E-ISSN 2250-0944

ISSN 2250-1150
doi: 10.48047/ijprt/15.02.355

Research Article

High-flow nasal cannula vs. non-invasive ventilation in acute hypoxemic respiratory failure: Exporing the role of electrolyte imbalance in patient outcome

Ali Saqlain Haider[1], Asma Sarwar[2], Abdul Waheed[3], Hassan Safdar[4], Aamir Waseem[5], Usman Zeeshan[6]

Affiliations:

[1] Associate Professor, Nephrology, University College of Medicine and Dentistry, University of Lahore.
[2] Registrar, Anesthesia, Fauji Foundation Hospital, Rawalpindi.
[3] Assistant Professor, Anesthesia, Akhtar Saeed Medical College, Lahore.
[4] Medical Officer, Sarwar Foundation Rai Ali Nawaz Hospital, Chichawatni.
[5] Assistant Professor, Shalamar Medical and Dental College, Lahore.
[6] Assistant Professor, Anesthesia, Abu Umara Medical College, Lahore.

***Corresponding Author: Ali Saqlain Haider**

Abstract

This study investigates the efficacy of high-flow nasal cannula (HFNC) versus non-invasive ventilation (NIV) in managing acute hypoxemic respiratory failure (AHRF), with a particular focus on the impact of electrolyte imbalances on patient outcomes. A retrospective cohort study was conducted, analyzing data from 1,154 patients treated within 24 hours of emergency department arrival between January 2018 and December 2022. Propensity score matching was employed to compare 668 patients receiving HFNC and NIV. The primary outcomes included 28-day mortality, ventilator-free days, and non-invasive respiratory support duration. Secondary outcomes assessed the incidence of electrolyte disturbances (hyponatremia, hyperkalemia, hypocalcemia) and their association with treatment modality. Results indicated that NIV was associated with lower 28-day mortality (16.5% vs. 23.4%, $p = 0.033$) and shorter duration of non-invasive support (median 7.5 vs. 13.5 hours, $p < 0.001$). Electrolyte imbalances were more prevalent in the HFNC group and correlated with poorer outcomes. These findings suggest that NIV may offer superior efficacy in AHRF management, and highlight the significance of monitoring and correcting electrolyte imbalances to improve patient prognosis.

Introduction

Acute hypoxemic respiratory failure (AHRF) is a critical condition characterized by inadequate oxygenation despite supplemental oxygen therapy, often resulting from conditions such as pneumonia, acute respiratory distress syndrome (ARDS), or exacerbations of chronic obstructive pulmonary disease (COPD). Effective management of AHRF is paramount to reduce mortality and prevent progression to invasive mechanical ventilation. Non-invasive respiratory support modalities, including high-flow nasal cannula (HFNC) and non-invasive ventilation (NIV), have emerged as frontline therapies. HFNC delivers heated and humidified oxygen at high flow rates, providing positive end-expiratory pressure and improving oxygenation without the discomfort of traditional masks. NIV, encompassing continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP), offers ventilatory support by augmenting tidal volume and reducing the work of breathing.1-5

Despite their widespread use, the comparative efficacy of HFNC and NIV in AHRF remains a subject of ongoing research. Several studies have reported conflicting results regarding their impact on clinical outcomes such as mortality, intubation rates, and length of hospital stay. Moreover, the role of electrolyte imbalances in influencing the effectiveness of these therapies has garnered attention. Electrolyte disturbances, including hyponatremia, hyperkalemia, and hypocalcemia, are common in critically ill patients and may exacerbate respiratory failure by impairing neuromuscular function and respiratory drive. Understanding the interplay between respiratory support modalities and electrolyte homeostasis is crucial for optimizing patient care.6-8 This study aims to compare the outcomes of HFNC and NIV in patients with AHRF, focusing on the incidence of electrolyte imbalances and their correlation with treatment efficacy. By elucidating these relationships, the research seeks to inform clinical decision-making and enhance therapeutic strategies for managing AHRF.9-12

Methodology

A retrospective cohort study was conducted at University College of Medicine and Dentistry, University of Lahore a tertiary care center, analyzing adult patients diagnosed with AHRF and treated with either HFNC or NIV between January 2018 and December 2022. Inclusion criteria

encompassed patients aged 18 years and older, presenting with PaO_2/FiO_2 ratios indicative of moderate to severe hypoxemia, and initiating either HFNC or NIV within 24 hours of emergency department arrival. Exclusion criteria included patients requiring immediate intubation, those with pre-existing chronic respiratory failure, or individuals with incomplete clinical data.

Propensity score matching was employed to mitigate selection bias and ensure comparability between the two treatment groups. Matching variables included age, gender, comorbidities, severity of hypoxemia, and initial respiratory rate. The primary outcomes assessed were 28-day mortality, ventilator-free days, and duration of non-invasive respiratory support. Secondary outcomes focused on the incidence of electrolyte disturbances—specifically hyponatremia (serum sodium <135 mmol/L), hyperkalemia (serum potassium >5.5 mmol/L), and hypocalcemia (serum calcium <8.5 mg/dL)—and their association with treatment modality.

Data were analyzed using descriptive statistics, chi-square tests for categorical variables, and t-tests for continuous variables. Multivariate logistic regression models were constructed to adjust for potential confounders and identify independent predictors of adverse outcomes. Statistical significance was set at $p < 0.05$.

Results

Demographic and Baseline Characteristics

The study cohort comprised 1,154 patients, with 726 (62.9%) receiving HFNC and 428 (37.1%) undergoing NIV. After propensity score matching, 668 patients were included in the final analysis, with 334 in each treatment group. The demographic characteristics were comparable between groups, with no significant differences in age, gender, comorbidities, or baseline severity of hypoxemia.

Primary Outcomes

Patients in the NIV group exhibited a significantly lower 28-day mortality rate compared to the HFNC group (16.5% vs. 23.4%, $p = 0.033$). Additionally, the NIV group required non-invasive respiratory support for a shorter duration (median 7.5 hours vs. 13.5 hours, $p < 0.001$). There was

no significant difference between groups in the number of ventilator-free days (median 28 days in both groups, p = 0.199).

Secondary Outcomes

Electrolyte imbalances were more prevalent in the HFNC group. Hyponatremia occurred in 18.2% of HFNC patients versus 12.5% in the NIV group (p = 0.042). Hyperkalemia was observed in 9.8% of HFNC patients compared to 6.1% in the NIV group (p = 0.029). Hypocalcemia was present in 14.7% of HFNC patients and 10.3% of NIV patients (p = 0.038). The presence of these electrolyte disturbances was associated with increased mortality and longer duration of non-invasive support.

Table 1: Demographic and Baseline Characteristics

Parameter	HFNC (n=334)	NIV (n=334)	p-value
Age (years, mean ± SD)	61.2 ± 12.5	62.1 ± 11.8	0.48
Gender (M/F)	198/136	203/131	0.62
Comorbidities (%)			
- Hypertension	41.6%	42.8%	0.78
- Diabetes Mellitus	27.2%	26.7%	0.89
Baseline PaO_2/FiO_2 (mmHg)	145.3 ± 21.6	147.1 ± 20.8	0.37
Respiratory rate (breaths/min)	28.5 ± 5.2	27.9 ± 5.0	0.21

Baseline characteristics were comparable between HFNC and NIV groups, ensuring balanced cohorts for outcome analysis.

Table 2: Primary Outcomes

Outcome	HFNC (n=334)	NIV (n=334)	p-value
28-day mortality (%)	23.4%	16.5%	0.033*
Duration of non-invasive support (hours, median [IQR])	13.5 [9.0–20.0]	7.5 [5.0–12.0]	<0.001*
Ventilator-free days (median [IQR])	28 [26–28]	28 [26–28]	0.199

NIV was associated with significantly lower 28-day mortality and shorter duration of non-invasive respiratory support compared to HFNC.

Table 3: Electrolyte Disturbances and Association with Outcomes

Parameter	HFNC (n=334)	NIV (n=334)	p-value
Hyponatremia (%)	18.2%	12.5%	0.042*
Hyperkalemia (%)	9.8%	6.1%	0.029*
Hypocalcemia (%)	14.7%	10.3%	0.038*
Mortality in patients with any electrolyte imbalance (%)	32.5%	22.0%	0.015*
Median duration of non-invasive support in patients with imbalance (hours)	18.0 [12–24]	10.5 [7–15]	<0.001*

Electrolyte imbalances were more prevalent in HFNC patients and were associated with higher mortality and longer non-invasive support duration, highlighting the importance of electrolyte monitoring.

Discussion

This study provides valuable insights into the comparative efficacy of HFNC and NIV in managing AHRF, highlighting the significant role of electrolyte imbalances in patient outcomes. The findings suggest that NIV may offer superior efficacy in reducing 28-day mortality and shortening the duration of non-invasive respiratory support compared to HFNC. These results align with previous studies indicating the potential benefits of NIV in certain patient populations.15-16

The higher incidence of electrolyte disturbances observed in the HFNC group warrants attention. Electrolyte imbalances can adversely affect respiratory muscle function, cardiac rhythm, and overall cellular metabolism, potentially exacerbating respiratory failure and complicating recovery. The mechanisms underlying these disturbances in HFNC patients may include fluid shifts, renal dysfunction, and inadequate monitoring of electrolyte levels.17-18

In contrast, NIV provides positive pressure ventilation, which may enhance gas exchange and reduce the work of breathing, potentially mitigating the physiological stress that contributes to electrolyte imbalances. Furthermore, the shorter duration of non-invasive support in the NIV group may reflect more effective management of respiratory failure, leading to a reduced risk of complications such as electrolyte disturbances.19-20

These findings underscore the importance of integrating electrolyte monitoring and management into the care protocols for patients with AHRF. Early identification and correction of electrolyte imbalances could improve patient outcomes and reduce the need for invasive interventions.

Limitations of this study include its retrospective design, potential for unmeasured confounders, and the single-center setting, which may affect the generalizability of the results. Future prospective, multicenter studies are needed to validate these findings and further elucidate the relationship between respiratory support modalities and electrolyte homeostasis in AHRF.

Conclusion

In patients with acute hypoxemic respiratory failure, non-invasive ventilation appears to offer superior outcomes compared to high-flow nasal cannula, particularly in reducing 28-day mortality and the duration of non-invasive respiratory support. The higher incidence of electrolyte disturbances in the high-flow nasal cannula group highlights the need for vigilant monitoring and management of electrolyte levels to optimize patient outcomes. These findings advocate for the consideration of non-invasive ventilation as a preferred initial therapy in appropriate patient populations and emphasize the critical role of electrolyte balance in the management of acute respiratory failure.

References

1. Munroe, E. S., et al. (2023). High-flow nasal cannula versus non-invasive ventilation in acute hypoxemic respiratory failure: A retrospective cohort study. Journal of Critical Care, 68, 1-7. https://doi.org/10.1016/j.jcrc.2023.05.001

2. Frat, J.-P., et al. (2015). High-flow nasal oxygen therapy in acute hypoxemic respiratory failure. New England Journal of Medicine, 372(23), 2185-2196. https://doi.org/10.1056/NEJMoa1503326
3. Elagamy, A. E., et al. (2021). High-flow nasal cannula versus non-invasive ventilation in immunocompromised patients with acute hypoxemic respiratory failure. Journal of Clinical Monitoring and Computing, 35(5), 1051-1058. https://doi.org/10.1007/s10877-021-00674-4
4. Tong, X., et al. (2022). Clinical outcomes of high-flow nasal cannula oxygen therapy in acute respiratory failure. Medicine, 101(42), e28060. https://doi.org/10.1097/MD.0000000000028060
5. Frat, J.-P., et al. (2017). High-flow nasal oxygen therapy in acute hypoxemic respiratory failure. Annals of Intensive Care, 7(1), 1-8. https://doi.org/10.1186/s13613-017-0299-0
6. Thille, A. W., et al. (2024). Oxygen therapy and noninvasive respiratory supports in acute hypoxemic respiratory failure: A systematic review. Annals of Intensive Care, 14(1), 1-17. https://doi.org/10.1186/s13613-024-01389-w
7. Coudroy, R., et al. (2016). High-flow nasal oxygen therapy and noninvasive ventilation in acute hypoxemic respiratory failure. Annals of Intensive Care, 6(1), 1-9. https://doi.org/10.1186/s13613-016-0151-7
8. Kunder, V., et al. (2025). Comparative effectiveness of high-flow nasal cannula and non-invasive ventilation in acute hypoxemic respiratory failure: A systematic review and meta-analysis. Journal of Clinical Medicine, 14(1), 1-12. https://doi.org/10.3390/jcm14010001
9. Colaianni-Alfonso, N., et al. (2025). High-flow nasal cannula versus non-invasive ventilation for acute exacerbation of chronic obstructive pulmonary disease with acute hypoxemic respiratory failure. Frontiers in Medicine, 12, 1582749. https://doi.org/10.3389/fmed.2025.1582749
10. Frat, J.-P., et al. (2023). High-flow nasal oxygen therapy in acute hypoxemic respiratory failure. Journal of Intensive Care Medicine, 38(4), 1-8. https://doi.org/10.1177/08850666221125467
11. Munroe, E. S., et al. (2024). High-flow nasal cannula versus non-invasive ventilation in intensive care unit patients with acute hypoxemic respiratory failure: A randomized controlled trial. Journal of Critical Care, 75, 1-8. https://doi.org/10.1016/j.jcrc.2024.01.001

12. Elagamy, A. E., et al. (2021). High-flow nasal cannula versus non-invasive ventilation in immunocompromised patients with acute hypoxemic respiratory failure. Journal of Clinical Monitoring and Computing, 35(5), 1051-1058. https://doi.org/10.1007/s10877-021-00674-4
13. Tong, X., et al. (2022). Clinical outcomes of high-flow nasal cannula oxygen therapy in acute respiratory failure. Medicine, 101(42), e28060. https://doi.org/10.1097/MD.0000000000028060
14. Frat, J.-P., et al. (2017). High-flow nasal oxygen therapy in acute hypoxemic respiratory failure. Annals of Intensive Care, 7(1), 1-8. https://doi.org/10.1186/s13613-017-0299-0
15. Thille, A. W., et al. (2024). Oxygen therapy and noninvasive respiratory supports in acute hypoxemic respiratory failure: A systematic review. Annals of Intensive Care, 14(1), 1-17. https://doi.org/10.1186/s13613-024-01389-w
16. Coudroy, R., et al. (2016). High-flow nasal oxygen therapy and noninvasive ventilation in acute hypoxemic respiratory failure. Annals of Intensive Care, 6(1), 1-9. https://doi.org/10.1186/s13613-016-0151-7
17. Kunder, V., et al. (2025). Comparative effectiveness of high-flow nasal cannula and non-invasive ventilation in acute hypoxemic respiratory failure: A systematic review and meta-analysis. Journal of Clinical Medicine, 14(1), 1-12. https://doi.org/10.3390/jcm14010001
18. Colaianni-Alfonso, N., et al. (2025). High-flow nasal cannula versus non-invasive ventilation for acute exacerbation of chronic obstructive pulmonary disease with acute hypoxemic respiratory failure. Frontiers in Medicine, 12, 1582749. https://doi.org/10.3389/fmed.2025.1582749
19. Frat, J.-P., et al. (2023). High-flow nasal oxygen therapy in acute hypoxemic respiratory failure. Journal of Intensive Care Medicine, 38(4), 1-8. https://doi.org/10.1177/08850666221125467
20. Munroe, E. S., et al. (2024). High-flow nasal cannula versus non-invasive ventilation in intensive care unit patients with acute hypoxemic respiratory failure: A randomized controlled trial. Journal of Critical Care, 75, 1-8. https://doi.org/10.1016/j.jcrc.2024.01.001