e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(8); 1378-1383

Original Research Article

Predictors of High Flow Nasal Cannula Failure in Acute Respiratory Failure

Manish Kumar Jha[1], Manash Jyoti Saikia [2],Farjana Begum[3], Basanta Hazarika [4], Suresh Sharma[5]

[1]Senior Resident, Dept of Pulmonary Medicine, Gauhati Medical College Hospital
[2]Assistant Professor, Dept of Pulmonary Medicine, Gauhati Medical College Hospital
[3]Assistant Professor, Dept of Pulmonary Medicine, Gauhati Medical College Hospital
[4]Professor & HOD, Dept of Pulmonary Medicine, Gauhati Medical College Hospital
[5] Professor, Dept of Pulmonary medicine, Gauhati Medical College Hospital

Received: 01-05-2025 / Revised: 15-06-2025 / Accepted: 21-07-2025
Corresponding author: Dr. Manish Kumar Jha
Conflict of interest: Nil

Abstract

Background and Objective: Respiratory failure is defined as inability of respiratory system to either oxygenate the blood or remove CO2 from blood. The initial treatment for hypoxemia in ARF patients is oxygen therapy. It is applied using devices such as nasal cannulas, face masks or masks with reservoir bags, HFNC etc. HFNC makes use of heated, humidified air combined with oxygen.[1] High oxygen flows (60 L/min) are delivered by HFNCs, and their FiO2 is in the range of 0.21 to 1. Failure of HFNC is characterized by the necessity of endotracheal intubation in spite of HFNC administration.[2] Therefore, in order to assess the predictors for HFNC failure in patients with ARF, we conducted an observational study at the hospital.

Method: This was a hospital-based observational study in which adult patients more than 18 yrs presenting with ARF and managed with HFNC in the Department of Pulmonary Medicine and Allied Specialties were included. Important parameters included in the study were GCS, RR, FiO_2, SpO_2, ROX index, and arterial blood gas parameters, including pH, PaO_2, and PO_2. Outcome characteristics Included survival or mortality, and failure or success of HFNC treatment.

Result: The majority of patients experienced HFNC failure (60%). Causes of respiratory failure ($p>0.05$), FiO_2 ($p=0.199$), $PaCO_2$ ($p=0.381$), PaO_2 ($p=0.702$) were comparable among patients with success and failure of HFNC. The ROX index was significantly lower in HFNC failure patients than HFNC success patients at 1 hour ($p=0.022$) and 12 hours ($p=0.004$) after HFNC treatment**.**

Conclusion: ROX index has good performance in prediction of failure of HFNC treatment; however, the sensitivity and specificity are higher at 12 hours after HFNC treatment than at 1 hour.

Keywords: Acute Respiratory Failure (ARF), High Flow Nasal Cannula (HFNC), Glassgow Coma Score (GCS), Respiratory Rate (RR).

Introduction

Respiratory failure is defined as inability of respiratory system to either oxygenate the blood or remove CO2 from blood. Decreased Partial pressure of oxygen with decreased or normal partial pressure of carbon dioxide (PaCO2) is defined as Type 1 RF, while rise in arterial carbon dioxide (PaCO2) more than 45 mm of Hg with a pH less than 7.35 is termed as Type 2 RF or hypercapnic RF.

The initial treatment for hypoxemia in ARF patients is oxygen therapy. It is applied using devices such as nasal cannulas, face masks or masks with reservoir bags, HFNC etc. HFNC makes use of heated, humidified air combined with oxygen. Different sized nasal cannulas or tracheotomy cannula connectors can be used to administer this gas mixture. [3-4] High oxygen flows (60 L/min) are delivered by HFNCs, and their FiO2 is in the range of 0.21 to 1. Failure of HFNC is characterized by the necessity of endotracheal intubation in spite of HFNC administration. [5]

The likelihood of HFNC treatment failure varies between 10 and 20 percent, depending on the indication of HFNC use and the patient's characteristics. [6-8] Delays in intubating patients who need this function are known to have negative effects.5The SpO2/FiO2 (SF) ratio is frequently

utilized to determine the severity of respiratory illness because SpO2 is routinely monitored in patients with respiratory issues. [9] The ratio of SpO2/FiO2 toRRis the basis for the respiratory rate-oxygenation (ROX) index, which is able to predict HFNC failure.

However, the predictive factors for HFNC failure have not been thoroughly studied, and the findings of various studies have been inconsistent. Therefore, in order to assess the predictors for HFNC failure in patients with ARF, we conducted an observational study at the hospital.

Aims & Objectives: To study the predictors of high-flow nasal cannula failure in acute respiratory failure (ARF) patients.

Materials & Methods

This was a hospital-based observational study performed over a period of 12 months i.e., from January 2023 to December2023in the Department of Pulmonary Medicine and Allied Specialties of Gauhati Medical College, Assam. Adult patients more than 18 yrs presenting with acute respiratory failure (ARF) and managed with HFNC in the Department of Pulmonary Medicine and Allied Specialties were included. Excluded patients were those patients who HFNC as a palliative management in malignancies, patient given HFNC as a tool to wean from mechanical ventilation and patient not willing to give consent.

Important parameters included in the study were Glassgow coma score (GCS), respiratory rate, FiO_2, SpO_2, ROX index, and arterial blood gas parameters, including pH, PaO_2, and PO_2.Outcome characteristics Included survival or mortality, and failure or success of HFNC treatment.

Observations and Results

In comparing of age of patients among success and failure group of HFNC mean age of success group was 63.3 years and failure group was 66.47 years showing no statistically significant difference. Also there was no significant difference in gender observed between success and failure of HFNC (p=1.000).

Table1: Shows comparison of causes of respiratory failure among success and failure of HFNC

Causes	Failure (N=15)	Success (N=10)	p
Pneumonia	9 (60.00%)	6 (60.00%)	1.000
Interstitial lung disease	1 (6.67%)	1 (10.00%)	0.763
Fluid overload	1 (6.67%)	1 (10.00%)	0.763
Cancer	1 (6.67%)	0 (0.00%)	0.405
Atelectasis	0 (0.00%)	1 (10.00%)	0.211
Haemoptysis	1 (6.67%)	0 (0.00%)	0.405
ARDS	1 (6.67%)	0 (0.00%)	0.405
Pleural effusion	1 (6.67%)	0 (0.00%)	0.405
Pulmonary embolism	0 (0.00%)	1 (10.00%)	0.211

2. Comparison of GCS score before HFNC among success and failure of HFNC

Independent sample t test indicated no significant difference in GCS score before HFNC observed between success and failure of HFNC (p=0.076).

3. Comparison of FiO2 before HFNC among success and failure of HFNC: Independent sample t test indicated no significant difference in FiO2 within HFNC failure patients and HFNC success patients (p=0.199).

Comparison of FiO2 1hr after HFNC among success and failure of HFNC: v Independent sample t test indicated no significant difference in FiO2 within HFNC failure patients and HFNC success patients (p=0.154).

Comparison of FiO2 12hr after HFNC among success and failure of HFNC

Independent sample t test indicated no significant difference in FiO2 12hr after HFNC observed between success and failure of HFNC (p=0.106).

4. Comparison of patients according to respiratory rate before HFNC

Independent sample t test indicated significant increase in respiratory rate within HFNC failure patients than HFNC success patients (p=0.002).

Comparison of respiratory rate 1hr after HFNC among success and failure of HFNC

Independent sample t test indicated no significant difference in respiratory rate 1hr after HFNC observed between success and failure of HFNC (p=0.130).

Comparison of patients according to respiratory rate 12hr after HFNC: Independent sample t test indicated no significant difference in respiratory rate 12hr after HFNC observed between success and failure of HFNC (p=0.195).

5. Comparison of SpO2 before HFNC among success and failure of HFNC: Independent sample t test indicated no significant difference in SpO2

before HFNC observed between success and failure of HFNC (p=0.144).

Comparison of SpO2 1hr after HFNC among success and failure of HFNC: Independent sample t test indicated no significant difference in SpO2 1hr after HFNC observed between success and failure of HFNC (p=0.145).

Comparison of SpO2 12hr after HFNC among success and failure of HFNC: Independent sample t test indicated no significant difference in SpO2 12hr after HFNC observed between success and failure of HFNC (p=0.145).

6. Comparison of ROX 1hr and 12hr after HFNC among success and failure of HFNC

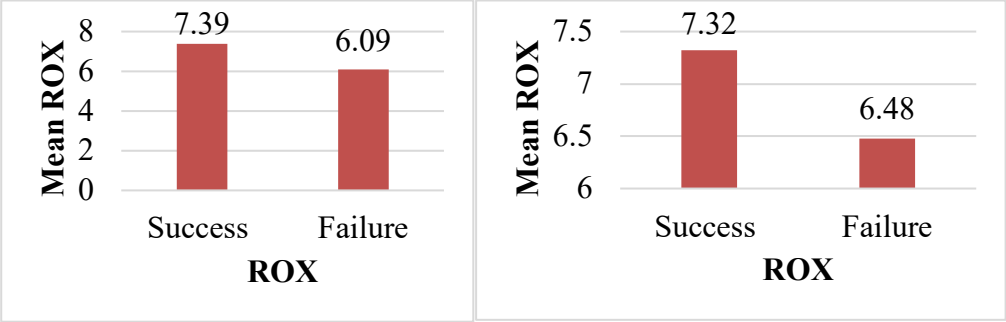

Figure 1:

Independent sample t test indicated significantly lower ROX within HFNC failure patients than HFNC success patients at 1hr (p=0.022) and at 12hr(p=0.004).

7. Comparison of pH among success and failure of HFNC

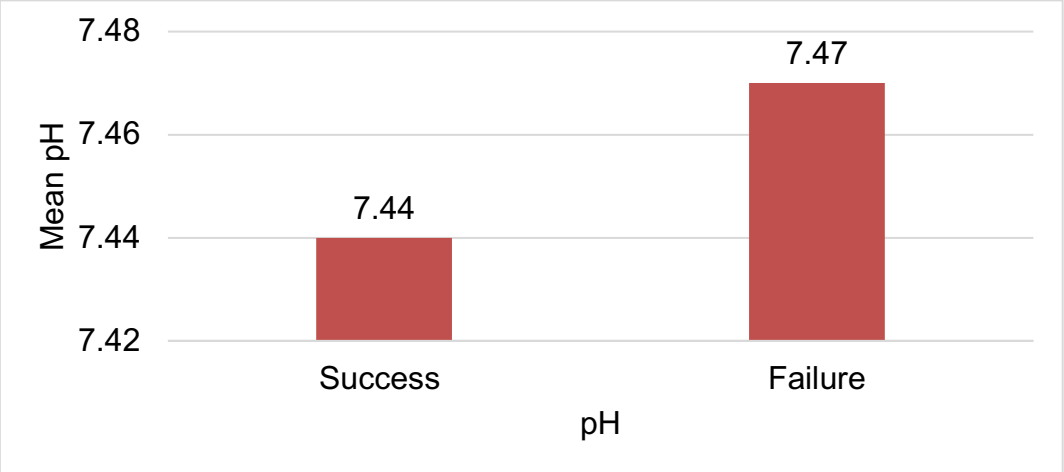

Figure 2:

Independent sample t test indicated significantly higher pH within HFNC failure patients than HFNC success patients (p=0.005).

8. Comparison of PaCO2 among success and failure of HFNC: Independent sample t test indicated no significant difference in PaCO2 observed in HFNC failure and HFNC success patients (p=0.381).

9. Comparison of PaO2 among success and failure of HFNC: Independent sample t test indicated no significant difference in PaO2 observed in HFNC failure and HFNC success patients (p=0.702).

10. Comparison of survival among success and failure of HFNC: Chi-square test revealed significant higher proportion of mortality found in HFNC failure patients than HFNC success patients (p<0.0001)

11. Multivariate analysis of the predictive factors for success of HFNC

Table 1:

Characteristics	Success (10)	Failure (15)	OR	95% CI	p
ROX	7.39 ± 1.10	6.09 ± 0.91	0.195	0.048 – 0.790	0.022
FiO2	0.51 ± 0.03	0.54 ± 0.07	0.001	0.000 – 19.15	0.109

The analysis revealed that ROX score was a significant predictor of success of HFNC (p=0.022), while FiO2 was not.

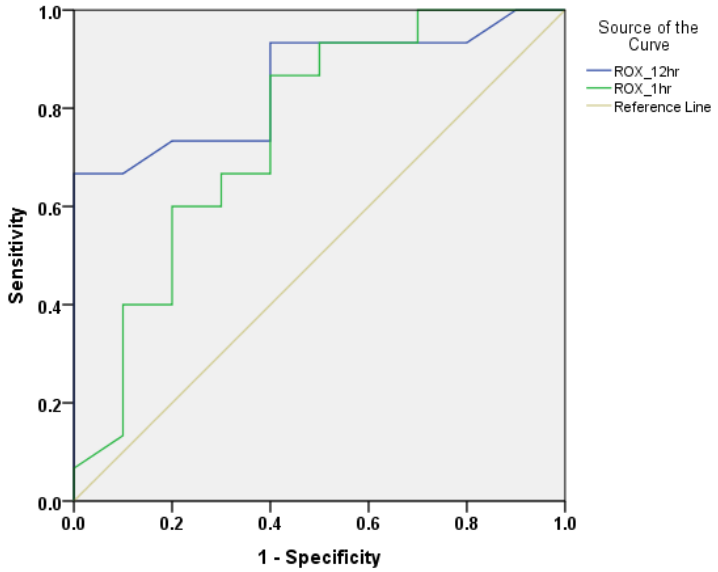

Figure 3: ROC curve analysis of ROX index at 1hr and 12hr in patients with respiratory failure

At a cut-off value of 6.9 ROX index at 1hr had a sensitivity and specificity of 66.7% and 70.0%, respectively (AUC: 0.750, 95% CI: 0.542-0.958; p-value: 0.038). At a cut-off value of 6.4 ROX index at 12hr had a sensitivity and specificity of 73.3% and 80.0% (AUC: 0.853, 95% CI: 0.704-1.000; p-value: 0.003).

Discussion

Causes: In the present study, there was no significant difference between the causes of success and failure in the HFNC groups (p>0.05). It is consistent with thestudies done by Goh and associates10&Liu and associates [11].

FIO2 Levels before HFNC, and 1 Hour and 12 Hours after HFNC: In the present study, there was no significant difference in FiO_2 between HFNC failure and success patients before HFNC (p=0.199), 1 hour after HFNC (p=0.154), and 12 hours after HFNC (p=0.106). it is consistent with ofstudy by Alshahrani and associates [12]

Respiratory Rate before HFNC, and 1 Hour and 12 Hours after HFNC: In the present studyno significant differences in respiratory rate were observed at 1 hour (p=0.130) and 12 hours (p=0.195) after HFNC between success and failure groups. Consistent with the findings of the study by Lun and associates [13]

SPO_2 Levels before HFNC, and 1 Hour and 12 Hours after HFNC: In this study, there was no significant difference in SpO_2 levels before HFNC (p=0.144), 1 hour after HFNC (p=0.145) and 12 hours after HFNC (p=0.145) between success and failure outcomes. In alignment with the findings of this study, Alshahrani and associates [12]

GCS Scores before HFNC: In the current study, there was no significant difference in GCS scores before HFNC (p=0.076. In contrast to the findings of the present study, Lun and associates reported a significantly higher GCS scores upon ICU admission (p=0.024) and at 12 hours after HFNC (p=0.027) in patients with HFNC success compared patient with HFNC failure. [13] Similarly, Liu and associates revealed a significant difference in GCS scores between HFNC success and failure patients within the 0-24 hour period (p<0.05).[11]This variation in findings could be ascribed to difference in etiologies of respiratory failure.

Rox Index 1 Hour and 12 Hours after HFNC: In present study, there was a significantly lower ROX index in HFNC failure group of patients in comparison to HFNC success group of patients both at 1 hour (p=0.022) and 12 hours (p=0.004) after HFNC. Aligned with the present findings, Lun and associates [13]

pH, paco2, pao2: In the present study, there was a significantly high baseline pH in HFNC failure patients than HFNC success patients (p=0.005). In case of paco2, pao2 there was no significant difference. In consistent with the present findings, Lun and associates [13]

Survival: In the present study, significantly higher mortality was found in HFNC failure patients than HFNC success patients (p<0.0001). Consistent with the findings of this study, Lun and associates [13]

Predictors of Failure of High-Flow Nasal Cannula: In the present study, ROX index was a significant predictor of failure of high-flow nasal cannula (p=0.022). Consistent with the results of

the current study, Ferrer and associates found that ROX index is a significant predictor of failure of HFNC treatment (p=0.015). [14] Similarly, Alshahrani and associates, [12] Roca and associates [15] andLun and associates [13] reported that ROX index significantly predicted the failure of HFNC treatment (p=0.008, 0.002, and 0.012, respectively). Thus, the ROX index is a consistent predictor of HFNC failure.

Roc Curve Analysis: The ROC curve analysis of ROX index at 1 hour and 12 hours in patients with respiratory failure. At a cut-off value of 6.9 and at 1 hour, ROX index had a sensitivity of 66.7 and specificity of 70.0% (AUC: 0.750, 95% CI: 0.542-0.958; p=0.038). At a cut-off value of 6.4 and at 12 hours, ROX index had a sensitivity of 73.3% and specificity of 80.0% (AUC: 0.853, 95% CI: 0.704-1.000; p=0.003). In consensus with the results of current study, Ferrer and associates found that in ROC curve analysis, at a cut-off value of 5.41 ROX index at 1 hour had a sensitivity of 86% and specificity of 56% (AUC 0.80, 95%CI 0.70–0.80, p=0.000). At a cut-off value of 5.27 ROX index at 12 hours had a sensitivity of 93% and specificity of 71% (AUC 0.88, 95%CI 0.77–0.99, p=0.000).91 Similarly, Lun and associates found that in ROC curve analysis, at a cut-off value of 5.626 ROX index at 12 hours had a sensitivity of 88% and specificity of 41% (AUC 0.659, p=0.014). [13]

Study Limitations: The standards and eligibility requirements for HFNC may differ amongst institutions, as this was a single-centre study.Because of this study's small sample size, the findings cannot be applied to all patients suffering from RF.

Summary

- The majority of patients experienced HFNC failure (60%). Causes of respiratory failure (p>0.05), FiO_2 (p=0.199), $PaCO_2$ (p=0.381), PaO_2 (p=0.702) were comparable among patients with success and failure of HFNC.
- Approximately 66% of patients who failed HFNC succumbed.
- There was no significant difference in FiO_2 between HFNC failure and success patients before HFNC (p=0.199) as well as 1 hour (p=0.154) and 12 hours (p=0.106) after HFNC treatment.
- The RR was significantly more in patients with HFNC failure when compared to those with success HFNC before HFNC initiation (p=0.002) but was comparable at 1 hour (p=0.130) and 12 hours (p=0.195) after HFNC treatment.
- The GCS scores, SpO_2, and flow rate were comparable before HFNC (p=0.076, 0.144, and 1.000, respectively), 1 hour after HFNC (p=0.540, 0.145, and 1.000, respectively) and 12 hours after HFNC treatment (p=0.146, 0.145, and 1.000, respectively) between success and failure outcomes.
- The ROX index was significantly lower in HFNC failure patients than HFNC success patients at 1 hour (p=0.022) and 12 hours (p=0.004) after HFNC treatment.
- The patients with HFNC failure had significantly higher pH (p=0.005) and mortality (p<0.0001) compared to patients with HFNC success.
- The ROX index was a significant predictor of failure of HFNC treatment (p=0.022).
- At a cut-off value of 6.9 and at 1 hour, ROX index had a sensitivity of 66.7% and specificity of 70.0% (AUC: 0.750, 95% CI: 0.542-0.958; p-value: 0.038).
- At a cut-off value of 6.4 and at 12 hour, ROX index had a sensitivity of 73.3% and specificity of 80.0% (AUC: 0.853, 95% CI: 0.704-1.000; p-value: 0.003).

Conclusion

To conclude, most of the patients with ARF experience HFNC failure. Moreover, those with HFNC failure have a high mortality rate. ROX index has good performance in prediction of failure of HFNC treatment; however, the sensitivity and specificity is higher at 12 hours after HFNC treatment than at 1 hour. Further research with larger samples and prospective designs is needed to confirm these results.

References

1. Vargas F, Saint-Leger M, Boyer A, Bui NH, Hilbert G. Physiologics effects of high-flow nasal cannula oxygen in critical care subjects. Respiratory Care. 2015; 60(10):1369-76.
2. Tobin MJ, Laghi F, Jubran A. Ventilatory failure, ventilator support, and ventilator weaning. Comprehensive Physiology. 2012; 2: 2871–2921.
3. Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated humidified highflow nasal oxygen in adults. Mechanism of action and clinical implications. Chest. 2015; 148(1):253---61.
4. Roca O, Hernández G, Diaz-Lobato S, Carratalá JM, Gutiérrez R, Masclans JR. and the Spanish Multidisciplinary Group of High Flow Supportive Therapy (HiSpaFlow). Current evidence for the effectiveness of heated and humidified high flow nasal cannula supportive therapy in adult patients with respiratory failure. Critical Care. 2016; 20:109.
5. Kang BJ, Koh Y, Lim C-M, Huh JW, Baek S, Han M, et al. Failure of high flow nasal cannula therapy may delay intubation and increase mortality. Intensive Care Medicine. 2015; 41(4): 623–632.

6. O'Brien S, Craig S, Babl FE, Borland ML, Oakley E, Dalziel SR. 'Rational use of high-flow therapy in infants with bronchiolitis. What do the latest trials tell us?' A Paediatric Research in Emergency Departments International Collaborative perspective. J Paediatr Child Health. 2019; 55(7):746-52.
7. Er A, Çağlar A, Akgül F, Ulusoy E, Çitlenbik H, Yılmaz D, Duman M. Early predictors of unresponsiveness to high-flow nasal cannula therapy in a pediatric emergency department. Pediatr Pulmonol. 2018; 53(6):809-815.
8. Kamit CF, Anil AB, Anil M, Zengin N, Durak F, Alparslan C, et al. Predictive factors for the outcome of high flow nasal cannula therapy in a pediatric intensive care unit: Is the SpO(2)/FiO(2) ratio useful? Journal of critical care. 2018; 44:436-44.
9. Saelim K, Thirapaleka B, Ruangnapa K, Prasertsan P, Anuntaseree W. Predictors of high flow nasal cannula failure in pediatric acute respiratory distress. Clin ExpPediatr 2022; 65(12):595–601.
10. Goh KJ, Chai HZ, Ong TH, Sewa DW, Phua GC, Tan QL. Early prediction of high flow nasal cannula therapy outcomes using a modified ROX index incorporating heart rate. Journal of intensive care. 2020; 8:1-4
11. Liu J, Li D, Luo L, Liu Z, Li X, Qiao L. Analysis of risk factors for the failure of respiratory support with high-flow nasal cannula oxygen therapy in children with acute respiratory dysfunction: A case–control study. Frontiers in Pediatrics. 2022; 10:979944.
12. Alshahrani MS, Alshaqaq HM, Alhumaid J, Binammar AA, AlSalem KH, Alghamdi A, et al. High-Flow nasal cannula treatment in patients with COVID-19 acute hypoxemic respiratory failure: A prospective cohort study. Saudi J Med MedSci 2021; 9:215-22
13. Lun CT, Leung CK, Shum HP, So SO. Predictive factors for high-flow nasal cannula failure in acute hypoxemic respiratory failure in an intensive care unit. Lung India 2022; 39:5-11.
14. Ferrer S, Sancho J, Bocigas I, Bures E, Mora H, Monclou E, Mulet A, Quezada A, Royo P, Signes-Costa J. ROX index as predictor of high flow nasal cannula therapy success in acute respiratory failure due to SARS-CoV-2. Respiratory Medicine. 2021; 189:106638.
15. Roca O, Messika J, Caralt B, García-de-Acilu M, Sztrymf B, Ricard J-D, et al. Predicting success of high-flow nasal cannula in pneumonia patients with hypoxemic respiratory failure: the utility of the ROX index. Journal of Critical Care. 2016; 35: 200–205.