.8%). Transient tachypnoea of the newborn was the most frequent diagnosis (41.6%) among the study population, followed by Respiratory Distress Syndrome (RDS) (24.0%), meconium aspiration syndrome (21.6%), and other conditions. In the study conducted by Thandaveshwara D et al., the main indication for N-CPAP was RDS (69.9%), followed by congenital pneumonia (9.6%). Transient tachypnoea of newborns was diagnosed in 8.7%, and meconium aspiration syndrome in 7% [8]. This prevalence is still higher in the study by Krishnegowda S et al., where 79% were treated for RDS [7]. This difference can be anticipated, as the majority of present cases were term babies, making TTN the indication for NIV support.

In present study, 68.0% of the subjects were supported with NIPPV, while 32.0% received N-CPAP, which differs from other studies where all cases were supported exclusively with N-CPAP [4,7,8]. Additionally, 24.8% of the cases experienced failure of respiratory support. In the study by Thandaveshwara D et al., 66.0% of subjects were successfully treated with CPAP [8], whereas in the study by Krishnegowda S et al., 26% experienced failure of NIV [7].

A very high correlation was observed between SOPI and $AaDO_2$ in present study, with a correlation coefficient of 0.903 and p-value <0.001. In the study conducted by Thandaveshwara D et al., a positive correlation was found between the same parameters, with a correlation coefficient of 0.815 (p-value=<0.001) [8]. In the study by Krishnegowda S et al., SOPI was found to have a positive correlation with $AaDO_2$, with a coefficient of 0.847 (p-value <0.001) [7].

The cut-off value of 1.33 for SOPI was found to have high sensitivity (99.0%) and high specificity (96.7%) for predicting mild cases. The cut-off value for moderate cases was 1.59, which also exhibited high sensitivity and specificity, albeit slightly lower than those for mild cases. The cut-off value for severe distress was 1.77, which had a sensitivity of 97.7% and specificity of 67.6%. In the study conducted by Thandaveshwara D et al., SOPI values of 1.52, 1.57, and 1.60 predicted $AaDO_2$ values of 70, 85, and 100 with sensitivity exceeding 80% and specificity greater than 90%, respectively [8]. In the study conducted by Krishnegowda S et al., a SOPI value of 1.60 had a sensitivity of 80% and specificity of 90% in predicting an $AaDO_2$ of 70, which was considered indicative of severe illness [7].

In the study conducted by Doreswamy SM et al., SOPI values of less than 2, 2 to 3.7, and greater than 3.7 indicated mild, moderate, and severe pulmonary disease, respectively, with high sensitivity and specificity [4]. A significant association was also found between the RDS score and SOPI in present study (p-value=0.048). SOPI has the potential to be used for assessing the severity of acute pulmonary disease in infants receiving CPAP and NIPPV.

Limitation(s)

Data were collected from a single rural area of Karnataka with a smaller sample size, which limits the ability to draw causal inferences. A multicentric study would be beneficial in validating the results.

CONCLUSION(S)

In the present study, SOPI serves as a crucial non invasive monitoring tool for evaluating the severity of respiratory distress, as there is a positive correlation (Spearman's correlation of 0.903, with p-value <0.001) between SOPI and $AaDO_2$. It also facilitates continuous monitoring of neonates on NIV, thereby reducing the necessity for invasive blood gas analysis. Future research should focus on determining and validating the optimal SOPI cut-off values for different levels of respiratory distress and various neonatal conditions. Long-term studies are needed to evaluate the prognostic value of SOPI in predicting outcomes for neonates on NIV. Additionally, it would be valuable to compare SOPI with other existing non invasive monitoring tools to assess its relative effectiveness and potential advantages in managing neonates with respiratory distress.

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