Original Research Article

DYNAMIC CHANGES IN ROX INDEX AND PERFUSION INDEX AS EARLY PREDICTORS OF HIGH-FLOW NASAL CANNULA OUTCOME IN PEDIATRIC ACUTE RESPIRATORY DISTRESS: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: High-flow nasal cannula (HFNC) is widely used in paediatric respiratory distress, but early prediction of treatment failure remains challenging. Existing predictors are largely based on static measurements and may not reflect evolving physiology. This study evaluates the role of dynamic changes in ROX index and perfusion index as early predictors of HFNC outcomes. The objective to evaluate the predictive accuracy of dynamic changes in ROX index (ΔROX) and Perfusion index (ΔPI) in determining HFNC outcomes in children with acute respiratory distress, and to compare them with conventional indices.

Materials and Methods: This was a prospective observational study conducted in a tertiary-care PICU. 110 children aged 1 month–18 years initiated on HFNC were enrolled. ΔROX and ΔPI were recorded every 6 hours until 48 hours or escalation. Conventional indices (P/F, S/F, OI, OSI, and lactate) were measured 12-hourly. The primary outcome was HFNC failure (escalation to NIV/intubation). Predictive accuracy was assessed using ROC analysis.

Results: ΔROX and ΔPI consistently outperform all conventional parameters at every time point. ΔROX 0-6 hr (AUC 0.96) is the single best early predictor, while ΔPI 0-6 hr (AUC 0.90) is the best perfusion marker. PF/SF ratio shows steady moderate accuracy up to 48h, but remains inferior to ΔROX and ΔPI. OI/OSI and lactate show fair discrimination only, reinforcing ΔROX and ΔPI indices as superior dynamic predictors.

Conclusion: Dynamic changes in ROX index and perfusion index are reliable early predictors of HFNC outcomes in children with acute respiratory distress. ΔROX, particularly within the first 6 hours, showed the highest predictive accuracy, outperforming conventional static indices. The addition of ΔPI provides complementary insight into perfusion status, enabling a more comprehensive assessment. These dynamic indices can facilitate early identification of HFNC failure and support timely escalation of respiratory care.

Keywords: High-flow nasal cannula; ROX index; Perfusion index; Paediatric respiratory distress; Predictive markers.

INTRODUCTION

Acute respiratory distress is a leading cause of paediatric morbidity and hospital admissions worldwide, particularly in infants and young children, with common etiologies including bronchiolitis, pneumonia, and asthma-like illnesses. The burden is especially significant in low- and middle-income countries, where timely access to advanced respiratory support may be limited. Early recognition and appropriate management of respiratory failure are therefore critical to improving outcomes and reducing mortality.

High-flow nasal cannula (HFNC) therapy has emerged as an effective and increasingly utilized modality for non-invasive respiratory support in children with acute respiratory distress. By delivering heated and humidified oxygen at high flow rates, HFNC reduces nasopharyngeal resistance, washes out dead space, provides a degree of positive airway pressure, and improves oxygenation and ventilation.[1] These physiological advantages have led to its widespread adoption across paediatric intensive care units, emergency departments, and general wards as an alternative to conventional oxygen therapy and, in selected cases, as a bridge to avoid invasive mechanical ventilation.[1,2]

Several studies have demonstrated the clinical benefits of HFNC therapy, including reduced work of breathing, improved oxygenation, and decreased need for intubation in children with respiratory failure. In conditions such as moderate to severe bronchiolitis, HFNC has been shown to reduce treatment failure rates and duration of oxygen therapy compared to conventional oxygen delivery systems.[3] However, despite its effectiveness, a substantial proportion of patients do not respond adequately to HFNC and require escalation to non-invasive or invasive ventilation. In the present study, HFNC failure was observed in 25% of patients, highlighting the ongoing clinical challenge of identifying non-responders early.

Failure of HFNC therapy is clinically significant, as delayed recognition and escalation of respiratory support have been associated with adverse outcomes, including increased mortality. Evidence suggests that delayed intubation following HFNC failure may result in poorer clinical outcomes compared to early escalation, underscoring the importance of timely identification of patients unlikely to benefit from HFNC.[4] Therefore, reliable and early predictors of HFNC outcome are essential to guide clinical decision-making and optimize patient care.

In recent years, several indices and clinical parameters have been evaluated for their ability to predict HFNC outcomes. Among these, oxygenation-based indices such as the ratio of peripheral oxygen saturation to fraction of inspired oxygen (SpO_2/FiO_2 or SF ratio) have been widely studied as non-invasive surrogates for arterial oxygenation. The SF ratio has been shown to correlate well with the PaO_2/FiO_2 ratio and can serve as a practical bedside tool for assessing respiratory status.[5] Lower SF ratios at initiation or failure to achieve improvement within the first few hours of therapy have been associated with higher risk of HFNC failure.[6,7]

The respiratory rate oxygenation (ROX) index, which incorporates both oxygenation and respiratory effort, has gained prominence as a predictor of HFNC success. It has demonstrated good predictive accuracy in both adult and paediatric populations, with specific cutoff values at different time intervals helping to stratify patients at risk of failure.[8,9] Modified indices such as the paediatric ROX (pROX) and other composite scores have further improved predictive performance by incorporating age-specific physiological parameters.[6,10]

In addition to oxygenation indices, clinical scoring systems such as the Clinical Respiratory Score (CRS) and Paediatric Early Warning Scores (PEWS) have also been used to predict disease severity and need for escalation of care. These scores provide a holistic assessment of respiratory distress by incorporating clinical signs, including respiratory rate, retractions, and oxygen requirements, and have demonstrated good predictive value in identifying children at risk of deterioration.[6,11]

Despite these advances, a key limitation of existing predictors is their reliance on static measurements at single time points, which may not adequately reflect the dynamic physiological changes occurring during the course of HFNC therapy. Respiratory failure is a continuously evolving process, and early trends in response to therapy may provide more meaningful insights than isolated measurements. Studies evaluating early changes in parameters such as the SF ratio and ROX index suggest that temporal trends may improve predictive accuracy; however, systematic evaluation of dynamic indices remains limited.[6,7,9]

Furthermore, most existing predictors focus primarily on respiratory parameters, with relatively little attention given to perfusion and circulatory status, which play a crucial role in overall tissue oxygen delivery. The perfusion index (PI), derived from pulse oximetry, is a non-invasive measure of peripheral perfusion and may provide additional information regarding hemodynamic status. However, its role in predicting HFNC outcomes in paediatric respiratory distress remains inadequately explored.

In this context, there is a need to explore dynamic, multimodal predictors that can accurately identify HFNC failure at an early stage. Evaluating changes in indices such as the ROX index (ΔROX) and perfusion index (ΔPI) over time may provide superior predictive performance compared to conventional static parameters. Early identification of non-responders using such dynamic markers could facilitate timely escalation of respiratory support, reduce complications associated with delayed intervention, and improve clinical outcomes.

Therefore, the present study was undertaken to evaluate the predictive accuracy of dynamic changes in ROX index and perfusion index in determining HFNC outcomes in children with acute respiratory distress and to compare their performance with conventional indices.

Objective: To evaluate the predictive accuracy of dynamic changes in ROX index (ΔROX) and Perfusion index (ΔPI) in determining HFNC outcomes in children with acute respiratory distress, and to compare them with conventional indices.

MATERIALS AND METHODS

This Prospective observational analytical study was conducted in the Pediatric Intensive Care Unit (PICU) of Government General Hospital, Vijayawada, Andhra Pradesh, India among Children aged 1 month to 13 years admitted with acute respiratory distress requiring HFNC support. The duration of the study was from April 2025 to August 2025. The sample size 110 was calculated based on the results of previous study done by Roca et al., [8]in 2016 on evaluating ROX index performance in respiratory failure. In that study, the Area under the curve (AUC) for ΔROX was 0.84, with null hypothesis AUC of 0.70, alpha error of 0.05, and power of 80%, the sample size was estimated to be 110. So, a total of 110 children were enrolled in this study. Convenient sampling technique was used to select the study participants who fulfill the eligibility criteria admitted during the study period.

Inclusion Criteria

- Children with clinical diagnosis of acute respiratory distress initiated with HFNC therapy
- Children with parents/guardians willing to give informed consent

Exclusion Criteria

- Children who need immediate intubation at presentation
- Children with severe congenital heart disease
- Children with chronic lung disease

Data collection: After obtaining permission from the Institutional Ethical Committee, data collection was started. The parents of the study subjects were explained about the study, and written informed consent was obtained from each. Data collection was done using the semi-structured questionnaire. Demographic and clinical data including age, gender, diagnosis, and outcome were recorded. At the time of HFNC initiation (baseline, 0 hour), detailed clinical and physiological parameters were recorded. ΔROX and ΔPI were recorded at baseline and every 6 hours up to 48 hours or until escalation. Conventional parameters (P/F ratio, S/F ratio, OI, OSI, lactate) were recorded every 12 hours. Patients were followed up for 48 hours after HFNC initiation. Based on clinical course, patients were categorized into: **HFNC Success**: No escalation of respiratory support within 48 hours. **HFNC Failure**: Requirement of escalation to non-invasive ventilation (NIV) or invasive mechanical ventilation

Statistical analysis: Data were entered into a Microsoft Excel spreadsheet and analysed using SPSS Version 20.0(trial version). Qualitative data were expressed in frequencies and percentages. Quantitative data were expressed in mean and standard deviation. The diagnostic attributes of various indices were analysed in terms of sensitivity, specificity, PPV, NPV. ROC curve analysis was used to evaluate the predictive value of each index for HFNC outcomes and for the aforementioned statistical tests, a p-value of < 0.05 was considered as statistically significant.

Ethical consideration: Informed consent was obtained from the parents/guardians of the study subjects. The doubts of patients were answered to avoid any confusion. No inconvenience was caused to the subjects. Confidentiality was maintained throughout the study.

RESULTS

The study had a total of 110 participants. The mean (±SD) age of the participants was 3.72(±3.35) years. Out of the total participants, 67(60.9%) were male children and 43(39.1%) were female children. On the basis of diagnosis, majority of the children (40.9%) were suffered from bronchiolitis, 34.5% were diagnosed with pneumonia, 16.4% had asthma-like illness.

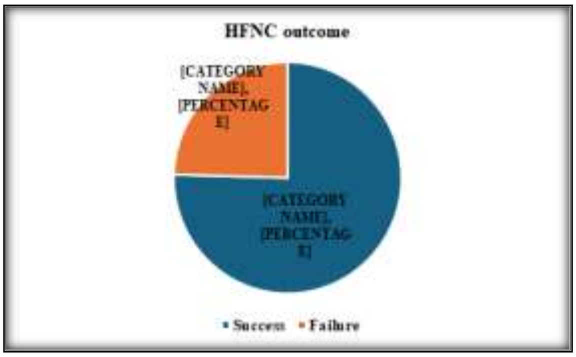

Figure 1: Distribution of participants based on HFNC outcome

Diagnostic accuracy of Delta ROX in predicting HFNC outcome: The ΔROX index maintained an exceptionally high predictive strength across all time points. The 0-6-hour measurement showed the best overall diagnostic performance with perfect specificity and highest AUC, indicating strong early prediction of HFNCoutcome. At 0–12 hour and 0–24-hour interval diagnostic accuracy remained high with balanced sensitivity and specificity. The 0–48-hour measurement provided the highest negative predictive value, making it useful for identifying patients unlikely to fail HFNC therapy. All Delta

ROX measurements were statistically significant predictors of HFNC outcome (p < 0.001).

Table 1: Diagnostic accuracy of Delta ROX in predicting HFNC outcome

	Sensitivity	Specificity	PPV	NPV	AUC	p-value
Delta ROX- 0to6h	92.8%	100%	100%	81.8%	0.964	<0.001
Delta ROX-0to12h	90.4%	96.3%	98.7%	76.5%	0.933	<0.001
Delta ROX-0to24h	95.2 %	81.5%	94%	84.6%	0.883	<0.001
Delta ROX-0to48h	95.2%	88.9%	75.5%	96.3%	0.920	<0.001

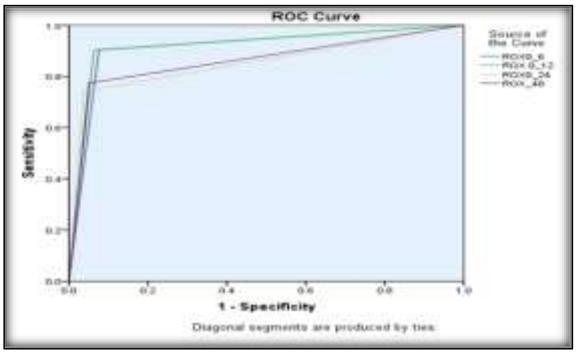

Figure 2: ROC curves showing excellent diagnostic accuracy of ΔROX levels at various intervals in diagnosing HFNC Outcome

Diagnostic accuracy of Delta PI in predicting HFNC outcome

[Table 2] shows that Delta PI is an effective predictor of HFNC outcome at all evaluated time intervals. The 0–6-hour Delta PI measurement demonstrated excellent diagnostic performance with high sensitivity, specificity, and an AUC of 0.902, indicating strong early predictive accuracy. At 0–12 hours and 0–24 hours, diagnostic performance remained good with consistently high specificity and PPV, although sensitivity and NPV showed a gradual decline. The 0–48-hour measurement showed the highest sensitivity and NPV, suggesting improved ability to identify patients likely to fail HFNC therapy at later assessment. All time intervals showed statistically significant predictive value (p < 0.001). The tight alignment of ΔROX and ΔPI curves suggests that their combined interpretation captures the dual physiology of recovery - respiratory and circulatory - within the first 12 hours of HFNC therapy. In contrast, conventional indices—PF/SF ratio, OI, OSI, and lactate showed only fair discrimination, underscoring their slower reflection of physiological improvement. [Figure 8]

Table 2: Diagnostic accuracy of Delta PI in predicting HFNC outcome

	Sensitivity	Specificity	PPV	NPV	AUC	p-value
Delta PI-0to6h	91.6%	88.9%	96.2%	77.4%	0.902	<0.001
Delta PI-0to12h	89.2%	88.9%	96.1%	72.7%	0.828	<0.001
Delta PI-0to24h	86.7 %	88.9%	96%	68.6%	0.891	<0.001
Delta PI-0to48h	97.6%	81.5%	94.2%	91.7%	0.895	<0.001

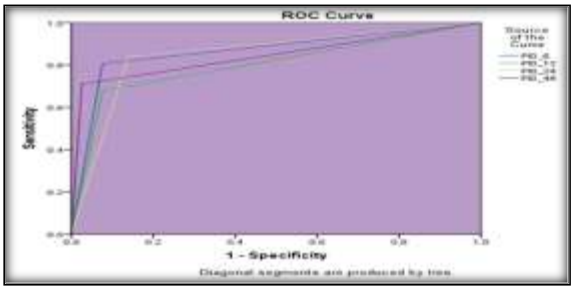

Figure 3: ROC curves showing excellent diagnostic accuracy of ΔPI levels at various intervals in diagnosing HFNC Outcome.

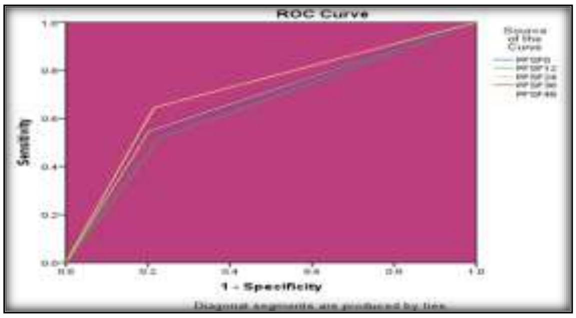

Figure 4: ROC curves showing moderate diagnostic accuracy of PF-SF ratio at various intervals in predicting HFNC Outcome

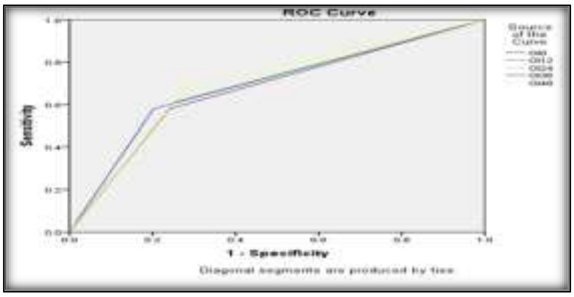

Figure 5: ROC curves showing moderate diagnostic accuracy of OI at various intervals in diagnosing HFNC Outcome

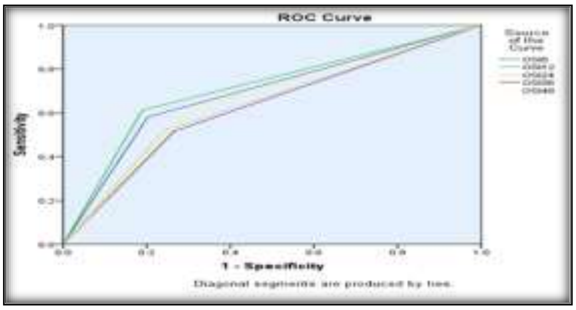

Figure 6: ROC curves showing moderate diagnostic accuracy of OSI at various intervals in diagnosing HFNC Outcome

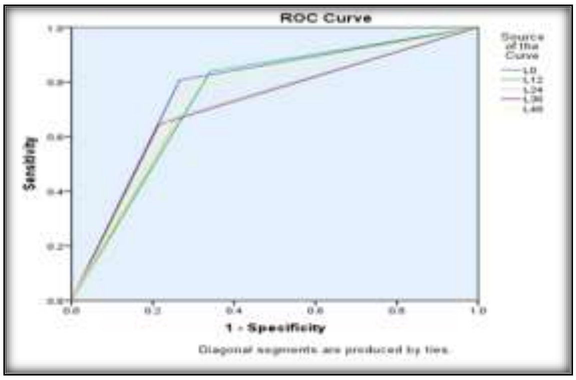

Figure 7: ROC curves showing moderate diagnostic accuracy of lactate levels at various intervals in diagnosing HFNC Outcome

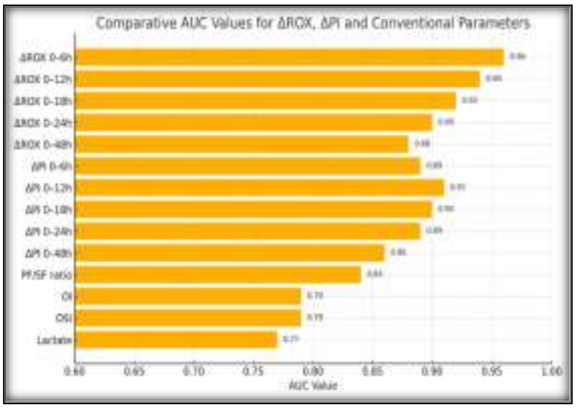

Figure 8: Comparative AUC values for ΔROX, ΔPI and conventional parameters

Table 3: Diagnostic accuracy of PF-SF ratio in predicting HFNC outcome

	Sensitivity	Specificity	PPV	NPV	AUC	p-value
PF-SF ratio - 0hr	85.4%	59.3%	86.4%	57.1%	0.663	0.081
PF-SF ratio - 12hr	84.1%	55.6%	85.2%	53.6%	0.644	0.069
PF-SF ratio - 24hr	82.9%	40.7%	81%	44%	0.673	0.060
PF-SF ratio - 36hr	82.9%	59.3%	86.1%	53.3%	0.679	0.123
PF-SF ratio - 48hr	78.3%	59.3%	85.5%	47.1%	0.715	0.001

Table 4: Diagnostic accuracy of OI in predicting HFNC outcome

	Sensitivity	Specificity	PPV	NPV	AUC	p-value
OI - 0hr	78.3%	59.3%	85.5%	47.1%	0.689	0.081
OI - 12hr	72.3%	59.3%	84.5%	41%	0.680	0.069
OI - 24hr	75.9%	63%	86.3%	45.9%	0.670	0.060
OI - 36hr	69.9%	63%	85.3%	40.5%	0.670	0.123
OI - 48hr	68.7%	63%	85.1%	39.5%	0.699	0.001

Table 5: Diagnostic accuracy of OSI in predicting HFNC outcome

	Sensitivity	Specificity	PPV	NPV	AUC	p-value
OSI - 0hr	72.1%	52.3%	73.3%	51.3%	0.688	0.002
OSI - 12hr	77.1%	55.6%	84.1%	44.1%	0.712	0.001
OSI - 24hr	73.5%	48.1%	81.3%	37.1%	0.638	0.025
OSI - 36hr	71.1%	48.1%	80.8%	35.1%	0.625	0.042
OSI - 48hr	67.7%	62%	84.1%	38.5%	0.655	0.012

Table 6: Diagnostic accuracy of Lactate level in predicting HFNC outcome

	Sensitivity	Specificity	PPV	NPV	AUC	p-value
Lactate - 0hr	71.1%	81.5%	92.2%	47.8%	0.770	0.001
Lactate - 12hr	66.3%	82.6%	86.5%	47.2%	0.748	0.001
Lactate - 24hr	69.9%	63%	85.3%	40.5%	0.706	0.001
Lactate - 36hr	75.9%	63%	86.3%	45.9%	0.715	0.001
Lactate - 48hr	72.3%	85.2%	93.8%	50%	0.745	0.001

DISCUSSION

In the present study, dynamic changes in the ROX index (ΔROX) and perfusion index (ΔPI) demonstrated excellent predictive accuracy for high-flow nasal cannula (HFNC) outcomes in children with acute respiratory distress. Among these, ΔROX within the first 6 hours showed the highest diagnostic performance (AUC 0.96), indicating its strong utility as an early predictor of HFNC success or failure. Overall, HFNC failure was observed in 25% of patients, which is comparable to previously reported failure rates ranging from approximately 12% to 30% in paediatric populations.[6,10,12-15]

Early identification of HFNC failure is clinically crucial, as delayed escalation of respiratory support has been associated with worse outcomes, including increased mortality.[4] This underscores the importance of reliable bedside predictors that can guide timely clinical decision-making. Traditionally, several indices such as the SpO_2/FiO_2 (SF) ratio, ROX index, and clinical scoring systems have been used to predict HFNC outcomes. However, most of these rely on static measurements at single time points, which may not adequately capture the evolving pathophysiology of respiratory distress.

The findings of the present study highlight the superiority of dynamic monitoring, particularly ΔROX, over conventional static indices. Previous studies evaluating the ROX index have demonstrated its usefulness in predicting HFNC success, with cutoff values at different time intervals correlating with outcomes.[8,9] In paediatric populations, modified indices such as pROX have also shown good predictive performance.[6,16] However, these studies primarily assessed ROX values at fixed time points. In contrast, our study demonstrates that changes in ROX over time (ΔROX) provide significantly higher predictive accuracy, suggesting that temporal trends in oxygenation and respiratory effort are more informative than isolated measurements.

Similarly, oxygenation-based indices such as the SF ratio have been widely used as non-invasive surrogates for arterial oxygenation and have shown moderate predictive value for HFNC outcomes.[5,14,15] Lower SF ratios at baseline and failure to achieve improvement early during therapy have been associated with increased risk of HFNC failure.[7,10] While these findings support the utility of SF ratio as a practical bedside tool, our results indicate that its predictive performance remains inferior to ΔROX, particularly in the early phase of therapy. This may be because SF ratio reflects only oxygenation status and does not account for respiratory effort or dynamic physiological changes.

An important novel finding of the present study is the strong predictive value of ΔPI (perfusion index). While most previous studies have focused predominantly on respiratory parameters, the role of perfusion and circulatory status in determining HFNC outcomes has been relatively underexplored. The perfusion index, derived from pulse oximetry, reflects peripheral perfusion and may serve as an indirect marker of systemic hemodynamic status. In our study, ΔPI demonstrated consistently high diagnostic accuracy across all time intervals, with early measurements (0–6 hours) showing excellent predictive performance (AUC 0.90).

The combined interpretation of ΔROX and ΔPI suggests that successful response to HFNC therapy is not solely dependent on improvement in oxygenation but also involves restoration of adequate tissue perfusion. This aligns with the understanding that respiratory failure is a complex interplay between ventilation, oxygenation, and circulatory dynamics. The integration of respiratory and perfusion-based parameters therefore provides a more comprehensive assessment of patient status compared to conventional indices.

In comparison, other clinical predictors such as the Clinical Respiratory Score (CRS) and Paediatric Early Warning Scores (PEWS) have demonstrated utility in identifying children at risk of deterioration.[6,11,12] However, these scores are largely subjective and may vary based on observer interpretation. Moreover, they do not provide continuous quantitative assessment of physiological changes. The objective and reproducible nature of indices such as ΔROX and ΔPI makes them particularly suitable for bedside monitoring and early decision-making.

The present study also compared dynamic indices with conventional parameters such as PaO_2/FiO_2 (PF) ratio, SF ratio, oxygenation index (OI), oxygen saturation index (OSI), and lactate levels. These parameters showed only moderate predictive accuracy, consistent with previous studies.[5,14,15] The relatively lower performance of these indices may be attributed to their delayed response to physiological changes and their inability to reflect the dynamic course of respiratory distress. In contrast, Δ-based indices capture early trends in patient response, enabling more timely identification of non-responders.

Another important implication of our findings is the potential to reduce delays in escalation of respiratory support. Previous evidence suggests that prolonged use of HFNC in non-responders may delay intubation and worsen outcomes.[4] By providing highly accurate early prediction, particularly within the first 6–12 hours, ΔROX and ΔPI can facilitate prompt recognition of treatment failure and guide timely escalation to non-invasive or invasive ventilation.

The strengths of the present study include its prospective design, comprehensive evaluation of both respiratory and perfusion parameters, and repeated measurements over multiple time intervals. The use of dynamic indices provides a novel approach that addresses the limitations of existing static predictors. However, certain limitations should be acknowledged. Being a single-center study, the findings may have limited generalizability. Additionally, the sample size, although adequate for statistical analysis, may limit subgroup comparisons across different etiologies of respiratory distress. Further multicentric studies are required to validate these findings and establish standardized cutoff values for clinical use.

From a clinical perspective, the incorporation of ΔROX and ΔPI into routine monitoring protocols may enhance early risk stratification in children receiving HFNC therapy. These indices are simple, non-invasive, and easily obtainable at the bedside, making them practical tools for use in resource-limited settings. Future research may also explore the integration of these dynamic indices with advanced predictive models, including machine learning approaches, to further improve accuracy and clinical applicability.[17,18]

CONCLUSION

Dynamic monitoring using ΔROX and ΔPI provides highly accurate early prediction of high-flow nasal cannula (HFNC) outcomes in children with acute respiratory distress. Among these, ΔROX within the first 6 hours demonstrated the best overall predictive performance, while ΔPI offered valuable additional insight into the perfusion status, highlighting the importance of integrating both respiratory and circulatory parameters in clinical assessment. Compared to conventional static indices such as SF ratio, PF ratio, and oxygenation indices, dynamic changes showed superior diagnostic accuracy, particularly in the early phase of therapy.

The use of these dynamic indices enables timely identification of HFNC failure, thereby facilitating early escalation of respiratory support and potentially improving clinical outcomes by avoiding delays in intervention. Given their non-invasive nature, ease of measurement, and strong predictive ability, ΔROX and ΔPI can serve as practical bedside tools, especially in resource-limited settings. Further multicentric studies are warranted to validate these findings and to establish standardized cutoff values for broader clinical application.

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