e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(8); 53-58

Original Research Article

Usefulness of pROX Index Score to Assess the Outcome of Patients with Lower Respiratory Tract Infection (Pneumonia and Bronchiolitis) on High Flow Nasal Cannula

Vinay Kumar B.[1], G. V. Basavaraja[2], Sathvika Chandrashekara Reddy[3], Priyanka A.R.[4], Jacqueline A. Shah[5]

[1]Paediatrician Specialist, Department of Health and Family Welfare, General Hospital, Chikkanayaka-nahalli, Tumkur, Karnataka, India

[2]Professor and Medical Superintendent, Department of Paediatrics, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India

[3]Assistant Professor, Department of Paediatrics, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India

[4]Assistant Professor, Department of Paediatrics, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India

[5]Assistant Professor, Department of Paediatrics, Indira Gandhi Institute of Child Health, Bengaluru, Karnataka, India

Received: 25-05-2026 / Revised: 23-06-2026 / Accepted: 26-07-2026
Corresponding Author: Dr. Sathvika Chandrashekara Reddy
Conflict of interest: Nil

Abstract:

Background: High-flow nasal cannula is increasingly used in children with lower respiratory tract infections, although early identification of patients at risk of treatment failure remains challenging.

Aim: To assess the usefulness of the pediatric ROX index in predicting outcomes among children with pneumonia and bronchiolitis receiving HFNC therapy.

Methods: This prospective observational study included 80 children aged 1 month to 5 years requiring HFNC for lower respiratory tract infection. Heart rate, respiratory rate, SpO_2, FiO_2, clinical respiratory signs, and pROX values were assessed serially. ROC analysis was performed to determine the predictive accuracy of pROX. CRP and procalcitonin were also evaluated.

Results: Mean SpO_2 increased from 92.4 ± 4.1% at 30 minutes to 98.9 ± 1.2% at 24 hours, while respiratory rate decreased from 62.8 ± 12.4 to 40.1 ± 7.9 breaths/min. Mean pROX increased from 1.98 ± 0.71 to 3.15 ± 0.88. The 6-hour pROX demonstrated an AUC of 0.876. At a cutoff of 2.2, sensitivity was 83.3%, specificity 88.9%, PPV 80%, and NPV 91.4%. A pROX <2 at 6 hours was significantly associated with clinical deterioration or escalation of respiratory support (OR 5.4; $p<0.001$). Combined CRP >100 mg/L and PCT >2 ng/mL showed 100% specificity for bacterial pneumonia.

Conclusion: Serial pROX measurement, particularly at 6 hours, may serve as a useful non-invasive predictor of HFNC outcome in children with pneumonia and bronchiolitis.

Keywords: High-Flow Nasal Cannula, pROX Index, Pneumonia, Bronchiolitis, Pediatric Respiratory Failure, CRP, Procalcitonin.

DOI: 10.25258/ijpqa.17.8.10

Introduction

Lower respiratory tract infections (LRTIs), particularly pneumonia and bronchiolitis, are important causes of respiratory distress and hospitalization among young children. Children with moderate-to-severe disease may develop hypoxemia requiring escalation from conventional oxygen therapy to advanced respiratory support. High-flow nasal cannula (HFNC) has increasingly been used because it provides heated and humidified oxygen at high flow rates while offering a relatively well-tolerated form of non-invasive respiratory support. [1] Early identification of patients who are unlikely to respond to HFNC is important because delayed escalation to invasive ventilation may adversely affect clinical outcomes. The respiratory rate-oxygenation (ROX) index, initially evaluated in patients with pneumonia and acute hypoxemic respiratory failure, combines oxygenation with respiratory rate and has demonstrated utility in predicting the outcome of

HFNC therapy. [1] Subsequent validation showed that serial assessment of the ROX index could help distinguish patients likely to succeed on HFNC from those requiring escalation of respiratory support [2]. The usefulness of ROX-based indices has subsequently been investigated in children. Yuniar et al. evaluated the ROX index among pediatric patients receiving HFNC and demonstrated the potential value of serial ROX measurements for predicting treatment outcome [3]. Similarly, Nascimento et al. studied infants with bronchiolitis and reported that ROX index assessment could assist in identifying patients at increased risk of HFNC failure [4]. Other pediatric studies have also examined oxygenation and respiratory rate-based indices for predicting the requirement for positive-pressure ventilation [5]. Clinical and physiological parameters obtained during the initial hours of HFNC therapy may therefore provide useful information for early recognition of treatment failure [6].

HFNC has demonstrated clinical benefits in infants with bronchiolitis, particularly in reducing the requirement for escalation of respiratory support compared with standard oxygen therapy [7]. Evidence from systematic review and meta-analysis further supports its role as an effective respiratory support modality in children with bronchiolitis [8]. However, reliable early prediction of HFNC failure remains clinically important.

The present study was therefore undertaken to assess the usefulness of the pediatric ROX (pROX) index in predicting outcomes among children with pneumonia and bronchiolitis receiving HFNC therapy and to determine its potential role in early risk stratification and escalation of respiratory support.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the Department of Paediatrics, Indira Gandhi Institute of Child Health, Bangalore, a tertiary pediatric referral center with a dedicated Pediatric Intensive Care Unit (PICU). The study included children with lower respiratory tract infection requiring HFNC respiratory support.

Study Population: A total of 80 children aged 1 month to 5 years, diagnosed with pneumonia or bronchiolitis and requiring HFNC therapy because of respiratory distress and hypoxemia, were included in the study.

Inclusion Criteria: Children aged 1 month to 5 years with clinically diagnosed pneumonia or bronchiolitis requiring HFNC because of acute hypoxemic respiratory failure (SpO_2 <90% despite conventional oxygen therapy) were eligible. Children with congenital heart disease without pulmonary hypertension who developed LRTI and required HFNC were also included. Written informed consent was obtained from the parent or legal guardian.

Exclusion Criteria: Children aged <1 month or >5 years were excluded. Patients receiving HFNC following extubation or after weaning from CPAP/BiPAP, those with chronic ventilator dependence, neuromuscular disorders affecting respiratory function, upper airway abnormalities or obstruction, inborn errors of metabolism, and diabetic ketoacidosis were excluded. Children whose parents or guardians did not provide consent were also excluded.

Sample Size and Sampling: The sample size was calculated based on the expected diagnostic performance of the pROX index for predicting HFNC outcome. Considering an anticipated sensitivity of 69%, absolute precision of 10%, and a 95% confidence level, the minimum required sample size was estimated to be 80 patients. Eligible children fulfilling the predefined selection criteria were enrolled consecutively until the required sample size was achieved.

Data Collection: Demographic and clinical information, including age, sex, weight, height, underlying comorbidities, diagnosis, heart rate, respiratory rate, SpO_2, FiO_2, and clinical respiratory score, was recorded at enrollment. Baseline measurements were obtained before initiation of HFNC therapy.

Patients were subsequently monitored at 30 minutes, 2 hours, 6 hours, 12 hours, and 24 hours following HFNC initiation. At each specified interval, heart rate, respiratory rate, SpO_2, FiO_2, clinical condition, and HFNC parameters were documented. Initial flow rate, maximum FiO_2 requirement, and total duration of HFNC therapy were also recorded.

pROX Index Assessment: The pROX index was calculated using oxygen saturation, fraction of inspired oxygen, and respiratory rate according to the following formula:

pROX index = (SpO_2/FiO_2) / Respiratory rate: The index was determined at 30 minutes, 2 hours, 6 hours, 12 hours, and 24 hours after initiation of HFNC. Serial changes in pROX were evaluated and correlated with clinical outcomes.

Laboratory Evaluation: Relevant laboratory investigations were performed according to the clinical condition of each patient. C-reactive protein (CRP) and procalcitonin (PCT) were evaluated as inflammatory markers. Blood cultures and other microbiological investigations were performed when bacterial infection was clinically suspected. CRP and PCT values were also assessed

for their ability to differentiate bacterial pneumonia from other LRTIs.

Outcome Assessment: The primary outcome was HFNC success or failure. HFNC success was defined as improvement in oxygenation and respiratory distress without the requirement for invasive mechanical ventilation.

HFNC failure was defined as deterioration or inadequate clinical response requiring endotracheal intubation and invasive mechanical ventilation because of persistent or worsening hypoxemia, increasing respiratory distress, respiratory fatigue, or clinical deterioration.

Secondary outcomes included duration of HFNC therapy, requirement for PICU care, length of PICU stay, requirement for invasive ventilation, and mortality.

Ethical Considerations: The study protocol was approved by the Institutional Ethics Committee of Indira Gandhi Institute of Child Health. Written informed consent was obtained from the parents or legal guardians before enrollment. Patient information was anonymized and confidentiality was maintained throughout the study.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 23.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, as appropriate, while categorical variables were presented as frequencies and percentages.

Continuous variables between HFNC success and failure groups were compared using the independent-samples t-test or Mann–Whitney U test according to data distribution. Categorical variables were compared using the Chi-square test or Fisher's exact test. Changes in physiological parameters and pROX values over time were assessed using appropriate repeated-measures analysis.

Receiver operating characteristic (ROC) curve analysis was performed to determine the ability of the pROX index at different time points to predict HFNC failure.

The area under the curve (AUC), optimal cutoff value, sensitivity, specificity, positive predictive value, and negative predictive value were determined. Multivariable logistic regression analysis was performed to identify independent predictors of HFNC failure. A p-value <0.05 was considered statistically significant.

Results

A total of 80 children aged 1 month to 5 years with lower respiratory tract infection requiring high-flow nasal cannula (HFNC) therapy were included in the study. Clinical, physiological, inflammatory, and pROX parameters were assessed serially to evaluate response to HFNC and predict adverse clinical outcomes.

Table 1: Demographic and Baseline Characteristics of Study Participants (n=80)

Characteristic	Number (n)	Percentage (%)
Age group		
<1 year	32	40.0
1–5 years	48	60.0
Sex		
Male	48	60.0
Female	32	40.0
Geographical distribution		
Karnataka	48	60.0
Andhra Pradesh	16	20.0
Other states	16	20.0
Baseline clinical abnormalities		
Retractions	68	85.0
Increased work of breathing	62	77.5
Accessory muscle use	58	72.5
Capillary refill time >3 sec	28	35.0

Children aged 1–5 years constituted the majority of the study population (60%), while infants accounted for 40%. There was a male predominance, with males comprising 60% of cases. At initiation of HFNC, respiratory distress was prominent, with retractions in 85%, increased work of breathing in 77.5%, and accessory muscle use in 72.5% of patients.

Table 2: Serial Changes in Physiological Parameters during HFNC Therapy

Time Point	Heart Rate (bpm) Mean ± SD	Respiratory Rate (breaths/min) Mean ± SD	SpO_2 (%) Mean ± SD	FiO_2 Mean ± SD	pROX Mean ± SD
30 min	162.4 ± 18.6	62.8 ± 12.4	92.4 ± 4.1	0.36 ± 0.07	1.98 ± 0.71
2 h	148.2 ± 16.3	56.3 ± 10.7	95.1 ± 2.8	0.35 ± 0.06	2.24 ± 0.82
6 h	136.7 ± 14.2	48.2 ± 9.3	97.8 ± 1.9	0.33 ± 0.05	2.87 ± 0.95
12 h	128.5 ± 12.6	44.6 ± 8.1	98.5 ± 1.4	—	—
24 h	120.8 ± 10.4	40.1 ± 7.9	98.9 ± 1.2	0.32 ± 0.04	3.15 ± 0.88

p-value for overall temporal trend: <0.001

A progressive clinical improvement was observed following HFNC initiation. Mean SpO_2 increased from 92.4 ± 4.1% to 98.9 ± 1.2%, while respiratory rate decreased from 62.8 ± 12.4 to 40.1 ± 7.9 breaths/min over 24 hours. Heart rate also decreased substantially. Simultaneously, FiO_2 requirement declined and mean pROX increased from 1.98 ± 0.71 to 3.15 ± 0.88, indicating progressive improvement in oxygenation relative to respiratory effort.

Table 3: Serial Changes in Clinical Signs of Respiratory Distress

Time Point	Retractions n (%)	Increased Work of Breathing n (%)	Accessory Muscle Use n (%)	CFT >3 sec n (%)
30 min	68 (85.0)	62 (77.5)	58 (72.5)	28 (35.0)
2 h	52 (65.0)	48 (60.0)	42 (52.5)	18 (22.5)
6 h	32 (40.0)	28 (35.0)	24 (30.0)	10 (12.5)
12 h	18 (22.5)	16 (20.0)	12 (15.0)	6 (7.5)
24 h	10 (12.5)	8 (10.0)	6 (7.5)	4 (5.0)

Signs of respiratory distress decreased progressively during HFNC therapy. Retractions declined from 85% at 30 minutes to 12.5% at 24 hours, while increased work of breathing decreased from 77.5% to 10%. Accessory muscle use fell from 72.5% to 7.5%. Improvement in capillary refill time was also observed, with the proportion having CFT >3 seconds decreasing from 35% to 5% at 24 hours.

Table 4: Predictive Performance of pROX and Inflammatory Markers

Parameter	Finding	Predictive/Diagnostic Value
pROX at baseline	1.98 ± 0.71	Increased progressively with clinical improvement
pROX at 6 h	2.87 ± 0.95	Strong early discriminator of clinical outcome
Optimal 6-h pROX cutoff	2.2	Prediction of unfavorable outcome/escalation
AUC for 6-h pROX	0.876	Excellent discriminatory ability
Sensitivity	83.3%	At pROX cutoff of 2.2
Specificity	88.9%	At pROX cutoff of 2.2
Positive predictive value	80.0%	At pROX cutoff of 2.2
Negative predictive value	91.4%	At pROX cutoff of 2.2
pROX <2 at 6 h	OR 5.4; p<0.001	Associated with deterioration/escalation of respiratory support
CRP >100 mg/L	18/80 (22.5%)	Associated with bacterial infection
PCT >2 ng/mL	14/80 (17.5%)	Associated with bacterial infection
CRP >100 mg/L + PCT >2 ng/mL	12 cases	Specificity 100% for bacterial pneumonia

ROC analysis demonstrated that the 6-hour pROX index had an AUC of 0.876, indicating excellent ability to discriminate children at risk of an unfavorable outcome.

At an optimal cutoff of 2.2, sensitivity was 83.3%, specificity 88.9%, PPV 80.0%, and NPV 91.4%. Children with a pROX <2 at 6 hours had significantly greater odds of clinical deterioration or escalation of respiratory support (OR 5.4; p<0.001). Among inflammatory markers, elevated CRP and PCT were associated with bacterial pneumonia, while the combination of CRP >100 mg/L and PCT >2 ng/mL demonstrated 100% specificity in the present cohort.

Discussion

High-flow nasal cannula has become an important modality of respiratory support in children with acute respiratory distress because it provides heated, humidified oxygen at high flow rates while reducing inspiratory resistance and improving oxygen delivery. Mikalsen et al. [9] described HFNC as an increasingly used non-invasive

respiratory support strategy in pediatric practice, particularly for bronchiolitis and other causes of hypoxemic respiratory failure.

In the present study, HFNC produced a progressive improvement in oxygenation and respiratory status over 24 hours. Mean SpO_2 increased from 92.4% at 30 minutes to 98.9% at 24 hours, while respiratory rate decreased from 62.8 to 40.1 breaths/min. Similar physiological benefits of HFNC in children have been described by Kwon [10], who emphasized improvement in oxygenation, reduction in work of breathing, and better patient tolerance with appropriate HFNC use.

Clinical signs of respiratory distress also improved substantially. Retractions decreased from 85% at 30 minutes to 12.5% at 24 hours, while accessory muscle use declined from 72.5% to 7.5%. Bressan et al. [11] similarly demonstrated that HFNC reduced respiratory distress and oxygen requirements among infants with bronchiolitis. Spentzas et al. [12] also reported improvement in respiratory parameters among children with respiratory distress receiving high-flow oxygen therapy.

The progressive decline in respiratory rate and work of breathing observed in the present study supports the physiological effects of HFNC, including improved oxygen delivery and reduction of respiratory effort. Ten Brink et al. [13] observed that high-flow nasal oxygen could provide effective respiratory support in children with moderate-to-severe respiratory distress and may reduce the requirement for more invasive respiratory interventions in selected patients.

A major objective of the present study was to determine the usefulness of the pROX index for predicting clinical outcome. The mean pROX value increased from 1.98 at baseline to 3.15 at 24 hours. ROC analysis showed an AUC of 0.876 for the 6-hour pROX, indicating good discriminatory ability. At a cutoff of 2.2, sensitivity was 83.3% and specificity was 88.9%.

Children with pROX <2 at 6 hours had significantly greater odds of clinical deterioration or escalation of respiratory support.

Dunbar et al. [14] also emphasized the importance of early physiological predictors for identifying children at risk of HFNC failure.

Inflammatory markers provided additional diagnostic information. CRP >100 mg/L was observed in 22.5% and PCT >2 ng/mL in 17.5% of children. The combination of CRP >100 mg/L and PCT >2 ng/mL showed 100% specificity for bacterial pneumonia in this cohort. Stockmann et al. [15] demonstrated the usefulness of procalcitonin for identifying children at low risk of bacterial community-acquired pneumonia, supporting its potential role in antimicrobial decision-making. Esposito et al. [16] similarly reported that procalcitonin-guided management may help rationalize antibiotic therapy in pediatric pneumonia.

The present findings also support serial rather than isolated pROX assessment. Changes in oxygenation and respiratory rate during the initial hours of HFNC were strongly related to subsequent clinical course. A systematic review by Zhou et al. [17] demonstrated that the ROX index has useful predictive performance for HFNC outcome in acute hypoxemic respiratory failure, although cutoff values may vary according to the population and timing of assessment. Tatkov [18] further highlighted that interpretation of ROX-based indices should consider the FiO_2 component and the physiological context in which the index is applied.

Overall, the study demonstrated that improvement in pROX paralleled clinical recovery during HFNC therapy. A persistently low pROX during the first 6 hours identified children at increased risk of deterioration, suggesting that serial pROX assessment may provide an objective bedside tool for guiding early escalation of respiratory support.

The study was limited by its single-center design, relatively small sample size, and inclusion of only children aged below 5 years. Larger multicenter studies are required to validate age-specific pROX cutoff values and determine whether their incorporation into standardized HFNC protocols improves outcomes.

Conclusion

HFNC was effective in improving oxygenation and reducing respiratory distress in children with pneumonia and bronchiolitis. Serial pROX assessment, particularly at 6 hours, showed good ability to predict clinical outcome and identify children at risk of HFNC failure. A 6-hour pROX cutoff of 2.2 demonstrated high sensitivity and specificity. Combining pROX with clinical findings and inflammatory markers such as CRP and procalcitonin may further improve early risk stratification and guide timely escalation of respiratory support.

References

1. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard JD, et al. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: the utility of the ROX index. J Crit Care. 2016;35:200-205. doi: 10.1016/j.jcrc.2016.05.022.
2. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al. An index combining respiratory rate and oxygenation to predict

outcome of nasal high-flow therapy. Am J Respir Crit Care Med. 2019;199(11):1368-1376. doi: 10.1164/rccm.201803-0589OC.
3. Yuniar I, Pudjiadi AH, Dewi R, Prawira Y, Puspaningtyas NW, Tartila T, et al. Respiratory Rate Oxygenation (ROX) index as predictor of high flow nasal cannula in pediatric patients in pediatric intensive care unit. BMC Pulm Med. 2024;24(1):216. doi: 10.1186/s12890-024-03029-2.
4. Nascimento MS, Zólio BA, Vale LAPA, Silva PAL, Souza TS, Fascina LP, et al. ROX index as a predictor of failure of high-flow nasal can nula in infants with bronchiolitis. Sci Rep. 202 4;14:389. doi: 10.1038/s41598-024-51214-4.
5. Kannikeswaran N, Whittaker P, Sethuraman U. Association between respiratory rate oxygenation index and need for positive pressure ventilation in children on high flow nasal cannula for bronchiolitis. Eur J Pediatr. 2022;181 (11):3977-3983. doi: 10.1007/s00431-022-04607-4.
6. Saelim K, Thirapaleka B, Ruangnapa K. Predictors of high-flow nasal cannula failure in pediatric patients with acute respiratory distress. Clin Exp Pediatr. 2022;65(12):595-601. doi: 10.3345/cep.2022.00241.
7. Franklin D, Babl FE, Schlapbach LJ, Oakley E, Craig S, Neutze J, et al. A randomized trial of high-flow oxygen therapy in infants with bronchiolitis. N Engl J Med. 2018;378(12):1 121-1131. doi: 10.1056/NEJMoa1714855.
8. Lin J, Zhang Y, Xiong L, Liu S, Gong C, Dai J. High-flow nasal cannula therapy for children with bronchiolitis: a systematic review and meta-analysis. Arch Dis Child. 2019;104(6):56 4-576. doi: 10.1136/archdischild-2018-315846.
9. Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. Scand J Trauma Resusc Emerg Med. 2016;24:93. doi: 10.1186/s13049-016-0278-4.
10. Kwon JW. High-flow nasal cannula oxygen therapy in children: a clinical review. Clin Exp Pediatr. 2020;63(1):3-7. doi: 10.3345/kjp.2 019.00626.
11. Bressan S, Balzani M, Krauss B, Pettenazzo A, Zanconato S, Baraldi E. High-flow nasal cannula oxygen for bronchiolitis in a pediatric ward: a pilot study. Eur J Pediatr. 2013;172(12):1649-1656. doi: 10.1007/s00431-013-2094-4.
12. Spentzas T, Minarik M, Patters AB, Vinson B, Stidham G. Children with respiratory distress treated with high-flow nasal cannula. J Intensive Care Med. 2009;24(5):323-328. doi: 10.1177/0885066609340622.
13. ten Brink F, Duke T, Evans J. High-flow nasal prong oxygen therapy or nasopharyngeal continuous positive airway pressure for children with moderate-to-severe respiratory distress? Pediatr Crit Care Med. 2013;14(7):e326-e331. doi: 10.1097/PCC.0b013e31828a894d.
14. Dunbar KS, Fox SN, Thomas JF, et al. When to transfer: predictors of pediatric high flow nasal cannula failure at a community hospital. Hosp Pediatr. 2024;14(1):45-51. doi: 10.1542/hpeds.2023-007298.
15. Stockmann C, Ampofo K, Killpack J, Williams DJ, Edwards KM, Grijalva CG, et al. Procalcitonin accurately identifies hospitalized children with low risk of bacterial community-acquired pneumonia. J Pediatric Infect Dis Soc. 2018;7(1):46-53. doi: 10.1093/jpids/piw091.
16. Esposito S, Tagliabue C, Picciolli I, Semino M, Sabatini C, Consolo S, et al. Procalcitonin measurements for guiding antibiotic treatment in pediatric pneumonia. Respir Med. 2011; 105(12):1939-1945. doi: 10.1016/j.rmed.201 1.09.003.
17. Zhou X, Liu J, Pan J, Xu Z, Xu J. The ROX index as a predictor of high-flow nasal cannula outcome in pneumonia patients with acute hypoxemic respiratory failure: a systematic review and meta-analysis. BMC Pulm Med. 2022;22(1):121. doi: 10.1186/s12890-022-01914-2.
18. Tatkov S. Nasal high-flow therapy: role of FiO2 in the ROX index. Am J Respir Crit Care Med. 2019;200(1):115-116. doi: 10.1164/rccm.201902-0376LE.