Section: Anesthesiology

Original Research Article

# EFFECT OF EARLY VERSUS DELAYED THERAPY WITH HFNO ON CLINICAL OUTCOMES IN SEVERE COVID 19 PNEUMONIA. A RETROSPECTIVE STUDY IN LIMITED RESOURCE SETTINGS

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## Abstract

**Background:** In patients with hypoxic respiratory failure due to coronavirus disease 2019 (COVID-19), an important unanswered question is the choice of optimal type of respiratory support. High-flow nasal oxygen (HFNO) is one approach for delivering noninvasive support which has become first line therapy in many resource limited centers, avoiding the need for intubation and mechanical ventilation. **Materials and Methods:** 488 HFNC treated covid 19 pueumonia patients were categorized into two groups depending on delay in starting therapy as per the availability of HFNO device. Group A(Early therapy). Comprised of 280 patients who received HFNC therapy within 1-2 days of its indication. Group B(Delayed therapy). Comprised of 208 patients who received HFNC therapy between 5 – 10 days of its indication. The primary outcome was in hospital mortality between the two groups. Secondary outcomes included need of NIV, Mechanical ventilation, length of hospital stay. **Result:** Demographics, laboratory investigations and radiological findings were comparable between groups. Average time to HFNO therapy was 1.34± 0.47 days in group A and 7.4± 1.8 days in group B. Number of patients requiring NIV in group a was 26(9.02%) and 43(20.06%) in group B. Number of patients requiring Mechanical ventilation in group A was 25(8.68%) and 40(19.2%) in group B ($p<0.05$). Progression to ARDS was higher in group B as compared to group A. The mortality in late HFNC group was significantly higher than that in early HFNC ie.57 (27.4%) vs. 33 (11.4%), $p<0.05$. **Conclusion:** We conclude that early application of HFNC may be associated with reduced need for mechanic ventilation and mortality in critically ill patients with severe COVID-19 pneumonia.

## INTRODUCTION

The corona virus disease 2019 (COVID-19) had become the most serious public health emergency worldwide in the 21st century. Patients with severe illness may develop dyspnea and hypoxemia within one week after the onset of COVID-19 and may quickly progress to ARDS, a major cause of death in patients with COVID-19.[1,2] Thus, respiratory support and intensive care management are vital to saving lives. A guideline for the management of critically ill adults
with COVID-19 published in JAMA March 26, 2020 recommended the use of High flow nasal oxygen (HFNC) relative to Non invasive ventilation (NIV) in the circumstance of acute hypoxemic respiratory failure despite conventional oxygen therapy.[3] High flow nasal oxygen (HFNO) is increasingly used for adults hospitalized with Acute hypoxemic respiratory failure. This non-invasive technique delivers warmed, humidified oxygen with a fraction of inspired oxygen (FiO2) up to 1.0 and a maximum flow rate of 60 L/min. However, evidence is lacking regarding optimal timing to apply HFNC which together with equipment supply – demand mismatch in several epicenters of pandemic affected the clinical outcome.

We retrospectively analyzed the clinical data of 488 COVID-19 patients with severe covid 19 pneumonia, during second wave in India, who received HFNC therapy depending on the availability of device at


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variable time intervals and its impact on recovery and mortality.

## MATERIALS AND METHODS

This retrospective observational study was conducted in Department of Anesthesiology at Sheri Kashmir institute of medical sciences, Srinagar, India between April 2021 to July 2021 which was the peak of second wave of pandemic in north India. SKIMS being a tertiary care hospital serve as referral centre for treating severly ill covid 19 patients. Adult patients more than 18 years of age with labortary confirmed COVID-19 and classified as severe COVID-19 pneumonia according to WHO /ICMR guidelines and received HFNO therapy were included in the study.

Due to lack of understanding of this new disease, the timing of HFNC therapy was uncertain. Due to overwhelming case load there was equipment supply – demand mismatch in several epicenters of pandemic affecting the clinical outcome. HFNO treatment was considered first line for all patients whose oxygen requirement was more than 10 lit/min(or 200≤po2/fio2≤300) to maintain the saturation of 92-94 % which is keeping in with recent guidelines of reasonable Spo2 range for patients receiving oxygen.

A total of 515 patients were admitted during this period.10 patients who died within 24 hours of admission and 17 patients who never had access to the device during their stay were excluded from the study. Rest 488 HFNC treated patients were categorized into two groups depending on delay in starting therapy as per the availability of HFNO device.

Group A (Early therapy). Comprised of 280 patients who received HFNC therapy within 1-2 days of its indication.

Group B (Delayed therapy). Comprised of 208 patients who received HFNC therapy between 5 – 10 days of its indication. HFNO was started at lower Fio2 settings.

Data collection. Patients' medical records were reviewed and epidemiological, clinical, laboratory, radiological characteristics and treatment data were obtained. We collected data on age, sex, comorbidities, symptoms at onset, laboratory parameters, radiological findings. The primary outcome was in hospital mortality between the two groups. Secondary outcomes included need of NIV, Mechanical ventilation, length of hospital stay.

**Statistical Analysis:** Continuous variables were presented as mean with standard deviation (SD) when normally distributed and compared by independent sample t test, or expressed as median with interquartile range (IQR) if non-normally distributed and compared by Mann-Whitney U test. Categorical variables were expressed as n (%) and compared by Pearson's chi-square or Fisher's exact test between early HFNC and late HFNC groups. A two-sided α of less than 0.05 was considered statistically significant. All statistical analyses were performed with the SPSS (version 25) software.

## RESULTS

A total of 515 patients with confirmed SARS-CoV-2 infection were admitted in high dependency unit during the defined study time period. Of these, 17 patients who did not receive HFNC treatment were excluded, as were 10 patients who died within 24 hours after admission. Thus, a total of 488 patients were included in our study. Of these 488 patients, 280 patients (Group A) received early HFNC treatment, and 208 patients (Group B) received late HFNC treatment.

The mean age of patients in Group A and Group B were 58.87± 14.80 and 56.23± 12.56 years respectively. Most patients in both groups were males. The most common symptoms on admission in both groups were Dyspnea

Cough, Fever, and Myalgias. [Table 1]. The most common co morbidities in both the groups were hypertension and Diabetes Mellitus. [Table 2]

There were no significant differences in admission SPO2 or PaO2/FiO2 between early and late HFNC groups. Both groups received antibiotics, steroids and anti virals. [Table 3]. Major laboratory markers were tracked from hospital records and were comparable between the two groups. [Table 4].Of the 488 patients who received HFNC, average time to HFNO therapy was 1.34± 0.47 days in Group A and 7.4± 1.8 days in Group B. Average duration of oxygen therapy in Group A was19.26 ± 3.04 days and 27.80± 5.17 days in Group B. Number of patients requiring NIV in Group A was 26 and 43 in group B. Number of patients requiring Mechanical ventilation in Group A was 25 and 40 in group B. Progression to ARDS was higher in Group B as compared to Group A. Length of hospital stay was higher in Group B . A total of 398 patients had been discharged, and 90 patients had died. The mortality in late HFNC group was higher than that in early HFNC 57 (27.4%) vs. 33 (11.4%) as shown in [Table 5].

**Table 1: Demographic and clinical characteristics.**

| Parameter | Total | A | B | P value |
|---|---|---|---|---|
| Age (M+ SD) | | 58.87± 14.80 | 56.23± 12.56 | 0.543 |
| Sex | | | | |
| Male | 300(61.4) | 165 (57.2) | 135 (64.9) | 0.231 |
| Female | 188 (38.6) | 98 (34) | 90(43.2) | 0.342 |
| Symptoms(n%) | | | | |
| Fever | 170 (34.8) | 80 (27) | 90(43.2) | 0.671 |
| Cough | 200 (40.9) | 105 (36.4) | 95 (45.6) | 0.987 |


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| | | | | |
|---|---|---|---|---|
| Dyspnea | 215(44) | 115 (39.9) | 100 (48.7) | 0.325 |
| Myalgia | 130(26.6) | 70 (24.3) | 60 (28.8) | 0.451 |
| GI symptoms | 20(4) | 8 (2.7) | 12(5.7) | 0.423 |
| Sore throat | 65(13.3) | 35(12.1) | 40 (19.2) | 0.965 |
| Fatigue | 100(20.4) | 60 (20.8) | 40 (19.2) | 0.345 |
| Anosmia | 8 (1.6) | 2 (0.69) | 6 (2.2) | 0.211 |
| Altered sensorium | 35(7.1) | 15 (5.2) | 20 (9.6) | 0.876 |

**Table 2: Co morbidities in the two groups.**

| Comorbidity (n%) | Total | A | B | P value |
|---|---|---|---|---|
| HTN | 230(47.1) | 120 (41.6) | 95 (45.6) | 0.23 |
| DM | 180(36.8) | 87 (32.2) | 95 (45.6) | 0.765 |
| CKD | 42 (8.6) | 19 (6.59) | 23 (11) | 0.543 |
| CLD | 31(6.3) | 14 (4.8) | 17 (8.1) | 0.312 |
| Cardiac disease | 17 (3.4) | 9 (3.12) | 8 (3.8) | 0.675 |
| Malignancy | 27 (5.5) | 17 (5.9) | 10 (4.8) | 0.981 |
| Post transplant | 10 (2.1) | 6 (2.08) | 4 (1.92) | 0.455 |
| Thyroid disease | 18 (3.6) | 8 (2.77) | 10 (4.8) | 0.431 |

**Table 3: Treatment Received**

| Treatment | A | B | P value |
|---|---|---|---|
| Antibiotics(n%) | 275 (95.4) | 200 (96.1) | 0.341 |
| Steroids (n%) | 280(97.2)) | 208(100) | 0.965 |
| Anti virals (n%) | 190 (65.9) | 160 (76.9) | 0.123 |
| Anti coagulation | | | |
| Prophylactic | 213 (73.9) | 177 (85) | 0.34 |
| Therapeutic | 67 (23.2) | 31 (14.9) | 0.456 |

**Table 4: Laboratory and radiological characteristics.**

| Parameter | A | B | P value |
|---|---|---|---|
| Hemoglobin (gm/l) Mean S.D | 12.44± 1.32 | 11.78 ± 2.34 | 0.341 |
| WBC(109/l) Mean SD | 8.90 ±3.25 | 9.01± 2.80 | 0.231 |
| Platelets(109/l) Mean SD | 152.13±77.27 | 154± 75.34 | 0.562 |
| Creatinine Median(IQR)≥1.5mg/l | 1.04(0.41- 0.82) | 1.02(0.3-0.79) | 0.63 |
| Bilirubin Median(IQR) ≥1.5mg/l | 0.5(0.42-0.73) | 0.8( 0.4-0.9) | 0.721 |
| Sodium Mean SD | 133.5±10.75 | 133.3± 9.75 | 0.954 |
| Potassium (IQR) | (3.3- 4.10) | (3.3- 4.1) | `0.825 |
| Chest X ray findings | | | |
| Normal | 0 | 0 | 0.457 |
| Unilateral pneumonia | 35 (12.1) | 23 (11) | |
| Bilateral | 253 (87.8) | 185 (88.9) | |

**Table 5: characteristics of oxygen therapy and outcome.**

| Parameter | A | B | P value |
|---|---|---|---|
| Time to HFNO (M ± SD) | 1.34± 0.47 | 7.4± 1.8 | 0.001* |
| Total duration of oxygen therapy(M ± SD) | 19.26 ± 3.04 | 27.80± 5.17 | 0.001* |
| No. of patients requiring NIV (n%) | 26 (9.02) | 43 (20.6) | 0.001* |
| No. of patients requiring Mechanical ventilation.(n%) | 25 (8.68) | 40(19.2) | 0.001* |
| Length of hospital stay | 21.92± 3.57 | 28.48± 5.34 | 0.001* |
| Outcome (n%) | | | |
| Discharged | 247 (85.7) | 151 (72.5) | 0.001* |
| Death | 33 (11.4) | 57 (27.4) | 0.001* |

*Statistically significant

## DISCUSSION

High-flow nasal cannula therapy (HFNC) is a major oxygen supporting therapy for severely ill patients, and is recommended for use in COVID-19 patients. However, study is lacking regarding the optimal timing of high-flow nasal cannula (HFNC) application among critically ill COVID-19 patients. In resource limited settings like ours, HFNO devices were not readily available especially during the peak of covid wave due to overwhelming number of patients suffering from hypoxic respiratory failure.We retrospectively analysed the data of patients who had severe COVID-19 pneumonia and received HFNO therapy at different time intervals classified as early or late.

HFNC, as an innovative and effective modality for oxygen therapy, delivers titratable oxygen up to 60 litres/minutes with heating and humidification to produce a low-level positive end expiratory pressure and to achieve FiO2 as high as 95-100%.[4] HFNC has been shown to reduce the risk of requiring more advanced ventilation and relieve dyspnea better than conventional oxygen therapy and has been suggested as a first-line therapy even before making a clear diagnosis for dyspnea.[5]

In this retrospective, single centre cohort study involving 488 patients with laboratory confirmed


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COVID-19, prognosis was much better in 280 patients who received HFNC early within 48 hrs of its indication, compared to 208 patients who received HFNC treatment later as and when it became available.

Patients in both the groups were comparable with respect to demographic characteristics. Dyspnea was most common presenting symptom in both groups followed by cough and fever. Hypertension and DM were most common comorbidities in both groups. Patients who received early HFNC were less likely to require NIV and MV and had shorter hospital stay. Early application of HFNC was associated shorter lengths of ICU and hospital stay and reduced mortality. The mortality in late HFNC group was higher than that in early HFNC 57 (27.4%) vs. 33 (11.4%) In our study, 10.5% patients in the early HFNC group converted to invasive mechanic ventilation, which is in contrast to the 52.7% in the late HFNC group [Table 5]. These findings are comparable to other published reports. A cohort study in 17 COVID-19 patients indicated starting HFNC when PaO2/FiO2>200 reduced the need of mechanical ventilation, although the impact on mortality was not reported.[6] Better understanding the relationship between HFNO use and outcome in COVID patients is particularly relevant as existing literature finds that HFNO use can stave off intubation in many patients with COVID-19 pneumonia.[7] A 2020 retrospective single-center study found that early application of HFNO as first-line ventilatory support during COVID-19-related AHRF obviated the need for intubation in up to a third of cases.[8] In Early HFNC group , the therapy was started at lower Fio2 settings, however starting HFNC at a relatively late stage of disease such as moderate to severe ARDS may prompt the physician to apply high FiO2.High oxygen mediated oxidative lung damage,[9] may further exacerbate oxygenation, which may paradoxically push for the need of higher FiO2. In addition, oxidative stress during respiratory viral infection may also exacerbate a "cytokine storm".[10]

Our findings correlate with a multicentre study of critically ill patients with the Middle East Respiratory Syndrome (MERS) related to MERS-CoV infection which showed that non-survivors received significantly higher FiO2 than survivors on ICU day 1.[11] Our current study provides evidence that application of HFNC earlier during the mild stage of ARDS may be associated with reduced need for mechanic ventilation and mortality in critically ill patients with COVID-19 pneumonia.

## CONCLUSION

Our study concludes that early application of HFNC may be associated with reduced need for mechanic ventilation and mortality in critically ill patients with severe COVID-19 pneumonia, although larger scale prospective studies are needed to confirm its effectiveness.

## REFERENCES


1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. LANCET.395, 507-513.
2. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. (2020) Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Internal Medicine.
3. Lamontagne F and Angus DC. (2020) Toward Universal Deployable Guidelines for the Care of Patients With COVID-19. JAMA.https://doi.org/10.1001 / jama.2020.5110
4. Rochwerg B, Granton D, Wang DX, Helviz Y, Einav S, Frat JP, et al (2019) High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: a systematic review and meta-analysis. Intensive Care Med.45, 563-572.
5. Liu Q, Zhu C, Lan C and Chen R. (2020) High-flow nasal cannula versus conventional oxygen therapy in patients with dyspnea and hypoxemia before hospitalization. Expert Rev Respir Med.14,425-433.
6. Wang K, Zhao W, Li J, Shu W and Duan J. (2020) The experience of high-flow nasal cannula in hospitalized patients with 2019 novel coronavirus-infected pneumonia in two hospitals of Chongqing, China. Annals of Intensive Care.10, 37.https://doi.org/10.1186/s13613-020-00653-z
7. Nasa P, Azoulay E, Khanna AK, et al. Expert consensus statements for the management of COVID-19-related acute respiratory failure using a Delphi method. Crit Care. 2021;25:106.
8. Zucman N, Mullaert J, Roux D, Roca O, Ricard JD; Contributors. Prediction of outcome of nasal high flow use during COVID-19-related acute hypoxemic respiratory failure. Intensive Care Med. 2020;46:1924–1926.
9. Mach WJ, Thimmesch AR, Pierce JT and Pierce JD. (2011) Consequences of hyperoxia and the toxicity of oxygen in the lung. Nurs Res Pract.2011, 260482.
10. Liu Q, Zhou YH and Yang ZQ. (2016) The cytokine storm of severe influenza and development of immunomodulatory therapy. Cellular & Molecular Immunology.13, 3-10.
11. Arabi YM, Al-Omari A, Mandourah Y, Al-Hameed F, Sindi AA, AlraddadiB, et al. (2017) Critically Ill Patients With the Middle East Respiratory Syndrome: A Multicenter Retrospective Cohort Study. CRITICAL CARE MEDICINE.45, 1683-1695.




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