

Original Research Article

Serial changes in oxygenation indices and arterial blood gas parameters during high flow nasal cannula therapy in children with moderate to severe respiratory distress: a prospective observational study

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ABSTRACT

Background: Aims and objectives were to evaluate the impact of high-flow nasal cannula (HFNC) therapy on ABG parameters, oxygenation indices, and clinical outcomes in children with moderate to severe respiratory distress admitted to the PICU.

Methods: This prospective observational study was conducted over 10 months at a tertiary care center. A total of 133 children aged 1 month to 14 years with respiratory distress were included. Severity was assessed using the Pediatric respiratory severity score (PRESS). Clinical and laboratory parameters were recorded at baseline, 1 hour, 12 hours, and 24 hours after initiation of HFNC therapy. Oxygenation indices, including A-a gradient, respiratory index, P/F ratio, S/F ratio, ROX index, and modified ROX index, were analyzed. Statistical analysis was performed using SPSS version 25.0.

Results: Of the 133 children, 90.23% had severe respiratory distress. Significant improvements were observed in heart rate, respiratory rate, and SpO₂ over time ($p < 0.05$). ABG analysis showed significant reductions in pCO₂ and lactate, along with improvements in pO₂, HCO₃, and base excess ($p < 0.05$). Both ABG-dependent and independent oxygenation indices improved significantly within 24 hours ($p < 0.0001$). HFNC failure and need for mechanical ventilation were low (1.5% each). Median ICU and hospital stay were 4 and 6 days, respectively, with 100% survival.

Conclusions: HFNC therapy is a safe and effective non-invasive respiratory support modality in children with moderate to severe respiratory distress. It significantly improves oxygenation, ABG parameters, and clinical outcomes, while reducing the need for invasive ventilation.

Keywords: High-flow nasal cannula, Pediatric respiratory distress, Oxygenation indices, Arterial blood gas, Pediatric intensive care unit

INTRODUCTION

Acute respiratory distress is among the leading causes of pediatric intensive care unit (PICU) admissions worldwide and is associated with considerable morbidity and mortality. Heated Humidified HFNC (HHHFNC) has gained popularity recently and is considered a standard respiratory support tool for pediatric patients with acute respiratory distress. Given the rising use of HFNC in PICUs, there is a need to evaluate its effectiveness not

only in improving oxygenation parameters and ABGs but also in influencing clinical outcomes.

Acute respiratory distress is one of the leading causes of PICU admissions worldwide.^{1,2} Children with moderate to severe respiratory distress often require advanced respiratory support to prevent further deterioration and ensure adequate oxygenation.² Traditionally, invasive mechanical ventilation has been the cornerstone of management in such cases. While effective, it is

associated with significant drawbacks, including ventilator-associated pneumonia, barotrauma, airway injury, prolonged PICU stay, and sedation-related complications.³ These limitations underscore the need for safer, non-invasive respiratory support strategies.

HFNC therapy has emerged as a promising modality in recent years.^{4,5} By delivering heated, humidified oxygen at high flow rates that exceed inspiratory demand, HFNC provides several physiological benefits: improved oxygenation through reduced entrainment of room air, decreased work of breathing via washout of nasopharyngeal dead space, and enhanced secretion clearance owing to optimal humidification.^{4,6} Importantly, HFNC has shown potential in reducing the need for intubation, thereby minimizing the complications associated with invasive ventilation.^{5,7}

Several studies have demonstrated the efficacy of HFNC in infants with bronchiolitis and in children with hypoxemic respiratory failure.^{7,8} However, evidence regarding its impact specifically on ABGs, oxygenation indices, and clinical outcomes in children with moderate to severe respiratory distress remains limited.⁹ Understanding these effects is crucial, as early optimization of non-invasive support may significantly influence morbidity, length of PICU stay, and overall outcomes.

This study aims to evaluate the role of HFNC in improving ABG parameters, oxygenation indices, and clinical outcomes in children admitted with moderate to severe respiratory distress, thereby providing insights into its utility as a frontline non-invasive therapy in the pediatric critical care setting.

To our knowledge, this study is among the few that comprehensively evaluates both ABG-dependent and independent oxygenation indices in pediatric patients receiving HFNC.

Objectives

Objectives were to study the impact of HFNC therapy in children with moderate to severe respiratory distress admitted to PICUs with respect to various ABG dependent and ABG independent oxygen indices along with ABG parameters and clinical outcomes.

Inclusion criteria

Children aged 1 month to 14 years, admitted to PICU with respiratory distress of any etiology were included in the study.

Exclusion criteria

Children aged <1month and >14 years, surgical and trauma cases, children with congenital abnormalities and cerebral palsy children were excluded in the study.

Ethical clearance

This prospective observational study was approved by the institutional ethics committee of Sri Ramachandra Children's and Dental Hospital, Guntur, Andhra Pradesh, India (Approval No. SRCANDDH/EC/1/2021). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from the parents or legal guardians of all participants before enrolment.

METHODS

Type of the study

It was a prospective observational study. This study is reported in accordance with the STROBE guidelines.

Place of the study

Study conducted at Sri Ramachandra Children's and Dental Hospital, Guntur, Andhra Pradesh, India.

Duration of the study

Study conducted for 10 months.

Study subjects

The 133 Infants and children aged between 1 month to 14 years who were admitted with respiratory distress were included in the study.

Participant selection

Eligible participants were enrolled consecutively during the study period. Severity was assessed by PRESS score.

Demographic data was noted. Vital parameters like heart rate, and respiratory rate were noted.

ABG parameters (PH, PCO₂, PaO₂, HCO₃, base excess, and lactate), ABG dependent oxygen indices like AaDo₂, Respiratory index, and P/F ratio, and ABG independent parameters like P/F ratio, ROX index, and modified ROX index were taken at 0, 1, 12, and 24 hours, i. e., at "0" hour means at the time of admission, at "1"hour means approximately 1 hour after initiation of HFNC, at "12"hours means follow up ABGs after initiation of respiratory support, and at "24"hours means daily monitoring as a part of assessment of the child's condition.

Outcome parameters like total ICU stay, total hospital stay, and discharge were noted.

Master sheet was prepared with the collected data, and statistical analysis was done.

Bias control

Consecutive enrollment and standardized time-point measurements were used to reduce selection and measurement bias.

Sample size calculation

Based on repeated-measures analysis with four observations per participant, moderate effect size, alpha 0.05, and power 80%, the minimum sample size was estimated at approximately 128 participants. A total of 133 children were enrolled.

Statistical analysis

Categorical variables were presented as numbers and percentages, while quantitative data were expressed as mean $\pm$ SD (normal distribution) or median with interquartile range (non-normal distribution), with normality assessed by Kolmogorov-Smirnov test.

Non-normally distributed quantitative variables were analyzed using Mann-Whitney or Kruskal-Wallis tests, while normally distributed data were compared using independent or paired t-tests.

Qualitative variables were analyzed using Chi-square or Fisher's exact test, and correlations were assessed with Spearman's rank correlation.

Data entry was done in Microsoft excel and statistical analysis in SPSS version 25.0, with $p < 0.05$ considered significant.

RESULTS

Participant flow

A total of 133 eligible children were enrolled consecutively and included in the final analysis. No major missing data were noted for primary outcomes.

Baseline characteristics

There was male predominance (64.7%). Median age was 0.9 years (IQR 0.3-3.0), and median weight was 7.8 kg (IQR 4.7-11.8) (Table 1).

Table 1: Demographic characteristics.

Demographic characteristics	HFNC, (n=133)
Gender	
Female	47 (35.34%)
Male	86 (64.66%)
Age (in years)	0.9 (0.3-3)
Weight (in kg)	7.8 (4.7-11.8)

Severity of illness

Severe respiratory distress (PRESS 4-5) was present in 120 children (90.2%), while 13 (9.8%) had moderate distress (Table 2).

Table 2: Severity of respiratory distress by PRESS score.

Press score	HFNC, (n=133)
Moderate {2-3}	13 (9.77%)
Severe {4-5}	120 (90.23%)
Total	133 (100%)

Physiological response to HFNC

Trends of Heart rate, respiratory rate, and SpO₂ at "0", "1", "12", and "24" hours

Declining trend was seen in heart rate, and respiratory rate with respect to time. Significant reduction was seen in heart rate, and respiratory rate at follow up as compared to baseline value ($p < 0.05$) Increasing trend was seen in SpO₂ (%) with respect to time. Significant increase was seen in SpO₂ (%) at follow up as compared to baseline value ($p < 0.05$)

Trends of ABG parameters at different time intervals "0", "1", "12", and "24" hours

Significant reduction was seen in pCO₂, Lactate (mmol/L) at follow up as compared to baseline value ($p < 0.05$) Significant increase was seen in SpO₂ (%), pO₂, base excess (mmol/L), HCO₃ (mmol/L) at follow up as compared to baseline value ($p < 0.05$).

Trends of ABG dependent oxygen indices (AaDO₂, respiratory index, and P/F ratio) at different time intervals "0", "1", "12", and "24" hours

Significant reduction was seen in AaDO₂/(PAO₂-PaO₂), respiratory index {AaDO₂/(PAO₂)} at follow up as compared to baseline value ($p < 0.05$) Significant increase was seen in PaO₂/FiO₂ (P/F) ratio at follow up as compared to baseline value ($p < 0.05$).

Trends of ABG independent oxygen indices (S/F ratio, ROX, and modified ROX index) at different time intervals "0", "1", "12", and "24" hours

Increasing trend was seen SpO₂/FiO₂ ratio, ROX index and modified ROX index with respect to time. Significant increase was seen in SpO₂/FiO₂ ratio, ROX index and modified ROX index at follow up as compared to baseline value ($p < 0.05$) (Table 3).

Clinical outcomes

HFNC failure occurred in 2 children (1.5%). Two children (1.5%) required invasive mechanical ventilation.

Median duration of ICU stay was 4 days (IQR 3-5), hospital stay was 6 days (IQR 5-7), and HFNC duration

was 2 days (IQR 2-3). All children survived to discharge (Table 5).

Table 3: Trends of ABG dependent (AaDO₂, respiratory index, and P/F ratio) and independent (S/F ratio, ROX, and modified ROX index) oxygen indices.

Parameters	Mean±SD	Median (25 th -75 th percentile)	Range	P value
AaDO ₂ /(PAO ₂ -PaO ₂) at 0 hour	142.71±46.19	140.75 (118.55-168.425)	39.03-280.98	-
AaDO ₂ /(PAO ₂ -PaO ₂) at 1 hour	107.02±45.36	103.57 (75.075-132.975)	6.53-263.28	<0.0001 [¶]
AaDO ₂ /(PAO ₂ -PaO ₂) at 12 hours	95.31±38.98	93.15 (70.3-119.325)	11.78-211.72	<0.0001 [¶]
AaDO ₂ /(PAO ₂ -PaO ₂) at 24 hours	66.79±32.74	62.03 (41.625-82.8)	10.12-219.68	<0.0001 [¶]
Respiratory index {AaDO ₂ /(PAO ₂)} at 0 hour	2.45±1.23	2.47 (1.58-3.233)	0.24-6.31	-
Respiratory index {AaDO ₂ /(PAO ₂)} at 1 hour	1.43±0.99	1.21 (0.705-1.756)	0.04-4.88	<0.0001 [¶]
Respiratory index {AaDO ₂ /(PAO ₂)} at 12 hours	1.25±0.8	1.06 (0.691-1.636)	0.07-3.98	<0.0001 [¶]
Respiratory index {AaDO ₂ /(PAO ₂)} at 24 hours	0.81±0.59	0.63 (0.438-1.009)	0.08-3.34	<0.0001 [¶]
PAO ₂ /FiO ₂ (P/F) ratio at 0 hour	196.52±90.03	163.14 (135.143-222.857)	82.6-506.67	-
PAO ₂ /FiO ₂ (P/F) ratio at 1 hour	271.34±96.22	256.86 (209.429-327.667)	92-560	<0.0001 [¶]
PAO ₂ /FiO ₂ (P/F) ratio at 12 hours	286.2±93.5	281.7 (220-340)	116-583.33	<0.0001 [¶]
PAO ₂ /FiO ₂ (P/F) ratio at 24 hours	336.98±91.66	338.8 (272-398.4)	128.33-556	<0.0001 [¶]
SpO ₂ /FiO ₂ (S/F) ratio at 0 hour	251.81±40.62	262.86 (230-268.571)	120-324.14	-
SpO ₂ /FiO ₂ (S/F) ratio at 1 hour	288.7±38.1	282.86 (268.571-323.333)	178.18-344.83	<0.0001 [¶]
SpO ₂ /FiO ₂ (S/F) ratio at 12 hours	308.93±33.12	326.67 (282.857-330)	192-396	<0.0001 [¶]
SpO ₂ /FiO ₂ (S/F) ratio at 24 hours	347.25±40.17	333.33 (330-396)	196-400	<0.0001 [¶]
ROX index at 0 hour	3.8±0.93	3.77 (3.333-4.332)	1.4-6.97	-
ROX index at 1 hour	5.47±1.14	5.52 (4.714-6.282)	2.61-8.6	<0.0001 [¶]
ROX index at 12 hours	7.12±1.44	7.17 (6.149-8.167)	3.53-11	<0.0001 [¶]
ROX index at 24 hours	9.79±2.02	9.26 (8.684-11)	3.43-16.5	<0.0001 [¶]
Modified ROX index at 0 hour	2.23±0.75	2.16 (1.793-2.53)	0.74-5.03	-
Modified ROX index at 1 hour	3.65±1.06	3.5 (2.956-4.107)	1.61-7.63	<0.0001 [¶]
Modified ROX index at 12 hours	5.36±1.63	5.1 (4.33-6.138)	1.91-11.58	<0.0001 [¶]
Modified ROX index at 24 hours	8.54±2.69	7.85 (6.74-9.549)	2.2-17.31	<0.0001 [¶]

*[¶] Paired t test

Table 4: Outcome distribution of HFNC group.

Outcomes	N	Percentage
Ventilator	2	1.50%
HFNC failure	2	1.50%
Duration of ventilator (days)		
Mean±SD	2.5±0.7	
Median (25 th -75 th percentile)	2.5 (2.25-2.75)	
Range	2-3	

Table 5: Outcome distribution of HFNC group.

Outcomes	HFNC
Discharged	133 (100%)
Duration of ICU stay (days)	4 (3-5)
Duration of hospital stay (days)	6 (5-7)
Duration of HFNC requirement (days)	2 (2-3)

DISCUSSION

The present study evaluated the impact of HFNC therapy on arterial blood gas (ABG) parameters, oxygenation indices, and clinical outcomes in children with moderate to severe respiratory distress admitted to the PICU. Our

findings demonstrated significant improvements in the ABG parameters (pCO₂, pO₂, lactate, HCO₃, base excess), oxygenation indices (AaDO₂, P/F ratio, S/F ratio, ROX index), and clinical parameters (heart rate, respiratory rate, SpO₂) within 1 to 24 hours of initiating

HFNC therapy, reflecting rapid physiological stabilization.

These results are consistent with Chang et al who reported that HFNC significantly improves oxygenation and reduces the need for intubation in children with hypoxemic respiratory failure, supporting its role as a non-invasive alternative to conventional oxygen therapy and mechanical ventilation.¹⁰

Similarly, Milési et al emphasized that HFNC provides improved patient comfort, reduced work of breathing, and better secretion clearance compared to conventional oxygen therapy in pediatric patients.¹¹

Our study also showed a low rate of HFNC failure (1.5%) and ventilator requirement (1.5%), corroborating the findings of Mayordomo-Colunga et al who observed that appropriate patient selection and early application of HFNC are associated with high success rates in avoiding intubation in critically ill children.¹²

A study by Lodeserto et al proved that good responders to HFNC generally show improvements in RR, HR, and work of breathing (WOB) within the first 60-90 minutes.¹³

A study by Kelly et al showed the risk factors associated with HFNC failure were triage respiratory rate greater than 90th percentile for age (odds ratio [OR], 2.11; 95% confidence interval [CI], 1.01-4.43), initial venous PCO₂ greater than 50 mm Hg (OR, 2.51; 95% CI, 1.06-5.98), and initial venous pH less than 7.30 (OR, 2.53; 95% CI, 1.12-5.74). A final diagnosis of bronchiolitis was observed to be protective with respect to intubation (OR, 0.40; 95% CI, 0.17-0.96).¹⁴

In our study children with low levels of SpO₂/FiO₂ ratio, ROX index, and modified ROX index suggestive of worsening clinical condition, required HFNC therapy. In our study children with low SpO₂/FiO₂ ratio, ROX index, and modified ROX at time of admission required more number of days of ICU stay, and Hospital stay. No correlation was seen with PaO₂/FiO₂ ratio. In line with our study, study by Webb et al showed that, among 446 subjects, 111 (24.9%) failed HFNC therapy. HFNC failure was associated with lower ROX and ROX-HR indices at termination compared to HFNC liberation ($p < 0.001$). ROX-HR index < 3 significantly associated with a higher risk of HFNC failure at 1 (AUROC 0.76, $p = 0.01$) and 6 (AUROC 0.81, $p = 0.02$) hours.¹⁵

A study by Kim et al showed that cases of HFNC failure were classified as hypoxic respiratory failure (HRF) or non-HRF (NHRF) depending on the cause of intubation. The ratio of percutaneous oxygen saturation to the fraction of inspired oxygen (S/F), the ratio of S/F to RR (ROX), the ratio of S/F to RR/median RR (ROX-M), and the ratio of S/F to z-score of RR (ROX-Z) were calculated and compared between groups. Of the 152

cases, 45 (29.6%) failed to wean from the HFNC support, of which 21 (46.7%) were HRFs and 24 (53.3%) were NHRFs. The S/F and ROX-M at 6 h and 3 h, respectively, predicted HRF well with a high area under the curve. Initial hypercapnia and low weight were good predictors for NHRF.¹⁶

To our knowledge, this study is among the few that comprehensively evaluates both ABG-dependent and ABG-independent oxygenation indices in pediatric patients receiving HFNC, providing a more detailed insight into physiological changes during early HFNC therapy.

Overall, our findings support the growing body of evidence advocating HFNC as a safe and effective non-invasive respiratory support tool in pediatric critical care, particularly for patients with moderate to severe respiratory distress.

Standardized clinical protocols and larger studies are warranted to optimize its use and define clear indications, failure criteria, and cost-effectiveness in different healthcare settings.

Limitations

The study was conducted at a single tertiary care center, which may limit generalizability of the results to other settings/populations. As a prospective observational study without a control group, causality between HFNC use and observed improvements in oxygenation or clinical outcomes cannot be definitively established. Although 133 patients were included, the sample size remains relatively small for detecting rare outcomes such as HFNC failure/need for mechanical ventilation. The inclusion of respiratory distress from varied etiologies may introduce confounding factors affecting the response to HFNC therapy, but subgroup analysis was not detailed.

Strengths

The study assessed a broad spectrum of outcomes, including ABG parameters, ABG-dependent and independent oxygenation indices, clinical parameters (heart rate, respiratory rate, SpO₂), as well as duration of ICU and hospital stay. Employing the PRESS provided a standardized method to classify the severity of respiratory distress, enhancing comparability. Systematic measurement of key parameters at baseline, 1 hour, 12 hours, and 24 hours allowed tracking of early physiological responses to HFNC therapy. The study used appropriate statistical tests (Mann-Whitney, Chi-square, Spearman correlation) and clearly defined significance thresholds ($p < 0.05$).

CONCLUSION

HFNC therapy demonstrates significant benefits in the management of moderate to severe respiratory distress in

pediatric patients, with marked improvements in oxygenation indices, ABG parameters, and vital clinical signs within a short time of initiation.

Its use is associated with reduced work of breathing, enhanced oxygen delivery, and a low rate of escalation to invasive ventilation, highlighting its effectiveness as a safe, non-invasive respiratory support modality.

Despite some limitations, HFNC presents a promising frontline strategy in the pediatric intensive care setting, potentially reducing morbidity, shortening ICU and hospital stay, and minimizing complications associated with invasive mechanical ventilation.

"With growing evidence supporting HFNC therapy, future multi-center RCTs and standardized protocols will be key to optimizing its implementation and patient selection criteria."

Recommendations

Conduct large-scale multi-center RCTs comparing HFNC with other non-invasive and invasive respiratory support modalities to establish causality and strengthen evidence. Future research should investigate long-term outcomes such as recurrence of respiratory distress, post-discharge morbidity, and neurodevelopmental outcomes. Stratified studies based on the etiology of respiratory distress (e.g., bronchiolitis, pneumonia, sepsis) can provide more targeted recommendations regarding HFNC use. Assess the economic impact of HFNC therapy compared to conventional oxygen therapy and mechanical ventilation, considering hospital resource utilization and cost savings. Developing standardized clinical protocols and clear criteria for HFNC initiation and weaning could improve uniformity of care and allow benchmarking across centers. Exploring biomarkers predictive of HFNC success or failure may help in early identification of patients requiring escalation of care.

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