



## ***Intrahospital Transport of Critically Ill Patients Using High Flow Nasal Cannula or Non-Invasive Ventilation: A Randomised Comparative Study***

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### **Abstract**

**Background:** Intrahospital transport of critically ill patients is challenging and optimal respiratory support during transportation is a scarcely investigated field. High Flow Nasal Cannula (HFNC) and Non-Invasive Ventilation (NIV) are commonly used modalities in acute respiratory failure which can provide the needed oxygen support during transportation of such patients. Hence this study was planned to compare the efficacy and safety of HFNC and NIV during intrahospital transportation of the critically ill patients.

**Materials and Methods:** A randomized comparative study was conducted. Fifty critically ill patients who required intrahospital transport were allocated randomly to HFNC and NIV group. The patients' need for escalation of respiratory support, effect on oxygenation, length of ICU/hospital stay, hospital mortality and any adverse event during transportation were recorded.

**Results:** The HFNC group had lower duration of oxygen support than NIV group ( $2.84 \pm 1.60$  versus  $4.00 \pm 2.04$ ,  $p= 0.030$ , respectively) and lower requirement of  $FiO_2$  ( $0.48 \pm 0.16$  vs.  $0.67 \pm 0.24$ ,  $p= 0.004$ , respectively). The HFNC group had lower rates of escalation of respiratory support, lower duration of ICU stay, ICU mortality and hospital mortality than the NIV group, the difference, however, being non-significant.

**Conclusion:** The present study shows that HFNC can be a better modality than NIV for respiratory support during intrahospital transport of critically ill patients.

**Clinical Significance** – The present study highlights the preferred mode of respiratory support during intrahospital transport of critically ill patients.

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### List of Abbreviations

**HFNC:** High Flow Nasal Cannula

**NIV:** Non-Invasive Ventilation

**FiO<sub>2</sub>:** Fraction of Inspired Oxygen

**AE:** Adverse Events

**ICU:** Intensive Care Unit

**HCW:** Health Care Worker

**ARF:** Acute Respiratory Failure

**PEEP:** Positive End Expiratory Pressure

**CI:** Confidence Interval

**PaCO<sub>2</sub>:** Partial pressure of Carbon dioxide

**SAPS II:** Simplified Acute Physiology Score II

**COPD:** Chronic Obstructive Pulmonary Disease

**COVID-19:** Coronavirus Disease-19

**PICU:** Pediatric Intensive Care Unit

pulmonary edema and acute exacerbation of chronic-obstructive pulmonary disease [9]. The positive pressure in NIV augments better gas exchange and decreases the inspiratory effort [10]. However, good tolerance to NIV is not easily achieved due to frequent mask leaks, possibly causing patient-ventilator desynchrony and even intubation [11].

High-flow nasal cannula (HFNC) oxygen therapy is a relatively new modality that can deliver up to 60 l/min of fully humidified and heated oxygen leading to better patient compliance. The fraction of inspired oxygen (FiO<sub>2</sub>) ranges from 0.21 to 1.0 [12]. NIV has been addressed to prevent invasive mechanical ventilation and its complications in a wide range of hypoxicemic Acute respiratory Failure (ARF) patients; however, it is postulated that HFNC has the same effect as NIV with added advantages like easier tolerability, being more physiological, and patients can eat, drink, and talk while connected to HFNC [13,14].

While there are various studies evaluating and comparing HFNC and NIV in ICU settings, the present study was conducted with the aim to compare the efficacy of NIV with HFNC in the intrahospital transportation of critically ill patients.

### Materials and Methods

The study was performed in the adult medical ICU of our centre between July 2023 and July 2024. The Institution Ethical Committee approved the research protocol (registration number – ELMC&H/R-Cell/2023/32). The patients were enrolled in the study after informed consent from them or their next kin. The trial was registered with Clinical trial registry of India (CTRI number – CTRI/2023/07/054931).

However, critically ill patients are more prone to developing adverse events (AE) during transportation and moving them from the Intensive Care Unit (ICU) or other high-intensity care units is associated with an overall complication rate of up to 70% and a mortality rate of 2% [2-5]. These AEs may be attributed to various factors like unstable hemodynamics, ongoing organ support, presence of multiple devices or catheters, and even miscommunication between healthcare workers (HCWs) [6-8].

In the past two decades, strong evidence supported using non-invasive ventilation (NIV) for cardiogenic

The primary outcome of the study was to study the effect on oxygenation, by measuring SpO<sub>2</sub> during

transportation. The secondary outcomes were to record: duration of respiratory support (defined as the duration of combined invasive and non-invasive ventilation use in ICU), adverse events during transport (defined as cardiac arrest, need for resuscitation drugs), the need for escalation of respiratory support/invasive mechanical ventilation, the length of ICU and hospital stay, the ICU and hospital mortality.

Critically ill patients admitted to the adult ICU of our centre of age 18 years or above and requiring intrahospital transport were included in the study. Patients with severe respiratory failure requiring immediate tracheal intubation (respiratory frequency more than 40 breaths per min., severe hypoxia, severe respiratory acidosis with a pH <7.25, Glasgow Coma Scale <8), patients with contraindication to NIV (oral and facial trauma, excessive phlegm with poor expectoration ability, hemodynamic instability), patients with poor short term prognosis (very high risk of death within seven days or receiving palliative care), pregnant females, carriers of an implantable defibrillator or pacemaker and tracheostomised patients were excluded from the study.

## Sample Size

Sample size was calculated using the formula:

$$\frac{(\sigma_1^2 + \sigma_2^2 / \kappa)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

where, n= sample size,  $\sigma$  = Standard Deviation,  $\Delta$  = difference of means,  $\kappa$ = ratio,  $Z_{1-\alpha/2}$ = two-sided Z value,  $Z_{1-\beta}$ = Power

From the previous study by Agmy et al., the sample size calculated using the above formula was 42 [15]. Considering 20% attrition bias and 95% CI, the final sample size came out to be 50 (25 in each group).

## Methodology

A total of 57 patients were screened for enrolment of whom 5 didn't meet the inclusion criteria and 2 declined to participate in the study. Total 50 patients who met the inclusion criteria were randomised by Sequentially Numbered Sealed Envelopes (SNOSE) technique into HFNC or NIV groups. In group A (NIV group) patients were connected to a ventilator

for conventional NIV with a face mask. Positive end-expiratory pressure (PEEP) was initially adjusted between 2 and 10 cmH<sub>2</sub>O. The PEEP level or FiO<sub>2</sub> (or both) was later on set to keep the SpO<sub>2</sub> more than or equal to 92%. The pressure-support level was set to achieve 6–8 ml/kg expired tidal volume. In group B (HFNC) heated humidified oxygen (31–37°C) was continuously supplied through binasal large-bore prongs. The initially adjusted oxygen flow rate was 60 l/min with FiO<sub>2</sub> of 1.0. The FiO<sub>2</sub> was then adjusted to attain SpO<sub>2</sub> more than or equal to 92%.

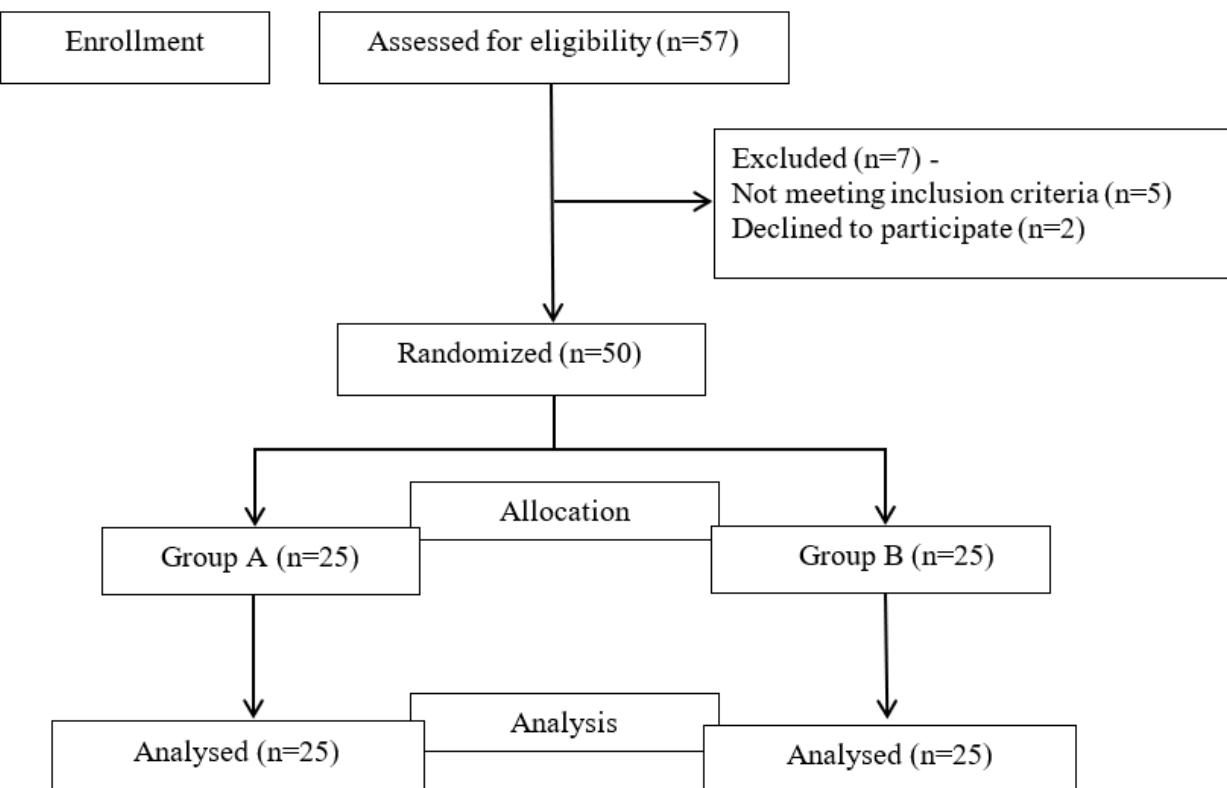
## Statistical Analysis

In order to compare patients receiving NIV or HFNC, just before the start of period 1, i.e. at baseline, Freeman-Halton's extension of Fisher's exact test was employed for categorical variables, and Wilcoxon's test for independent samples for quantitative variables.

A p value < 0.05 was considered statistically significant. Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, USA).

## Results

The present study was conducted in the medical ICU of our centre as a randomised comparative study. Figure 1 shows the patients' flowchart. Fifty patients met the inclusion criteria and each group included 25 patients.



**Figure 1:** Flow Chart of Patient Enrolment. 57 Patients were Assessed for Eligibility. 5 didn't Meet the Inclusion Criteria and 2 Denied to Participate in the Study. A Total of 50 Patients were Included in the Study (25 in Each Group).

Baseline demographic characters were comparable between the NIV and HFNC groups (Table 1). SpO<sub>2</sub> recorded during transportation was statistically non significant between the NIV and HFNC groups ( $97.68 \pm 3.16$  vs  $98.20 \pm 1.66$ ,  $p=0.470$ ). Hemoglobin levels of the cases in Group A were slightly higher as compared to Group B ( $9.92 \pm 1.51$  vs.  $9.76 \pm 2.43$  g/dL), however, no significant difference was found between the groups. On comparing SAPS-II score between the treatment groups, no significant difference was found for the score ( $39.6 \pm 8.72$  vs.  $37.48 \pm 10.71$ ).

**Table 1:** Baseline Patient Characteristics

Characteristics of the patient		Group A (NIV) (N=25)	Group B (HFNC) (N=25)	p value
Age (years) (mean $\pm$ SD)		53.60 $\pm$ 14.02	45.60 $\pm$ 17.14	p = 0.07
Male [n (%)]		11 (44.0)	14 (56.0)	p = 0.39
Female [n (%)]		14 (56.0)	11 (44.0)	p= 0.39
Weight (kg) (mean $\pm$ SD)		65.20 $\pm$ 8.98	64.68 $\pm$ 7.74	p=0.827
Comorbidities	Diabetes [n (%)]	7 (28.0)	4 (16.0)	p= 0.306
	COPD [n (%)]	7 (28.0)	3 (12.0)	p= 0.157
	CHF[n(%)]	2 (8.0)	3 (12.0)	p= 0.638
	Pneumonia [n (%)]	4 (8.0)	4 (8.0)	-
	Pulmonary edema [n (%)]	7 (28.0)	7 (28.0)	-
History of stroke [n (%)]		4 (16.0)	5 (20.0)	p= 0.713
SpO2 (%) (mean $\pm$ SD)		97.68 $\pm$ 3.16	98.20 $\pm$ 1.66	p= 0.470
Hb (gm/dL) (mean $\pm$ SD)		9.92 $\pm$ 1.51	9.76 $\pm$ 2.43	p= 0.776
SAPS II (mean $\pm$ SD)		39.6 $\pm$ 8.72	37.48 $\pm$ 10.71	p= 0.446

Data are reported as n (%) or mean (range)

HFNC High flow nasal cannula; NIV Non-invasive ventilation; COPD Chronic obstructive pulmonary disease; CHF- Congestive Heart Failure; SpO2 – Saturation of peripheral Oxygen; Hb – Hemoglobin; SAPS II Simplified acute physiology score II.

No significant difference was found between the two groups with respect to the baseline characteristics.

Table 2 and figure 2 demonstrate that cases in Group A as compared to Group B had higher duration of oxygen support (4.00 $\pm$ 2.04 vs 2.84 $\pm$ 1.60 days), ICU stay (4.58 $\pm$ 1.93 vs 4.32 $\pm$ 2.98 days) and but lower hospital stay (10.07 $\pm$ 2.97 vs 11.32 $\pm$ 4.47), albeit, a significant difference (p=0.030) was only found between the groups for duration of oxygen support. Another statistically significant difference was found in FiO2 which was higher in Group A as compared to Group B (0.67 $\pm$ 0.24 vs. 0.48 $\pm$ 0.16, p= 0.004) (Table 2). None of the cases in either of the groups reported adverse events (0.0%). Though a higher proportion of cases in Group A as compared to Group B required escalation of respiratory support (56.0% vs. 32.0%), had higher mortality during ICU stay (36.0% vs. 20.0%) and in-hospital mortality (8.0% vs. 0.0%), none of these parameters were significantly different between the groups (Figure 3).

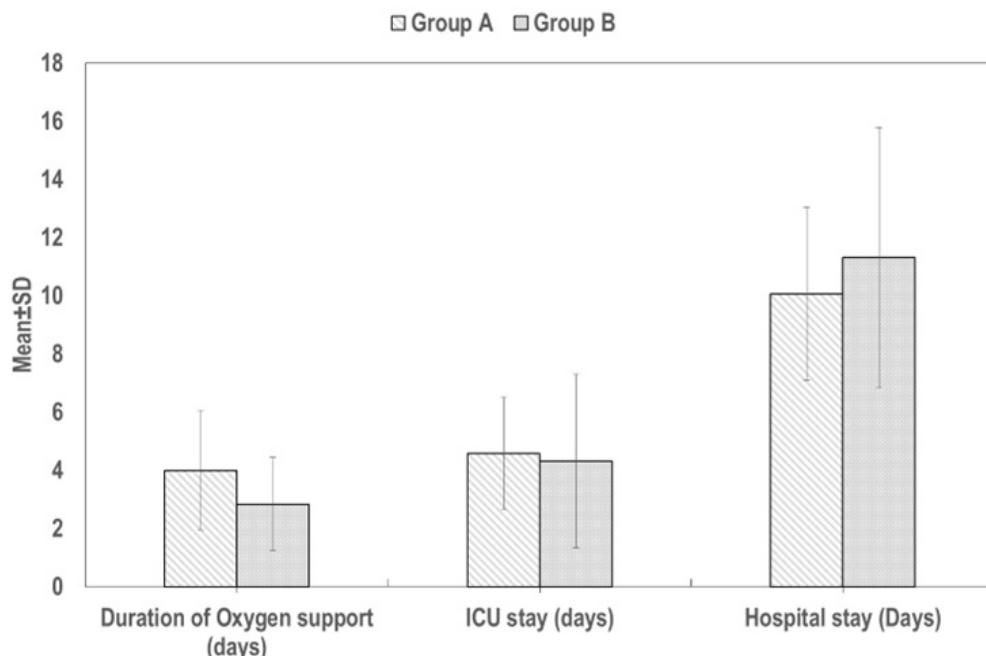
**Table 2:** Primary and Secondary Outcomes

End points	Group A (NIV)	Group B (HFNC)	p value
FiO2 (mean $\pm$ SD)	0.67 $\pm$ 0.24	0.48 $\pm$ 0.16	p= 0.004*
Duration of Oxygen support (days) (mean $\pm$ SD)	4.00 $\pm$ 2.04	2.84 $\pm$ 1.60	p = 0.030*
ICU stay (days) (mean $\pm$ SD)	4.58 $\pm$ 1.93	4.32 $\pm$ 2.98	p = 0.717
Hospital stay (days) (mean $\pm$ SD)	10.07 $\pm$ 2.97	11.32 $\pm$ 4.47	p = 0.374
Adverse Events [n(%)]	0 (0.0)	0 (0.0)	-
Escalation of Res. Support [n(%)]	14 (56.0)	8 (32.0)	p = 0.087
ICU mortality [n(%)]	9 (36.0)	5 (20.0)	p = 0.208
Hospital Mortality [n(%)]	2 (8.0)	0 (0.0)	p = 0.149

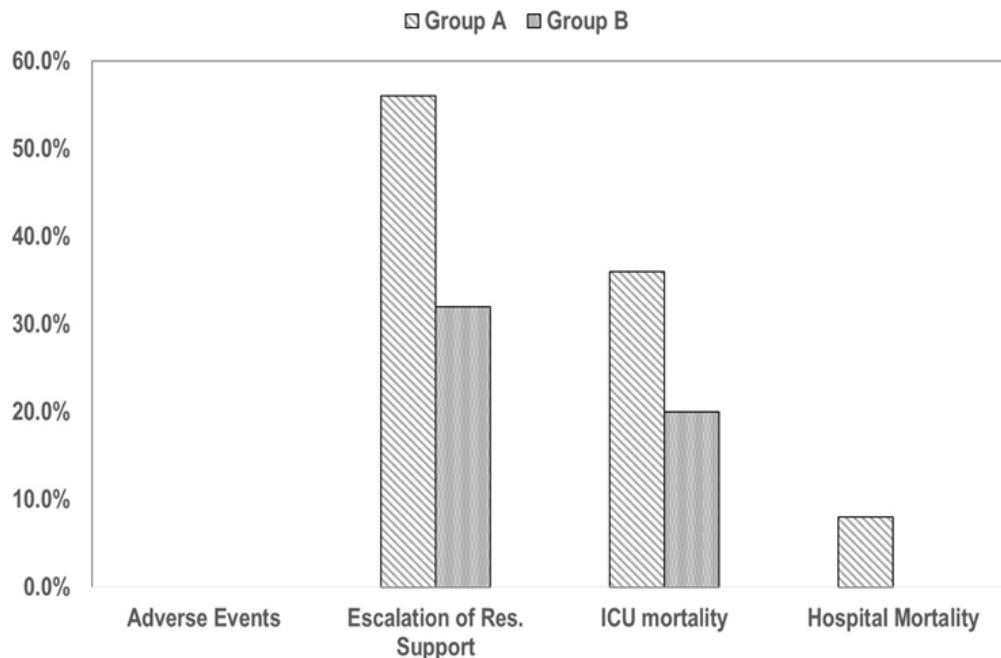
Data are reported as n (%) or mean (range)

HFNC High flow nasal cannula; NIV Non-invasive ventilation; FiO2 – Fraction of inspired oxygen; ICU – Intensive Care Unit.

The duration of oxygen support and the FiO2 requirement was significantly lower in group B than in group A ( $2.84 \pm 1.60$  vs  $4.00 \pm 2.04$ ,  $p = 0.030$  ;  $0.48 \pm 0.16$  vs  $0.67 \pm 0.24$ ,  $p= 0.004$ , respectively). The ICU length of stay, escalation of respiratory support, ICU and hospital mortality was lower in group B, the difference was non-significant.



**Figure 2:** The Duration of Oxygen Support, ICU Length of Stay was Lower in Group B than in Group A. However, Overall Length of Hospital Stay was Longer in Group B than in Group A.



**Figure 3:** Escalation of Respiratory Support, ICU and Hospital Mortality was Lower in Group B than in Group A.

## Discussion

Intrahospital transport of critically ill patients, necessary for obtaining services such as radiological scans and surgical procedures, presents significant risks and challenges. A recent article by Juneja et al, had suggested various strategies to reduce these challenges and complications [16]. However, providing optimum respiratory support to these patients still remains uncertain. For this purpose, the present study aimed to compare the efficacy of Non-Invasive Ventilation (NIV) and High Flow Nasal Cannula (HFNC) in the transportation of these patients.

Patients were randomized into 25 in each group and the process of randomisation allowed for matching of patient characteristics at baseline and hence the cases in both the groups were found to be similar in terms of age, gender, weight and comorbidities. Our findings align with Tan et al, who found that found that the baseline characteristics, including gender, age, and comorbidities, were comparable between patients managed with HFNC and NIV [17].

In the current study, it was observed that patients managed with HFNC had higher oxygen saturation levels compared to those managed with NIV, although this difference was not statistically significant. Additionally, NIV patients exhibited higher

levels of Fraction of Inspired Oxygen (FiO<sub>2</sub>) requirement. These findings are corroborated by Frat et al, who in their review article have reported that HFNC delivers a high FiO<sub>2</sub> and generates a low level of positive pressure, contributing to improved oxygenation and mechanical pulmonary properties [11]. They concluded HFNC to be better modality than standard oxygen and NIV as treatment for hypoxic respiratory failure. Similarly, Papachatzakis et al, found that HFNC was superior to NIV in reducing partial carbon dioxide arterial pressure (PaCO<sub>2</sub>) in patients with hypercapnic respiratory failure, highlighting the efficacy of HFNC in enhancing respiratory parameters [18]. The study included 40 patients who were randomized into HFNC and NIV group (20 patients in each group). No difference between the two groups was found regarding the duration of hospitalization and predicted death rate. However, respiratory rate in the HFNC group was lower than in the NIV group ( $p = 0.023$ ) and at discharge, PaCO<sub>2</sub> in the HFNC group was lower than in the NIV group ( $50.8 \pm 9.4$  mmHg vs.  $59.6 \pm 13.9$  mmHg,  $p = 0.024$ ).

In the present study, the Simplified Acute Physiology Score II (SAPS II) was lower in patients managed with HFNC compared to those managed with NIV, indicating a better overall physiological status in the HFNC group. Furthermore, the duration of oxygen

support was significantly shorter for the HFNC group compared to the NIV group, suggesting a more efficient resolution of respiratory failure with HFNC. These findings align with findings by Liu et al, who conducted a retrospective cohort study to study the effect of HFNC on patients with COPD and mild hypcapnia. 153 patients were included, 37 patients in the HFNC group and 116 patients in NIV group and they observed that HFNC resulted in lower heart rates and respiratory rates after 40-48 hours of treatment compared to NIV, reflecting improved physiological status and reduced need for prolonged respiratory support [HR (bpm):  $84.1 \pm 12.2$  vs.  $91.1 \pm 16.4$ , RR (times/min):  $19.8 \pm 4.9$  vs.  $21.6 \pm 4.1$ , both  $p < 0.05$ ] [19].

The present study reported a higher rate of escalation of respiratory support in NIV group than HFNC group although the difference was not significant. Similarly, higher number of ICU and hospital mortality was observed in NIV group, the difference again being non-significant. The same outcome was observed by Nair et al, who reported that HFNC was associated with lower intubation rates and hospital mortality in patients with acute hypoxic respiratory failure due to COVID-19, further supporting the superior efficacy of HFNC in managing respiratory distress [20]. The lower SAPS II score and reduced duration of oxygen support in the HFNC group can be attributed to the consistent delivery of high-flow, humidified oxygen, which enhances gas exchange and reduces the work of breathing, leading to quicker recovery and shorter dependence on respiratory support. Liu et al. also received similar outcome in their study where the patients managed with HFNC exhibited lower rates of escalation of respiratory support, ICU mortality, and hospital mortality, although these differences were not statistically significant [19]. Similar results were found in a study by Agmy et al, who showed that HFNC resulted in lower endotracheal intubation rates and in-hospital mortality compared to NIV in patients with ARF [14]. Similarly, a randomized controlled trial by Frat et al (Florali study) was conducted to compare three strategies of oxygenation: standard oxygen, HFNC and NIV [21]. The study included 310 hypoxic ARF ( $\text{PaO}_2/\text{FiO}_2 < 300$  mmHg) patients. Although the intubation rate among the three groups was not significantly different, 90-day mortality was lower in

patients treated by HFNC: 12% with HFNC vs. 23% with standard oxygen and 28% with NIV,  $p=0.02$ . This may have been caused by a significant lower intubation rate in the subgroup of severe hypoxic patients ( $\text{PaO}_2/\text{FiO}_2 < 200$ ) treated by HFNC than by the two other treatments: 35%, 53% and 58%, respectively,  $P=0.009$ .

The use of HFNC for transportation has been studied in pediatric patients also. A retrospective, single-center study by Schlapbach et al, enrolled children under 2 years old who were transported by a specialized pediatric retrieval team to PICU (Pediatric ICU). A total of 793 infants were transported [22]. They found that using HFNC was associated with a significant reduction in invasive ventilation initiated by the retrieval team (multivariate OR 0.51; 95 % CI 0.27–0.95;  $p = 0.032$ ). Similarly, a cohort study done by Shinya Miura et al, found that the implementation of HFNC on interhospital transport was associated with significant reduced PICU length of stay and respiratory support use among PICU admissions [23].

The present study observed that the duration of ICU stay was comparable between the HFNC and NIV groups. This is different from the study by Liu et al who observed that the length of ICU stay in HFNC group was significant longer than that of the NIV group [19]. In our study also, the overall hospital length of stay was higher in HFNC, difference however, being non-significant. The key practical recommendations by the International NIV committee have emphasized the importance of detailed planning and continuous monitoring during intra-hospital transport to prevent complications, suggesting that HFNC's stability and ease of use may contribute to better outcomes in critically ill patients [24].

The comparable ICU stay between the groups in the present study indicates that while both HFNC and NIV provide effective respiratory support, HFNC's lower escalation and mortality rates reflect its better tolerability and reduced risk of complications, which are crucial during intrahospital transport. The present study highlights that HFNC may offer advantages over NIV in the short-term management of critically ill patients, particularly during intrahospital transport. The improved physiological parameters, reduced duration of oxygen support, and better

tolerance suggest that HFNC could positively impact long-term outcomes, although further research is needed to confirm this. The results of present study as well as previous studies suggest that the benefits of HFNC extend beyond the immediate management of respiratory failure.

Our study had certain limitation. It is a single centre study with limited sample size. Future research should focus on large-scale randomized controlled trials to further validate the findings of this study and explore the long-term outcomes of HFNC versus NIV in various clinical scenarios. Additionally, studies should investigate the optimal protocols and guidelines for the use of HFNC during intra-hospital transport, including patient selection criteria, equipment requirements, and staff training, to ensure the safe and effective application of this technology in critical care.

## Conclusion

The findings of the study elucidate that the potential for HFNC to improve long-term outcomes by reducing the need for invasive mechanical ventilation and associated complications can have significant implications for critical care practice. The present study adds to the growing body of evidence supporting the use of HFNC as a superior alternative to NIV for the transportation and management of critically ill patients with respiratory failure. The integration of HFNC during transportation maintains the continuity of care, reduces the risk of complications, enhances patient comfort and improve overall outcomes in critical care settings.

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