

## **High Flow Nasal Cannula Oxygen Therapy as Primary Mode of Treatment in Children Aged 2 Months to 18 Years with Respiratory Distress Admitted into PICU: A Quasi Experimental Study**

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### **Abstract**

**Background:** High-flow nasal cannula (HFNC) oxygen therapy has emerged as a promising non-invasive respiratory support option for pediatric patients with acute respiratory distress. However, its efficacy and safety as a primary mode of treatment in children aged 2 months to 18 years admitted to the Pediatric Intensive Care Unit (PICU) remain underexplored in resource-limited settings.

**Objective:** To evaluate the efficacy and safety of HFNC as the primary mode of respiratory support in children aged 2 months to 18 years with respiratory distress admitted to the PICU.

**Methods:** This quasi-experimental study was conducted at a single-center PICU, enrolling 66 children aged 2 months to 18 years with acute respiratory distress. Patients received HFNC as the initial respiratory support, and outcomes were assessed based on responsiveness (defined as no need for escalation to non-invasive or invasive ventilation), respiratory clinical scores, and modified COMFORT scores at baseline, 60–90 minutes, and 12–24 hours post-initiation. Demographic data, socioeconomic status, locality, underlying medical history, and primary indications were analyzed for associations with responsiveness using SPSS v27, with a significance level set at  $p < 0.05$ .

**Results:** Of the 66 patients, 89.4% responded to HFNC therapy. Significant improvements were observed in respiratory clinical scores (from 11.20 to 6.68,  $p < 0.001$ ) and COMFORT scores (from 32.32 to 23.61,  $p < 0.001$ ) among responders at 12–24 hours. Males (65.2%) showed higher responsiveness ( $p = 0.003$ ), and rural locality (56.1%) was associated with better outcomes ( $p = 0.018$ ). Pneumonia (59.1%) was the most common indication, with significant associations between responsiveness and pneumonia ( $p = 0.010$ ), bronchiolitis ( $p = 0.012$ ), and status asthmaticus ( $p = 0.044$ ). Neurological comorbidities were linked to lower responsiveness ( $p = 0.001$ ).

**Conclusion:** HFNC is a safe and effective primary therapy for pediatric respiratory distress in the PICU, particularly for pneumonia, bronchiolitis, and status asthmaticus, with high success rates and improved clinical outcomes. Its use may reduce the need for invasive ventilation, especially in resource-limited settings.

**Keywords:** High-flow nasal cannula, pediatric intensive care, respiratory distress, HFNC efficacy, non-invasive ventilation.

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### **Introduction**

Respiratory illness is among the most common conditions encountered in routine pediatric practice. Respiratory distress is a leading reason for admission to pediatric intensive care units.

Clinically, respiratory distress encompasses increased work of breathing, obstructed airflow, altered respiratory patterns, and, in severe cases, respiratory failure.[1] It is also one of the principal

presenting complaints in emergency departments, alongside shock, seizures, and altered consciousness. In infants, the cardinal signs include tachypnea, use of accessory muscles, intercostal or subcostal retractions, hypoxemia, grunting, and cyanosis.[2] Pneumonia is the most frequent cause of respiratory illness in children and infants, with additional etiologies including acute bronchiolitis, bronchial asthma, epiglottitis, and neuromuscular disorders.[3]

Sustained respiratory distress with persistent use of accessory muscles leads to fatigue and, over time, progression to respiratory failure.[4] Consequently, respiratory distress contributes substantially to morbidity and mortality among critically ill pediatric patients, and the use of non-invasive ventilation imposes a considerable economic burden on families and health systems. Early identification of children at risk of respiratory failure, followed by prompt, appropriate supportive and targeted care, improves outcomes and reduces complications.[5] The primary therapeutic goals are rapid assessment of airway patency, adequacy of gas exchange, and circulatory status.

Immediate management focuses on correcting hypoxemia and supporting ventilation. These aims are achieved by ensuring a patent airway and delivering oxygen while minimizing agitation.[6] Airway patency can be promoted by optimal positioning; when inadequate, oropharyngeal or nasopharyngeal airways may be inserted. Oxygen desaturation is addressed with supplemental oxygen via nasal cannula or Venturi mask. However, conventional oxygen delivery methods are limited by higher failure rates related to insufficient oxygen flow. A standard nasal cannula typically provides 4–6 L/min, corresponding to an  $FiO_2$  of approximately 0.37–0.45.[7] Flows above this range can dry the nasal mucosa, increasing the risk of epistaxis with prolonged use and impairing the mucociliary function of the nasal and paranasal sinuses.

High-flow nasal cannula (HFNC) therapy mitigates these drawbacks, reducing complications and improving patient comfort and adherence. HFNC is a non-invasive respiratory modality that delivers fully humidified, heated gas mixtures via a nasal interface, with flows up to 60 L/min and  $FiO_2$  up to 1.0.[7] Over the past decade, HFNC has gained broad acceptance for managing critically ill patients across the age spectrum—from preterm neonates to adults—in diverse intensive care settings.[7,8] Against this background, the objective of the present study is to evaluate HFNC therapy as a primary treatment modality for children with respiratory distress, focusing on its safety and efficacy.

### Materials and Methods

This prospective quasi-experimental study evaluated the efficacy of HFNC oxygen therapy as

the primary treatment for children with acute respiratory distress. All eligible participants received HFNC according to a standardized protocol, and pre- and post-intervention assessments were performed to measure responsiveness. The study proceeded without a control group and focused on within-group changes and their associations with demographic and clinical factors. It was conducted in the Pediatric Intensive Care Unit (PICU) of the Department of Pediatrics and Neonatology at Melmaruvathur Adhiparasakthi Institute of Medical Sciences and Research (MAPIMS), Melmaruvathur, Tamil Nadu, India, a tertiary-care teaching hospital affiliated with The Tamil Nadu Dr. M.G.R. Medical University, Chennai. The study population comprised children aged 2 months to 18 years admitted to the PICU with acute respiratory distress, defined by the presence of tachypnea, use of accessory muscles, intercostal or subcostal retractions, hypoxemia ( $SpO_2 < 94\%$ ), grunting, or cyanosis despite initial supportive measures. Exclusion criteria encompassed the need for immediate non-invasive ventilation (e.g., CPAP/BiPAP) or invasive mechanical ventilation, contraindications to HFNC such as facial, nasal, or airway abnormalities or recent surgery preventing appropriate cannula fit, altered sensorium with a Glasgow Coma Scale (GCS) score below 12, shock, refusal or lack of consent, and age outside the 2-month to 18-year range.

Convenience sampling was employed. The sample size was calculated using a 95% confidence level and an anticipated prevalence of responsiveness to HFNC of 40.3% derived from prior literature; the standard formula for prevalence studies yielded a minimum required sample of 66 participants to ensure adequate statistical power. The study ran from January 2023 through June 2024. Upon admission, all eligible patients underwent comprehensive initial assessment that included detailed history taking (symptoms, prior episodes, and comorbidities), physical examination, and targeted laboratory investigations as clinically indicated, such as complete blood count (hemoglobin and platelet count), serum bilirubin, serum albumin, international normalized ratio, prothrombin time, and echocardiography when cardiac involvement was suspected. HFNC therapy was then initiated. The Optiflow™ system (Fisher & Paykel Healthcare, Auckland, New Zealand) or an equivalent device delivered heated, humidified oxygen; flow rates were weight-based at 2 L/kg/min for patients weighing  $\leq 10$  kg, with a maximum of 50 L/min for older children. The fraction of inspired oxygen ( $FiO_2$ ) was titrated to maintain  $SpO_2$  between 92% and 97%. Continuous monitoring captured heart rate, respiratory rate,  $SpO_2$ , and clinical signs of distress.

**Table 1: Sociodemographic and clinical characteristics of the study population**

		Frequency (n)	Percentage (%)
Age	2-23 months	12	18.2
	2-4 years	23	34.8
	5-12 years	22	33.3
	13-18 years	9	13.6
Socioeconomic class	Class I	15	22.7
	Class II	13	19.7
	Class III	12	18.2
	Class IV	26	39.4
Underlying medical history	Neurological disorder	11	16.7
	Hematological disorder/ malignancy	10	15.1
	Respiratory disorder	19	28.8
	Cardiac disorder	9	13.6
Primary indication	Pneumonia	39	59.1
	Sepsis	10	15.1
	Bronchiolitis	20	30.3
	Status asthmaticus	17	25.7
	Neurological disorder, seizures	9	13.6

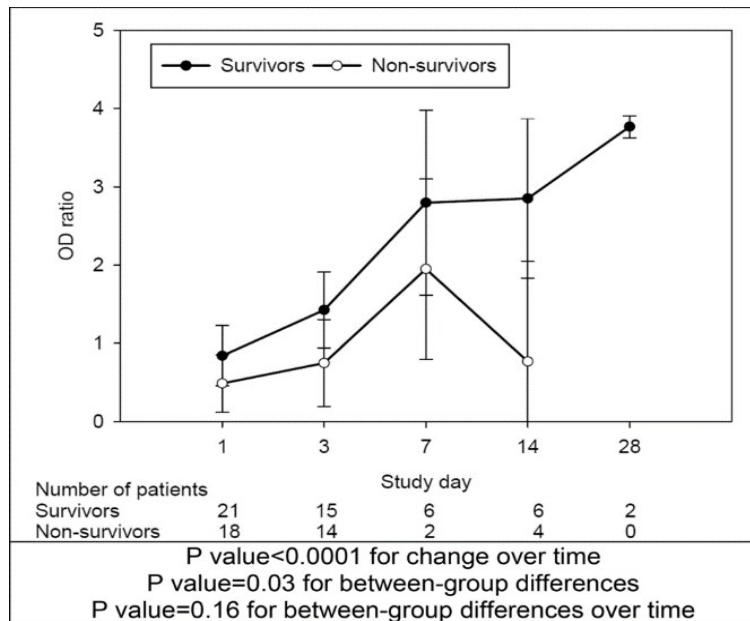
**Table 2: Factors associated with responsiveness to the high-flow nasal cannula**

		Responders (N = 59)		Non-responders (N = 7)		p-value
		n	%	n	%	
Age	2-23 months	11	16.7	1	1.5	0.811
	2-4 years	19	28.8	4	6.1	
	5-12 years	20	30.3	2	3.0	
	13-18 years	8	12.1	1	1.5	
Gender	Male	42	63.6	1	1.5	0.003*
	Female	17	25.7	6	9.1	
SES	Class I	11	16.7	4	6.1	0.137
	Class II	12	18.1	1	1.5	
	Class III	11	16.7	1	1.5	
	Class IV	25	37.9	1	1.5	
Locality	Urban	23	34.8	6	9.1	0.018*
	Rural	36	54.5	1	1.5	
Underlying medical history	Present	42	63.6	7	10.6	0.001*
	Absent	17	25.7	0	0	
Neurological disorder	Present	6	9.1	5	7.6	0.001*
	Absent	53	80.3	2	3	
Hematological disorder	Present	8	12.1	2	3	0.294
	Absent	51	77.3	5	7.6	
Respiratory disorder	Present	18	27.3	1	1.5	0.370
	Absent	41	62.1	6	9.1	
Cardiac disorder	Present	7	10.6	2	3	0.223
	Absent	52	78.7	5	7.6	
Pneumonia	Present	38	57.6	1	1.5	0.010*
	Absent	21	31.8	6	9.1	
Sepsis	Present	8	12.1	2	3	0.294
	Absent	51	77.3	5	7.6	
Bronchiolitis	Present	15	22.7	5	7.6	0.012*
	Absent	44	66.7	2	3	

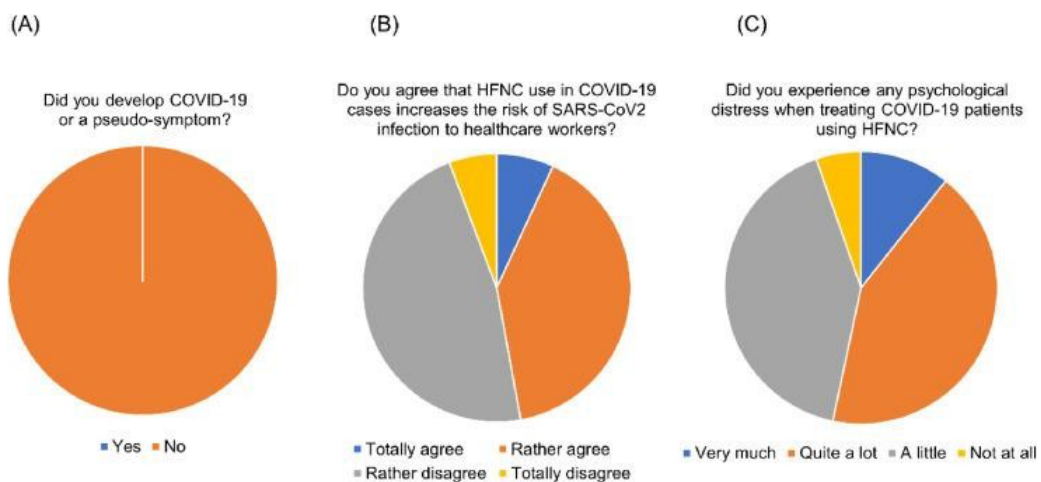
\*Statistically significant at p<0.05

**Table 3: Comparison of responders and non-responders by respiratory clinical scores and COMFORT scores**

	Responders (N = 59)	Non-responders (N = 7)	p-value
	Mean (SD)	Mean (SD)	
Respiratory clinical score – on admission	11.20 (0.85)	11.29 (0.69)	0.403
Respiratory clinical score – 60 to 90 minutes	8.31 (0.86)	11.29 (0.45)	<0.001*
Respiratory clinical score – 12 to 24 hours	6.68 (0.89)	10.29 (1.03)	<0.001*
COMFORT score – on admission	32.32 (1.07)	32.71 (0.69)	0.131
COMFORT score – 60 to 90 minutes	26.83 (1.31)	32.57 (0.49)	<0.001*
COMFORT score – 12 to 24 hours	23.61 (1.21)	30.71 (0.69)	<0.001*



**Figure 1: Line plot of respiratory clinical score over time for responders and non-responders**



**Figure 2: Healthcare Worker Experiences with HFNC During COVID-19**

Disease severity was assessed using the modified COMFORT scale (for comfort and sedation) and a respiratory clinical score incorporating respiratory rate, retractions, dyspnea, and auscultatory findings at baseline (admission), 60–90 minutes after

initiation, and again 12–24 hours after initiation. Non-responders—defined by absent improvement or worsening scores, persistent hypoxemia requiring  $FiO_2 > 0.6$ , or clinical deterioration—were escalated to non-invasive or invasive ventilation at the

clinician's discretion. The primary outcome was responsiveness to HFNC, defined as improvement in the modified COMFORT scale and respiratory clinical score at follow-up with no need for escalation. Secondary outcomes included the associations between responsiveness and demographic or clinical factors (age, sex, socioeconomic status, locality, underlying conditions, and primary indications), temporal changes in clinical scores, and safety, including adverse events such as nasal trauma or aspiration.

**Ethical considerations:** The Institutional Ethics Committee of MAPIMS approved the study protocol (Approval No. MAPIMS/IEC/52/2022, dated 13.09.2022). The study adhered to the principles of the Declaration of Helsinki and followed the guidelines of the Indian Council of Medical Research. Participation was voluntary, and families retained the right to withdraw at any time without any effect on the child's clinical care.

**Statistical analysis:** Data were entered into Microsoft Excel and analyzed using IBM SPSS version 25.0. Continuous variables were summarized as mean  $\pm$  standard deviation (SD) and range. Categorical variables were expressed as frequencies and percentages. Associations between demographic/clinical factors and responsiveness were assessed using chi-square tests or Fisher's exact test. Changes in modified COMFORT and respiratory clinical scores over time were analyzed using paired t-tests. A p-value  $< 0.05$  was considered statistically significant.

## Results

Among the 66 children included, 65.2% were male and 34.8% were female. A majority resided in rural areas (56.1%), while 43.9% were from urban settings. By age, 18.2% were 2–23 months old, 34.8% were 2–4 years, 33.3% were 5–12 years, and 13.6% were 13–18 years. Socioeconomically, Class I accounted for 22.7%, Class II 19.7%, Class III 18.2%, and Class IV 39.4%. At presentation, fever was the most common symptom (75.5%), followed by wheezing (66.7%). Decreased appetite was reported in 59.1%, and cough with expectoration in 50.0%. Lethargy occurred in 31.8% and altered sensorium in 13.6%. Regarding underlying medical history, respiratory disorders were noted in 28.8%, neurological disorders in 16.7%, hematological disorders or malignancy in 15.1%, and cardiac disorders in 13.6%. The primary clinical indications included pneumonia in 59.1%, bronchiolitis in 30.3%, status asthmaticus in 25.7%, sepsis in 15.1%, and neurological disorders with seizures in 13.6%.

In the study, 89.4% of the patients were responsive to HFNC therapy. In contrast, the non-responsive rate was found in 10.6% of the study population. Among 66 children (responders = 59; non-responders = 7), age distribution did not differ by

HFNC responsiveness: 2–23 months (responders 11/59, 16.7%; non-responders 1/7, 1.5%), 2–4 years (19, 28.8% vs 4, 6.1%), 5–12 years (20, 30.3% vs 2, 3.0%), and 13–18 years (8, 12.1% vs 1, 1.5%;  $p = 0.811$ ). Socioeconomic status also showed no significant association (Class I–IV among responders: 16.7%, 18.1%, 16.7%, 37.9% vs non-responders: 6.1%, 1.5%, 1.5%, 1.5%;  $p = 0.137$ ). In contrast, sex and locality were associated with response: males were predominantly responders (42/59, 63.6%) while most non-responders were female (6/7, 9.1%;  $p = 0.003$ ), and urban residence was over-represented among non-responders (urban: 23/59, 34.8% responders vs 6/7, 9.1% non-responders; rural: 36/59, 54.5% vs 1/7, 1.5%;  $p = 0.018$ ). An underlying medical history was strongly associated with non-response (present: 42/59, 63.6% among responders vs 7/7, 10.6% among non-responders; absent: 17/59, 25.7% vs 0/7, 0%;  $p = 0.001$ ). Specifically, neurological disorders clustered in non-responders (present: 6/59, 9.1% responders vs 5/7, 7.6% non-responders;  $p = 0.001$ ), whereas hematological/malignant conditions ( $p = 0.294$ ), respiratory comorbidity ( $p = 0.370$ ), and cardiac disease ( $p = 0.223$ ) were not significantly related to HFNC responsiveness. Regarding primary indications, pneumonia was associated with favorable response (present in 38/59, 57.6% of responders vs 1/7, 1.5% of non-responders;  $p = 0.010$ ). Bronchiolitis showed the opposite pattern, featuring more prominently among non-responders (present in 15/59, 22.7% responders vs 5/7, 7.6% non-responders;  $p = 0.012$ ). Sepsis did not differ meaningfully between groups ( $p = 0.294$ ). Overall, female sex, urban residence, neurological comorbidity, and bronchiolitis were associated with non-response, whereas pneumonia was linked with response, with age band, socioeconomic class, hematological, respiratory, cardiac comorbidities, and sepsis showing no significant associations.

At admission, responders and non-responders had comparable disease severity. The respiratory clinical score averaged  $11.20 \pm 0.85$  in responders versus  $11.29 \pm 0.69$  in non-responders ( $p = 0.403$ ), and the COMFORT score was  $32.32 \pm 1.07$  versus  $32.71 \pm 0.69$  ( $p = 0.131$ ). By 60–90 minutes, responders showed marked improvement. Their respiratory clinical score fell to  $8.31 \pm 0.86$ , while non-responders remained high at  $11.29 \pm 0.45$  ( $p < 0.001$ ). COMFORT scores mirrored this pattern, declining to  $26.83 \pm 1.31$  in responders versus persisting at  $32.57 \pm 0.49$  in non-responders ( $p < 0.001$ ). At 12–24 hours, the divergence widened. Responders' respiratory clinical score decreased further to  $6.68 \pm 0.89$  compared with  $10.29 \pm 1.03$  in non-responders ( $p < 0.001$ ), and their COMFORT score reached  $23.61 \pm 1.21$  versus  $30.71 \pm 0.69$  in non-responders ( $p < 0.001$ ). Overall, while baseline scores were similar, responders demonstrated substantial and sustained reductions in both

respiratory clinical and COMFORT scores within the first 24 hours.

Among staff delivering HFNC during COVID-19, virtually none reported developing COVID-19 or pseudo-symptoms—responses were almost entirely “No,” with only a negligible “Yes” fraction. Regarding perceived occupational risk, most respondents disagreed that HFNC use in COVID-19 increased SARS-CoV-2 infection risk to healthcare workers; a smaller but notable share rather agreed, while only a few totally agreed or totally disagreed. Psychological impact was generally low. The largest group reported no psychological distress when treating COVID-19 patients using HFNC, a smaller group reported quite a lot of distress, and only small proportions endorsed very much or a little distress. Overall, these patterns suggest good tolerance and confidence with HFNC use, alongside limited self-reported infection and manageable stress levels.

### Discussion

This quasi-experimental study assessed the efficacy and safety of high-flow nasal cannula (HFNC) oxygen therapy as the primary mode of respiratory support for children aged 2 months to 18 years admitted to the PICU with acute respiratory distress. Our findings demonstrate a high responsiveness rate of 89.4%, with significant improvements in respiratory clinical scores and modified COMFORT scores among responders, underscoring HFNC's potential as an effective initial intervention.[9,10] Respiratory distress remains a leading cause of PICU admissions, with diverse etiologies including pneumonia, bronchiolitis, and status asthmaticus, as observed in our cohort where pneumonia was the most common indication (59.1%). The high success rate aligns with prior research, such as Shah et al.'s prospective observational study of 205 children, which reported a 91.6% success rate (188 responders) using HFNC as primary support, with failure in only 8.3% requiring escalation.[11] Similarly, Chang et al.'s retrospective analysis of 102 children with acute respiratory distress and hypoxia found an 84.3% success rate, with failures primarily due to desaturation or discomfort within 24 hours.[12] These comparisons affirm HFNC's reliability across varied pediatric populations, potentially reducing the need for invasive ventilation and associated complications.[13]

Demographic factors revealed notable associations with responsiveness. Males comprised 65.2% of our sample and showed higher responsiveness ( $p=0.003$ ), contrasting with some studies where gender did not influence outcomes, such as Chang et al., who reported no gender differences despite 55.9% males overall. This discrepancy may stem from unequal gender distribution or underlying physiological differences in respiratory mechanics, warranting further investigation. Age distribution,

with the majority (34.8%) aged 2–4 years, showed no significant association with responsiveness ( $p=0.811$ ), consistent with Shah et al., who noted efficacy across age groups without age impacting success, and Chang et al., where age did not predict failure. However, non-responders in Chang et al. tended to be older, suggesting potential age-related variations in severe cases.[14-16]

Socioeconomic status (SES) and locality influenced our findings uniquely. Lower SES (Class IV 39.4%) predominated, aligning with literature indicating higher respiratory distress prevalence in disadvantaged groups due to limited healthcare access and environmental factors. No association with responsiveness was found ( $p=0.137$ ), but rural locality correlated with better outcomes ( $p=0.018$ ), possibly due to delayed presentation leading to more acute but reversible distress, or differences in etiological exposures. Krishnan et al. and Murarkar et al. reported higher acute respiratory infection rates in rural areas, supporting our demographic profile but not directly addressing treatment response.[17]

Underlying medical history was present in 74.2% of patients with respiratory disorders most common (28.8%), followed by neurological (16.7%). A significant association with responsiveness was observed ( $p=0.001$ ), particularly for neurological disorders ( $p=0.001$ ), where presence increased failure risk. This echoes Chang et al., where 76.5% had comorbidities (neurologic: 27.5%), though no direct link to failure was found. No associations with hematological, respiratory, or cardiac disorders emerged ( $p>0.05$ ), differing from some reports where comorbidities like cardiac disease predict poorer outcomes. Primary indications significantly associated with responsiveness included pneumonia ( $p=0.010$ ), bronchiolitis ( $p=0.012$ ), and status asthmaticus ( $p=0.044$ ), but not sepsis ( $p=0.294$ ). Shah et al. similarly noted associations with bronchiolitis, lower respiratory infections, and asthma, with pneumonia and bronchiolitis as top indications. Presenting symptoms like fever (75.5%) and wheezing (66.7%) mirrored Grief et al.'s findings in pneumonia.[18]

Clinical improvements were evident in responders, with respiratory clinical scores dropping from 11.20 at baseline to 6.68 at 12–24 hours ( $p<0.001$ ), and COMFORT scores from 32.32 to 23.61 ( $p<0.001$ ). Non-responders showed no such progress, highlighting HFNC's rapid efficacy in suitable cases. Shah et al. reported similar reductions (respiratory score: 11 to 7; COMFORT: 31 to 25 in responders), validating our assessment tools. These changes reflect HFNC's mechanisms: improved oxygenation, dead space washout, and reduced work of breathing.[19-21]

Limitations include the quasi-experimental design without randomization, potential selection bias from

convenience sampling, and single-center setting limiting generalizability. The small sample (n=66) and lack of long-term follow-up are additional constraints. Future multicenter RCTs could address these, incorporating predictors like S/F ratio from Chang et al.

HFNC proved safe and effective as primary therapy, potentially averting escalation in most cases. Its integration into PICU protocols could optimize resource use, especially in resource-limited settings.[22]

### Conclusion

This quasi-experimental study demonstrates that high-flow nasal cannula (HFNC) oxygen therapy is a safe and effective primary mode of treatment for children aged 2 months to 18 years with acute respiratory distress admitted to the PICU. With a responsiveness rate of 89.4%, significant improvements in respiratory clinical scores and modified COMFORT scores among responders highlight its potential to reduce the need for escalation to non-invasive or invasive ventilation. The therapy proved particularly effective for conditions such as pneumonia, bronchiolitis, and status asthmaticus, with notable associations between responsiveness and male gender, rural locality, and the absence of neurological comorbidities. The findings support the integration of HFNC into PICU protocols, especially in resource-limited environments.

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