Outcome of patients with COVID pneumonia on High Flow Nasal Oxygen Therapy

Rashmi Virmani[1], Megha Soni[2], Mamta Kumari[3], Lokesh Parashar[4]
[1,2,3]Department of Anaesthesia, [4]Department of Community Medicine,
ESIC Medical College & Hospital, Faridabad, Haryana, India.

Abstract

Background & Aims: The coronavirus pandemic has caused a rapid surge in patients requiring intensive care unit (ICU) admission. The mainstay of treatment is supplemental oxygen therapy by an oxygen mask, nonrebreathing mask, high flow nasal oxygen therapy (HFNOT), non-invasive and invasive mechanical ventilation. HFNOT is a relatively newer, easy-to-use technique with better patient compliance. This study aimed to assess the outcome of HFNOT in Corona Virus disease (COVID) patients in ICU.

Methods: This record based; retrospective study included 43 reverse transcriptase polymerase chain reaction (RTPCR) confirmed COVID patients whose respiratory support was initiated on HFNOT as per the inclusion criteria. The primary outcome of this study was to assess the number of patients requiring mechanical ventilation (HFNOT failure). The secondary outcome was to assess the association of HFNOT failure with age, co-morbidity index, and severity of illness.

Results: Out of forty-three patients, twenty-five patients (58%) required conversion to mechanical ventilation. Eighteen patients (42%) were managed with HFNOT alone. HFNOT failure was more with increasing age and higher comorbidity score (p value<0.05).

Conclusion: We concluded that HFNOT can be successfully used in COVID patients in ICU without the need for mechanical ventilation. However, it should be used cautiously in patients with higher 4C mortality scores.

Keywords: Acute Respiratory distress syndrome, Mechanical ventilation, COVID-19, Hypoxia, Risk assessment, Oxygen inhalation Therapy

Introduction

Corona Virus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). COVID-19 disease manifestations range from asymptomatic to acute respiratory distress syndrome requiring intensive care unit (ICU) admission and are associated with a high risk of mortality[1,2].

Various methods of providing respiratory support in ICU are high flow nasal oxygen therapy (HFNOT), non-invasive, and invasive mechanical ventilation. HFNOT has been shown to improve oxygenation and it also reduces the work of breathing[3,4]. Non-invasive mechanical ventilation is uncomfortable to the patients and requires significant man-machine cooperation[5]. High Flow Nasal oxygen therapy delivers heated humidified oxygen through nasal prongs at flow settings ranging from 20-60L/min and Fio2 settings ranging from 0.21-1.0[6]. We conducted this study to assess the outcome of patients who were initially started on HFNOT. In this study, we analyzed the proportion of patients who required conversion from HFNOT to non-invasive or invasive ventilation and the association of failure of HFNOT with baseline characteristics, associated co-morbidities, and severity of illness.

Methods

This observational study was carried out in COVID ICU of a tertiary care hospital, after approval of the institutional ethics committee. All demographic, clinical, laboratory, and, outcome data were extracted from clinical records using a standardized data collection form. Charlson Comorbidity Index and 4C mortality score were calculated using this data. RTPCR confirmed COVID-19 patients of ≥18 years of age with acute respiratory failure, who required ICU admission and were treated with High Flow Nasal

Address for Correspondence:
Dr. Rashmi Virmani
Department of Anaesthesia,
ESIC Medical College & Hospital, Faridabad
Email: rashmi.virmani@gmail.com

Oxygen Therapy from June 2020 to August 2020 were included in the study. Patients with hypercapnic respiratory failure, cardiogenic pulmonary edema, hemodynamic instability, altered sensorium, multiorgan dysfunction, or signs of exhaustion were excluded from the study. Patients, who were initiated on NIV or invasive mechanical ventilation and deescalated to HFNOT were not included in the study. Therapy was started using either "Optiflow Nasal High Flow therapy" or by using the high flow Oxygen therapy option on the Mindray ventilator (SV600). As per protocol in ICU therapy was started with a flow of 60 L/min and FiO2 100%. Flow and FiO2 adjustments were made to maintain a target oxygen saturation level of >92%. All patients who received High Flow nasal oxygen therapy wore a surgical mask and were encouraged to follow awake proning protocol[7,8,9]. Decision of intubation or initiation of non-invasive ventilation was made by a clinical team based on clinical assessment and arterial blood gas values. Successful HFNOT was defined as HFNO withdrawal and improved oxygenation, with no need for NIV/IMV or discharge. HFNOT failure was defined as the need for NIV/IMV and /or death while on HFNOT.

Statistical Analysis

Categorical variables were expressed as frequencies and percentages. Continuous variables were presented as means with standard deviations or median with interquartile range. All data was analyzed using SPSS 25 version. 't' test was used for the analysis of quantitative data and the "Chi-square" or Fisher exact test was used for qualitative data. "p" value less than 0.05 was considered significant.

Results

During the study period, forty-three patients were treated with HFNOT. Characteristics of patients at ICU admission are presented in table 1.

Table 1 Patient Characteristics

Characteristics	All patients (n=43)	HFNOT Success (n=18)	HFNOT Failure (n-25)	P value
Age (mean±SD)	52.84 + 15.23	39.94 +11.40	62.12 + 10.43	0.0001
Sex (Male)%	67.4%	72.2%	64%	0.581
Charlson Comorbidity Score, Median (IQR)	1 (0-2)	0	2 (0.75-2)	0.0001
4C mortality score Median (IQR)	8 (5-10)	5 (4-5.5)	9 (8-11.5)	0.0001
Duration of HFNOT (days) (mean±SD)	3.708 + 1.39	3.966 + 1.39	3.522 + 1.39	0.444
Length of hospital admission (days) (mean±SD)	11.44 + 4.40	10.72 + 2.98	11.96 + 5.20	0.3701

Primary endpoint

All the forty-three patients received HFNOT as the primary mode of respiratory support and out of these 58% of patients required ventilation during their ICU stay, either in the form of non-invasive or invasive mechanical ventilation (Table 2). Eighteen patients on HFNOT showed a good response (42%) and there was no escalation of therapy done (Fig. 1). 44% of patients who required ventilator recovered and 56% of patients on mechanical ventilation did not survive (Table 3, Fig 1).

Table 2 Failure rate of patients on HFNOT

	Number of patients	Percentage
HFNO failure	25	58.1
HFNO success	18	41.9
Total	43	100.0

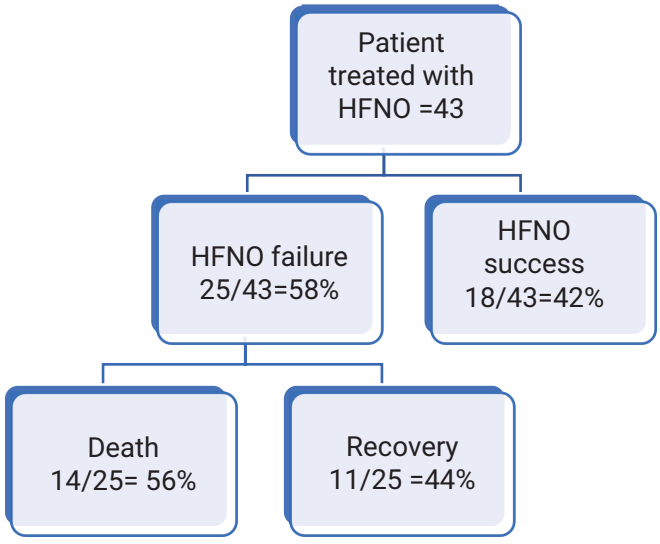

Fig. 1 Flow diagram showing outcome of patients on HFNOT

Table 3 Outcome of patients initiated on Mechanical Ventilation (HFNOT failure)

Mortality/ Discharge	Frequency	Percentage
Death	14	56%
Recovery	11	44%
Total	25	100

Secondary endpoint

The percentage of patients in the age group of 41 to 60 years was 39.5% and 34.9% of patients belonged to the age group of 61-80 yrs. (Mean age 52.84 ± 15.23 years). The failure rate of HFNOT was significantly high in the older age group ($p<0.05$) (fig.2). Out of forty-three patients 67.4% of patients, were males and 32.6% of patients were females (Table 1).

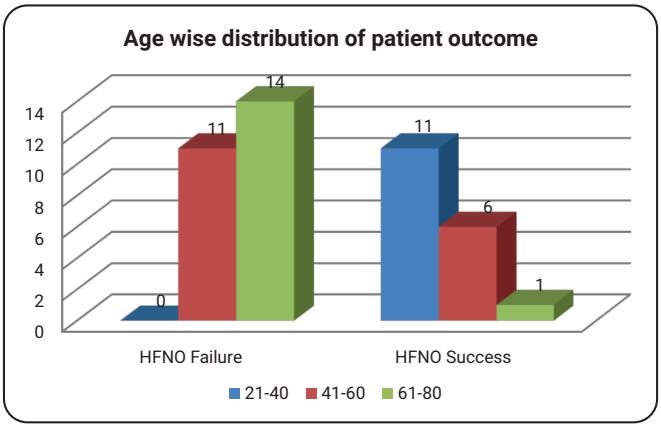

Fig 2. Age wise distribution of patient outcome

In our study, it was observed that in patients who were converted to mechanical ventilation, the median Charlson Comorbidity Index was two, and patients who did not require escalation of therapy had a median Charlson Comorbidity Index of 0 (p-value - 0.0001). 4C mortality score was nine in patients with HFNOT failure and 5 in patients who were successfully weaned off from HFNOT (p-value - 0.0001). Patients who had a greater number of co-morbidities and a higher 4 C Mortality scores had a significantly higher incidence of HFNOT failure.

The mean duration of high flow nasal oxygen therapy was 3.70 days ± 1.39 days. There was no significant difference in the average duration of therapy in patients in whom HFNOT was successfully used and in the other group ($p>0.05$). The average duration of ICU stay was 11.44 ± 4.40 days and the duration of ICU stay was not significantly different in the two groups.

Discussion

COVID-19 was declared a global pandemic in March 2020 by World Health Organization[10]. The primary concern is still the percentage of patients who develop acute respiratory failure requiring ICU admission. The life-threatening form of respiratory failure, acute respiratory distress syndrome (ARDS) is a frequent complication in COVID-19. The severity of ARDS is classified as mild, moderate, and severe, depending on the degree of hypoxemia. Patients with moderate-to-severe ARDS require invasive mechanical ventilation (IMV) and have a poor prognosis[11]. HFNC use has been suggested as first-line therapy in patients with ARF including ARDS[12]. This study was conducted to evaluate the outcome of COVID patients with respiratory failure who were initiated on HFNOT in the intensive care unit.

The main finding of this study is that HFNOT can be used successfully in the management of patients with respiratory failure associated with COVID-19. Many studies have described the role of humidified high-flow nasal oxygen in the management of hypoxemia associated with respiratory distress in non-COVID critically ill patients[13,14]. In our study, HFNOT was successfully used in approximately 41% of patients and this is similar to a study published by Calligaro G.L. et al[14]. In their study, mean SpO2 was substantially lower (90%); the median ratio of PaO2/FiO2 pre-HFNO was 68. Out of 293 patients, 137/293 (47%) patients [PaO2/FiO2 76] were successfully weaned from HFNOT. They noticed that 26 patients in the HFNO group died unexpectedly, however, no such death was encountered in our study. In another retrospective study done by Demoule et al similar observations were noticed. It was observed that out of 146 patients who were initiated on HFNC within 24 hours of admission, the proportion of patients requiring invasive mechanical ventilation on Day 28 was 56%[15]. However, in a study by Hu M et al 65 patients out of 105 patients (61.9%) were successfully withdrawn from HFNC. This could be due to the inclusion of relatively fewer hypoxemic patients in the study and their indication to start HFNOT was more liberal as compared to our study. They included patients with SpO2 ≤92% and/or RR ≥25 under nasal tube oxygen inhalation 10L/min or mask oxygen supply[16].

In this study out of forty-three patients who were initially started on HFNOT, twenty-five patients (58%) required ventilator support either in the form of Non-invasive or invasive mechanical ventilation. The result of a retrospective study done by Bonnet N et al also shows comparable results. They studied the role of HFNOT to avoid invasive mechanical ventilation in SARS-CoV-2 pneumonia in 76 patients and they concluded that in the HFNOT group, 39 patients out of 76 (51%) patients received mechanical ventilation[17]. A multicenter observational study by Artigas RM et

al to analyze the predictors of failure with HFNOT in COVID-19 patients also observed that out of 259 patients initially treated with HFNOT 140 (54%) patients require invasive mechanical ventilation. Because of a long course of disease patients on mechanical ventilators tend to develop complications like barotraumas and ventilator-induced lung infections[18]. Therefore, judicious use of HFNOT has many advantages and is worth considering for COVID-19 patients with respiratory failure as approximately 42% of patients could be successfully weaned off from high flow nasal oxygen therapy in our study.

In this study, HFNOT failure was significantly associated with old age (fig.2), a higher 4 C mortality score, and more comorbidities. In patients who required mechanical ventilatory support, the median Charlson Comorbidity Index (CCI) was 2 and, patients who did not require escalation of therapy had a median CCI of 0. In a systematic review and metanalysis of CCI score and a composite of poor outcomes in COVID-19 by Tuty Kuswardhini RA, they concluded that compared to a CCI score of 0, a CCI score of 1-2 and CCI score of ≥3 was prognostically associated with mortality and associated with a composite of poor outcomes. Per point increase of CCI score also increased mortality risk by 16%. Moreover, a higher mean CCI score is also significantly associated with mortality and disease severity [19].

In a retrospective cohort study conducted by Hu M et al significant association in HFNO outcome with age was observed [16]. In another retrospective, observational study conducted by Xia J et al failure rate of HFNOT was 46.5% and HFNO failure was more likely in older patients[20].

Artigas RM in a multi-center prospective observational study predicted that among adult critically ill patients with COVID-19 initially treated with HFNO, the SOFA score, and the ROX index may help to identify patients with a higher likelihood of intubation[18]. However, 4 C mortality score is an easy-to-use risk stratification tool to stratify COVID-19 patients into different management groups. Patients with a score higher than or equal to 9 were at higher risk of death (40%) [21]. Ali R et al studied the ISARIC-4C mortality score as a predictor of In Hospital mortality and concluded that ISARIC - 4C mortality score can be used for stratifying and predicting mortality in COVID-19[22]. In this study we found that patients with higher 4C mortality scores had a significantly higher failure rate of HFNOT.

Nunn K P et al observed that HFNOT is possibly more efficacious with self proning[23].

We also observed that a high-flow nasal cannula is a comfortable patient interface in both the supine and prone positions and has not had compliance issues allowing continuous usage. High Flow Nasal Cannula might be considered an alternative for patients with NIV intolerance[24]. Considering the ease of use, high-flow nasal cannula has also been successfully used in resource-constrained settings[14,25].

The following limitations of this study deserve mention. This was a single-center retrospective study; the sample size was relatively small and the timing of initiation of mechanical ventilation was dependent on the experience and judgments of a physician. Besides, as the awake proning was routinely performed in the intensive care unit, the exact impact of HFNOT without proning could not be determined.

Conclusion

In conclusion, high flow nasal oxygen therapy was used successfully in almost half of the patients with hypoxemic respiratory failure associated with COVID-19. They could be successfully weaned without the need for mechanical ventilation. However, it should be used cautiously in elderly patients with co-morbidities and patients with higher 4C mortality scores.

References

1. *Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020; 323:1061-9.*
2. *Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020; 323:1574-81.*
3. *Mauri T, Turrini C, Eronia N, Grasselli G, Volta CA, Bellani G. Physiologic Effects of High-Flow Nasal Cannula in Acute Hypoxemic Respiratory Failure. Am J Respir Crit Care Med. 2017; 195:1207-15.*
4. *Mauri T, Alban L, Turrini C, Cambiaghi B, Carlesso E, Taccone P, et al. Optimum support by high-flow nasal cannula in acute hypoxemic respiratory failure: effects of increasing flow rates. Intensive Care Med. 2017; 43:1453-63.*
5. *Procopio G, Cancelliere A, Trecarichi EM, Mazzitelli M, Arrighi E, Perri G, et al. Oxygen therapy via high flow nasal cannula in severe respiratory failure caused by Sars-Cov-2 infection: a real-life observational study. Ther Adv Respir Dis. 2020; 14:1-10.*
6. *Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. Respir Care. 2010; 55:408-13.*
7. *Montiel V, Robert A, Robert A, Nabaoui A, Marie T, Mestre NM, et al. Surgical mask on top of high-flow nasal cannula improves oxygenation in critically ill COVID-19 patients with hypoxemic respiratory failure. Ann Intensive Care. 2020; 10:125.*
8. *Li J, Fink JB, Elshafei AA, Stewart LM, Barbian HJ, Mirza SH, et al. Placing a mask on COVID-19 patients during high-flow nasal cannula therapy reduces aerosol particle dispersion. ERJ Open Res. 2021; 7:00519-2020.*
9. *Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. Crit Care. 2020; 24:28.*
10. *Cucinotta D, Vanelli M. WHO Declares COVID-19 a Pandemic. Acta Biomed. 2020; 91:157-60.*
11. *Tzotzos SJ, Fischer B, Fischer H, Zeitlinger M. Incidence of ARDS and outcomes in hospitalized patients with COVID-19: a global literature survey. Crit Care. 2020; 24:516.*

12. *Messika J, Ben Ahmed K, Gaudry S, Miguel-Montanes R, Rafat C, Sztrymf B, et al. Use of High-Flow Nasal Cannula Oxygen Therapy in Subjects With ARDS: A 1-Year Observational Study. Respir Care. 2015; 60:162-9.*
13. *Sztrymf B, Messika J, Bertrand F, Hurel D, Leon R, Dreyfuss D, et al. Beneficial effects of humidified high flow nasal oxygen in critical care patients: a prospective pilot study. Intensive Care Med. 2011 Nov; 37:1780-6.*
14. *Calligaro GL, Lalla U, Audley G, Gina P, Miller MG, Mendelson M, et al. The utility of high-flow nasal oxygen for severe COVID-19 pneumonia in a resource-constrained setting: A multi-centre prospective observational study. EClinicalMedicine. 2020; 28:100570.*
15. *Demoule A, Vieillard Baron A, Darmon M, Beurton A, Géri G, Voiriot G, et al. High-Flow Nasal Cannula in Critically III Patients with Severe COVID-19. Am J Respir Crit Care Med. 2020; 202:1039-42.*
16. *Hu M, Zhou Q, Zheng R, Li X, Ling J, Chen Y, et al. Application of high-flow nasal cannula in hypoxemic patients with COVID-19: a retrospective cohort study. BMC Pulm Med. 2020; 20:324.*
17. *Bonnet N, Martin O, Boubaya M, Levy V, Ebstein N, Karoubi P, et al. High flow nasal oxygen therapy to avoid invasive mechanical ventilation in SARS-CoV-2 pneumonia: a retrospective study. Ann Intensive Care. 2021; 11:37.*
18. *Mellado-Artigas R, Mujica LE, Ruiz ML, Ferreyro BL, Angriman F, Arruti E, et al. Predictors of failure with high-flow nasal oxygen therapy in COVID-19 patients with acute respiratory failure: a multicenter observational study. J Intensive Care. 2021; 9:23.*
19. *Tuty Kuswardhani RA, Henrina J, Pranata R, Anthonius Lim M, Lawrensia S, Suastika K. Charlson comorbidity index and a composite of poor outcomes in COVID-19 patients: A systematic review and meta-analysis. Diabetes Metab Syndr. 2020; 14:2103-9.*
20. *Xia J, Zhang Y, Ni L, Chen L, Zhou C, Gao C, et al. High-Flow Nasal Oxygen in Coronavirus Disease 2019 Patients With Acute Hypoxemic Respiratory Failure: A Multicenter, Retrospective Cohort Study. Crit Care Med. 2020; 48:1079-86.*
21. *Knight SR, Ho A, Pius R, Buchan I, Carson G, Drake TM, et al. Risk stratification of patients admitted to hospital with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. BMJ. 2020; 370:m3339.*
22. *Ali R, Qayyum F, Ahmed N, Haroon MZ, Irshad R, Sajjad S, et al. Isaric 4c Mortality Score As A Predictor Of In-Hospital Mortality In COVID-19 Patients Admitted In Ayub Teaching Hospital During First Wave Of The Pandemic. J Ayub Med Coll Abbottabad. 2021; 33:20-5.*
23. *Nunn KP, Blackstock MJ, Ellis R, Sheikh G, Morgan A, Rhodes JKJ. The Considerations and Controversies in Using High-Flow Nasal Oxygen with Self-Prone Positioning in SARS-CoV-2 COVID-19 Disease. Case Rep Crit Care. 2021; 2021:5541298.*
24. *Tu G, He H, Yin K, Ju M, Zheng Y, Zhu D, et al. High-flow Nasal Cannula Versus Noninvasive Ventilation for Treatment of Acute Hypoxemic Respiratory Failure in Renal Transplant Recipients. Transplant Proc. 2017; 49:1325-30.*
25. *Guy T, Créac'hcadec A, Ricordel C, Salé A, Arnouat B, Bizec J-L, et al. High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU. Eur Respir J. 2020; 56:2001154.*

Conflict of interest: Nil
Source of funding: Nil

Date received: Nov 29, 2021
Date accepted: Apr 22, 2022