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ORIGINAL ARTICLE

Outcome of high-flow nasal cannula (HFNC) therapy in respiratory failure due to lower respiratory tract infections in PICU - a single center experience in Karachi, Pakistan.

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ABSTRACT… Objective: To evaluate the outcome of high-flow nasal cannula (HFNC) therapy by ROX index in critically ill children with acute respiratory failure due to lower respiratory tract infections in pediatric intensive care unit (PICU). **Study Design:** Analytical, Observational, Cross-sectional study. **Setting:** The PICU of the Indus Hospital, Karachi, Pakistan. **Period:** November 2022 to October 2023. **Methods:** We enrolled children of either gender, aged above 1 month up to 16 years and presenting with acute respiratory insufficiency due to lower respiratory tract infections. The use of HFNC was monitored for 72-hours. HFNC failure was characterized by requiring either noninvasive mechanical ventilation or invasive mechanical ventilation due to an unstable state. **Results:** In a total of 62 children, 39 (62.9%) were male. The mean age was 27.01±30.96 months. The most common diagnosis at the time of admission were pneumonia, and bronchiolitis noted in 25 (40.3%), and 33 (53.2%) children, respectively. Gradual improvement in ROX index was observed among children with HFNC success while a declining ROX index predicted HFNC failure. Outcome of HFNC was successful in 45 (72.6%) children. Mortality was observed in 12 (19.4%) children. Presence of comorbidity was significantly associated with unsuccessful HFNC outcomes. **Conclusion:** ROX index was found to be a good predictor of HFNC outcome. Overall, HFNC therapy in PICU demonstrated 72.6% success rate. HFNC outcomes are hampered particularly in cases involving comorbidities highlighting the need for tailored interventions.

Key words: Bronchiolitis, High-flow Nasal Cannula, Pneumonia, Respiratory Failure, ROX Index.

INTRODUCTION

The admission of critically ill children to Pediatric Intensive Care Units (PICU) is often attributed to acute respiratory distress or failure. In these cases, a common approach for non-invasive respiratory support is the use of High Flow Nasal Cannula (HFNC).[1] HFNC is employed to enhance tissue oxygenation, alleviating the work for breathing, and minimizing the need for invasive mechanical ventilation.[2] HFNC is cost effective, requires less nursing care, and prevent patients from minor to major vent related complications.[2,3] The literature highlights HFNC therapy as a method that demonstrates a decrease in intubation rates among critically ill infants in PICU, coupled with a superior safety profile.[3-5] It is crucial to note that improper usage of HFNC in critically ill children can potentially lead to adverse outcomes. A study involving adult patients with respiratory failure suggested that prolonged application of HFNC before intubation might have detrimental effects.[6] In recent research, the failure of HFNC necessitating a transition to mechanical ventilation was reported at 23%,[1] whereas earlier studies indicated a range of 8-18%.[3,5]

HFNC is a new emerging therapy, number of variables available to predict the mechanical ventilation outcome like S/F ratio, P/F ratio, OI ratio, similarly we used ROX - index in HFNC which is a modified form of S/F ratio to predict the HFNC outcome.[6] In clinical settings, assessing the effectiveness of High-Flow Nasal Cannula (HFNC) therapy is crucial. Roca et al introduced

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a practical bedside tool, the ROX index, which utilizes SpO2, FiO2, and respiratory rate to predict the success or failure of HFNC therapy.[7] This index, validated for both adults and children, offers a reliable method to anticipate HFNC therapy outcomes. Moreover, alongside the ROX index, the ROX heart rate (ROX-HR) index further contributes to predicting HFNC therapy failure, providing clinicians with objective measures for decision-making and optimizing patient care. To this date, not much data is available to predict the outcome such as success or failure of HFNC in children getting admitted in PICU in Pakistan.

HFNC use is increasing in pediatric patients and globally it is found that its outcome is very good.[9] Objective measures that predict HFNC outcomes are lacking. The purpose of this study was to use the objective parameters to determine the HFNC outcome to prevent the risks associated with delay in intubation among children admitted in PICU. This study was thought to provide vital data for managing critically ill pediatric patients on HFNC therapy which help us early escalation or de-escalation of therapy in PICU of a tertiary care hospital. The research was planned to evaluate the outcome of HFNC therapy by using ROX index in critically ill children with acute respiratory failure due to lower respiratory tract infections in PICU.

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METHODS

This analytical, observational, cross-sectional study was conducted at the PICU of The Indus Hospital, Karachi, Pakistan from November 2022 to October 2023 after the approval of "Institutional Review Board" (letter number: IHHN_IRB_2022_12_037). A sample size of 62 was calculated considering the the success of HFNC as 88.5% in PICU[10], with 8% margin of error and 95% confidence level.

Inclusion criteria were children of either gender, aged above 1 month up to 16 years and presenting with acute respiratory insufficiency with restlessness, cough, fatigue, increased heart rate and tachypnea (1-2 months, respiratory rate 60 times/min; 2-12 months, respiratory rate 50 times/min; 1-5 years, respiratory rate 40 times/min; 5-16 years, respiratory rate 30 times/min). Exclusion criteria is were children who required elective or emergency intubation or those who had upper airway obstruction, facial trauma, deformity, or poor upper airway protection, or those who had known cardiac disorders. Children with known intolerance to HFNC were also not included. Children reporting difficulty in removing large amounts of sputum or risk of aspiration were also excluded. Children discharged within 24 hours after admission or those who had incomplete data were also not included. Written and informed consents were taken from all parents/guardians after explaining the objectives of this research and ensuring the confidentiality of the data involved in this study.

Children as per inclusion and exclusion criteria were enrolled. Age, gender, weight, diagnosis at the time of admission and comorbidity (if any) were recorded. The use of HFNC was monitored for 72 hours. HFNC therapy is an oxygen supply system capable of delivering up to 100% humidified and heated oxygen. Outcome was evaluated according to ROX-index. The ROX (respiratory rate oxygenation) index is a ratio of pulse oximetry/fraction of inspired oxygen (P/F ratio) to respiratory rate per minute. There is no universal agreement on the cut-off value of the ROX index. Lower and high values of ROX index are associated with failure and success of HFNC in pediatric acute respiratory failure respectively.[6,7] During HFNC therapy, fraction of inspiration O2 (FiO2) was adjusted to reach a pulse oximetry SpO2 between 92 and 97%, and the flow setting was based on the patients' body weight: 0–10 kg: 2 L/kg/min; and above 10 kg: 1 L/kg/min. We monitored clinical parameters and ROX index score [(SpO2/FiO2)/RR] every 4 hour after starting HFNC till 72 hours or before discontinuation of HFNC (if interruption was needed before 72 hours). HFNC failure was characterized by the requirement of either noninvasive mechanical ventilation (NIMV) or invasive mechanical ventilation (IMV) due to an unstable state. Instability encompassed conditions such as apnea, changes in mental status, inadequate perfusion indicated by cool extremities or capillary refill exceeding 3 seconds,

and instances of bradycardia.

Data was analyzed using IBM-SPSS Statistics, version 26. Gender, diagnosis at the time of admission, comorbidity, and categorical clinical parameters were shown as frequency and percentages. Numeric data were shown as mean and standard deviation. Chi- square test and t-test were apply where applicable to analyze between variables for the effectiveness of HFNC (success or failure). P value < 0.05 was taken as significant.

RESULTS

In a total of 62 children, 39 (62.9%) were male and 23 (37.1%) female children. The mean age and weight were 27.01±30.96 months (ranging between 1.5 to 120 months) and 9.04±5.84 kg (ranging between 3.5 to 31.0 kg), respectively. The most common diagnosis at the time of admission were pneumonia, and bronchiolitis noted in 25 (40.3%), and 33 (53.2%) children, respectively. Table-I is showing demographic and clinical characteristics of children.

The mean baseline ROX index score was 3.4±1.0 and it improved to 6.4±1.8 by the end of 72-hour evaluation period. Following administration of HFNC, ROX index improved during the course of 72 hours evaluation period as shown in Figure-1.

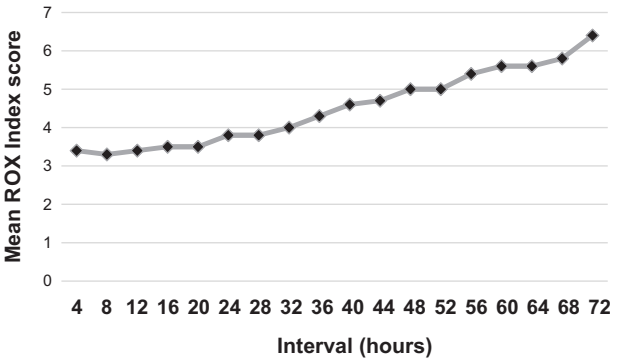

Figure-1. ROX Index score throughout the study period

Characteristics		Frequency (%)
Gender	Male	39 (62.9%)
	Female	23 (37.1%)
Age (months)	1-12	34 (54.8%)
	13-60	20 (32.3%)
	>60	8 (12.9%)
Diagnosis	Bronchiolitis	25 (40.3%)
	Pneumonia	33 (53.2%)
	Others	4 (6.5%)
Frequency of Most common comorbidities	Leukemia	7 (11.3%)
	Post-Measles	5 (8.1%)
	Asthma	4 (6.5%)
	Down syndrome	2 (3.2%)
	Nephrotic syndrome	2 (3.2%)
	Primary immunodeficiency	2 (3.2%)

Table-I. Demographics and clinical characteristics of children (n=62)

Interval (h)	Fever	RR (bpm)	HR (bpm)	Abnormal GCS	FiO_2 (%)	Flow Rate (L/min)	Saturation (%)	SO_2/FiO_2 Ratio	ROX Index
4	20 (32.3%)	53±10	150±18	18 (29.0%)	58±10	11±4	96±2	170±32	3.4±1.0
8	10 (16.1%)	53±10	152±19	16 (25.8%)	59±10	11±4	95±2	167±34	3.3±1.1
12	15 (24.2%)	53±9	150±20	12 (19.3%)	58±10	11±4	95±2	171±34	3.4±0.9
16	9 (14.5%)	52±9	147±18	14 (22.6%)	58±10	11±4	95±2	171±35	3.4±0.9
20	6 (9.7%)	51±9	146±18	13 (21.0%)	57±10	11±4	95±2	173±36	3.5±0.9
24	10 (16.1%)	52±9	144±19	18 (29.0%)	57±12	11±4	95±2	175±38	3.5±1.2
28	2 (3.2%)	50±8	142±19	13 (21.0%)	55±14	11±4	95±3	183±43	3.8±1.5
32	2 (3.2%)	49±8	142±17	13 (21.0%)	54±15	10±4	96±3	183±43	4.0±1.4
36	2 (3.2%)	47±8	139±19	6 (9.7%)	52±12	9±3	96±2	195±44	4.3±1.2
40	1 (1.6%)	47±9	137±18	6 (9.7%)	50±12	9±3	96±2	204±53	4.6±1.5
44	-	46±10	135±18	6 (9.7%)	50±12	9±3	96±2	202±50	4.7±1.7
48	-	45±9	130±16	6 (9.7%))	49±15	9±3	96±2	210±55	5.0±1.9
52	-	45±9	131±17	4 (6.5%)	48±13	8±3	96±2	213±49	5.0±1.7
56	-	44±9	129±20	4 (6.5%)	45±12	8±3	96±2	229±52	5.4±1.5
60	-	44±10	128±19	4 (6.5%)	43±11	8±3	97±2	233±49	5.6±1.9
64	-	45±9	127±17	4 (6.5%)	43±11	8±3	97±2	238±48	5.6±1.5
68	-	44±9	125±19	4 (6.5%)	41±11	8±3	96±2	246±50	5.8±1.6
72	-	42±9	125±20	3 (4.8%)	40±11	8±3	96±2	255±52	6.4±1.8

Table-II. Evaluation of clinical and laboratory parameters following HFNC administration

bpm: beats per minute; RR: Respiratory rate; HR: Heart rate: GCS: Glasgow coma score; FiO2: Fraction of Inspired Oxygen

The mean duration of HFNC was 4.04±4.6 days. Outcome of HFNC was successful in 45 (72.6%) children while failure was reported in 17 (27.4%) children. Throughout the 72-hours evaluation period for ROX index, it was found that a gradual improvement in ROX index was observed among children with HFNC success. On the other hand, a declining ROX index predicted HFNC failure (Figure-2).

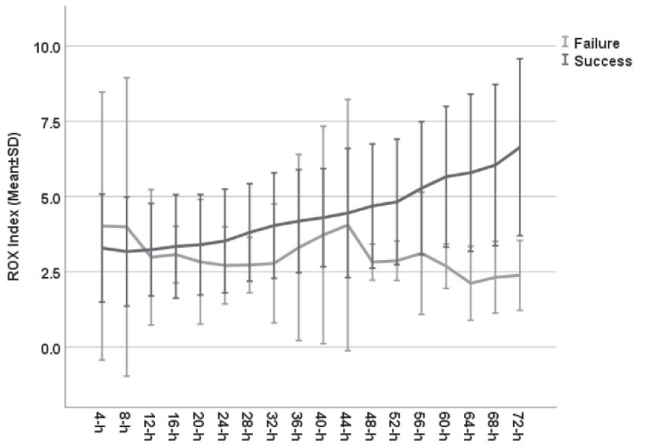

Figure-2. Patterns of ROX index with HFNC outcomes

Multiorgan dysfunction syndrome was noted among 7 (11.3%) children. The mean duration of PICU stay was 11.26±9.42 days (ranging between 2 to 45 days). Mortality was observed in 12 (19.4%) children. Presence of comorbidity was significantly associated with unsuccessful HFNC outcomes (Table-III). Female gender (p=0.018), and presence of comorbidy were significantly associated with mortality and the details are shown in Table-IV.

DISCUSSION

The study conducted at PICU in Karachi, Pakistan, delved into the outcomes of HFNC therapy in acute respiratory illness due to lower respiratory tract infections. In this study, 93.5% cases were primarily diagnosed with bronciolitis and pneumonia. Our findings are similar to what others have found showing pneumonia and bronchiolitis to be the commonest causes in childern with respiratory distress.[11] The evaluation revealed promising insights into the impact of HFNC therapy. Over a 72-hour period, the ROX index, exhibited improvement, emphasizing the positive influence of HFNC on vital and clinical parameters. HFNC demonstrated success in 72.6% of cases, but failure was reported in 27.4%, reflecting the complexity of managing lower respiratory tract infections in children within a critical care setting.

Variables		Outcome		P-Value
		Successful (n=45)	Unsuccessful (n=17)	
Gender	Male	31 (68.9%)	8 (47.1%)	0.112
	Female	14 (31.1%)	9 (52.9%)	
Age (months)	1-12	27 (60.0%)	7 (41.2%)	0.299
	13-60	12 (26.7%)	8 (47.1%)	
	>60	6 (13.3%)	2 (11.8%)	
Diagnosis	Bronchiolitis	8 (17.8%)	-	0.062
	Pneumonia	35 (77.8%)	17 (100%)	0.034
Comorbidities		19 (42.2%)	16 (94.0%)	0.001

Table-III. Comparison of baseline characteristics with HFNC outcome

Variables		Mortality		P-Value
		Yes (n=12)	No (n=50)	
Gender	Male	4 (33.3%)	35 (70.0%)	0.018
	Female	8 (66.7%)	15 (30.0%)	
Age (months)	1-12	5 (41.7%)	28 (56.0%)	0.085
	13-60	7 (58.3%)	14 (28.0%)	
	>60	-	8 (16.0%)	
Diagnosis	Bronchiolitis	-	8 (16.0%)	0.138
	Pneumonia	12 (100%)	38 (76.0%)	0.069
Commodities		12 (100%)	23 (46.0%)	0.001

Table-IV. Comparison of baseline characteristics with Mortality

Our results are aligned with an extensive retrospective study involving 26,423 admission by Morris et al.[12] The analyzed the utilization patterns of HFNC in PICUs as the primary mode of respiratory support, demonstrating a success rate of 73.1%. Notably, their findings revealed specific characteristics of patients who experienced HFNC failure like younger in age, presentation with more severe conditions, and cardiovascular diagnoses. Our study presented a comprehensive evaluation of the vital and respiratory parameters showing favorable impact of HFNC. Iplik et al from Turkey recently reported the relatively higher success rate of HFNC as 88.5% among children who were unable to maintain SpO_2 > 92% in the pediatric emergency on oxygen supplementation administration.[10] Iplik et al included cases adhering various etiologies while we only included cases who were reported with lower respiratory tract infections. Local study by Saeed et al reported the success of HFNC among children with acute respiratory insufficiency in PICU as 76.7%.[1]

HFNC represents a therapeutic approach that prioritizes patient comfort by delivering warm and humidified gas through nasal prongs. This method maintains a high FiO_2 while simultaneously generating a mild positive pressure within the upper airways.[13] This positive pressure is a result of the substantial flow of gas, which additionally facilitates the removal of stale air from the upper airway dead space.[14] Consequently, HFNC not only ensures optimal oxygen levels but also supports respiratory efficiency by improving the clearance of residual air in the upper airways.[15] The literature shows limitations exhibiting gaps in understanding the comprehensive respiratory dynamics and the direct impact of HFNC on the crucial parameters, our study addressed important evaluation of vitals and respiratory parameters during HFNC administration period adding valuable insights to the existing literature.[16,17]

The present study highlighted good utility of ROX index in predicting HFNC success as gradually improving ROX index predicted HFNC success or vice versa. These findings are consistent with the contemporary literature where dynamic evaluations of the ROX indexes presents a more comprehensive approach than single-point assessments. Continuously monitoring and analyzing changes in the ROX indexes over time offer valuable insights into a patient's response to HFNC therapy.[18] A recent meta-analysis by Zhou et al in pneumonia patients experiencing acute hypoxemic respiratory failure, assessing the ROX index within 12 hours following the initiation of HFNC therapy serves as a reliable predictor of successful weaning from HFNC. Early measurement of HFNC offers valuable predictive insights into the patient's response to HFNC, aiding clinicians in determining the feasibility of transitioning the patient off HFNC support. Monitoring the ROX index in this time-frame provides a crucial marker for anticipating the patient's readiness for weaning, facilitating timely and appropriate adjustments in their respiratory support. By observing trends and alterations in ROX index, clinicians gain a more nuanced understanding of a patient's respiratory status, aiding in timely adjustments to the therapy or interventions, thereby optimizing patient care and outcomes.

In this study, multi-organ dysfunction syndrome emerged in 11.3% of cases while mortality rate was 19.4% elucidates the gravity and protracted nature of care required in such cases. The presence of comorbidities notably affected HFNC success rates, corroborating existing literature that underscores the challenge of managing respiratory conditions in the presence of additional health issues.

This study emphasizes the efficacy of HFNC therapy in improving respiratory parameters but also highlighting its limitations, particularly in cases with comorbidities or where multiorgan dysfunction syndrome occurs. Such outcomes underscore the need for tailored interventions and continued research to optimize the management of lower respiratory tract infections in pediatric critical care settings.

CONCLUSION

ROX index was found to be a good predictor of HFNC outcome. Overall, HFNC therapy in

PICU demonstrated 72.6% success rate. HFNC outcomes are hampered particularly in cases involving comorbidities highlighting the need for tailored interventions. Further investigations should focus on refining patient selection criteria and exploring the efficacy of HFNC in diverse pediatric respiratory conditions to optimize its role in enhancing patient outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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2	Rabeea Tariq	Critical revisions, Literature review, Discussion, Approval for publication.	
3	Najmi Usman	Critical revisions, Literature review, Discussion, Approval for publication.	
4	Sadiq Mirza	Critical revisions, Literature review, Discussion, Approval for publication.	
5	Anwarul Haque	Critical revisions, Literature review, Discussion, Approval for publication.	
6	Sahrish Ameer	Critical revisions, Literature review, Discussion, Approval for publication.