LETTER TO THE EDITOR

Outcomes of HFNC Use in COVID-19 Patients in Non-ICU Settings: A Single-center Experience

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Sir,

Given the spate of coronavirus disease-2019 (COVID-19) cases faced by nations such as India, the total number of critically ill cases, especially during the peaks, has at times overwhelmed its healthcare infrastructure, leading to significant mortality and morbidity.[1] Maintaining oxygenation and adequate respiratory support with the help of noninvasive devices like nasal cannula, face mask, non-rebreathing mask, high-flow nasal cannula (HFNC), and noninvasive ventilation (NIV) have been the pillars of management of this deadly disease.[2] The rapid surge of cases and insufficient numbers of intensive care unit (ICU) beds have forced hospitals to utilize their general wards for the administration of noninvasive respiratory support including HFNC in severe COVID-19. However, there is a dearth of data on the success of such advanced levels of care outside the ICU setting. Therefore, we conducted an observational study at our center to assess the success of HFNC in managing severe COVID-19 cases outside the ICU (Fig. 1).

A retrospective cohort study was performed at our tertiary referral center located in North India between September and December 2020. Patients with severe COVID-19 pneumonia admitted to the ward were initiated on respiratory support via HFNC, if after a trial of high-flow oxygen, they failed to achieve SpO_2 of ≥90% or a respiratory rate of ≤30 breaths per min. Clinical, laboratory, and treatment information was retrieved from medical records. Outcome parameters included duration of oxygen or HFNC therapy, hospital length of stay, and HFNC failure (ICU transfer or mortality).

During this period, 31 patients received HFNC in the ward, with a median age of 62 (interquartile range [IQR], 50–69) years, including 24 (77%) males (Table 1). HFNC failure occurred in 10 (32%) patients, while 21 (68%) were discharged successfully. They required HFNC for a median of 9 (IQR, 5–12) days, and oxygen therapy was required for a median of 14 (IQR, 11–22) days during admission. Patients with HFNC failure had higher median D-dimer values at baseline (2.2 vs 0.6 mg/L, $p = 0.001$) and lower initial room-air SpO_2 (70 vs 80%, $p = 0.026$) compared to those in whom HFNC was successful. D-dimer levels predicted HFNC failure well (area under the receiver operating characteristic [AUROC] 0.86), and a cutoff of 1.7 mg/L was found to be optimal.

In hospitals with high influx of COVID-19 admissions and overburdened critical care units, HFNC use in wards could be

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a lifesaving modality for the patients suffering from severe respiratory compromise awaiting ICU care. Our retrospective cohort demonstrated successful outcomes with the use of HFNC in an outside of ICU setting among two-thirds of patients with severe COVID-19 pneumonia. Cohorts studying patients in ICU[3] from Japan have found higher levels of D-dimer in those with HFNC failure compared with HFNC success (4.8 vs 2.6 mg/L, $p = 0.02$). Similar results were reported from few studies done in ward settings, such as Calligaro et al. (1.03 vs 0.56 mg/L, $p = 0.002$).[4] Similarly, we found a D-dimer level of ≥1.7 mg/L to correctly predict 87% of HFNC failure cases. D-dimer in the appropriate clinical setting may thus help triaging patients at high likelihood of HFNC failure to early ICU transfer and a lower threshold for endotracheal intubation. Predictably, patients with severe COVID-19 pneumonia who have lower oxygen saturation, denoting more extensive pulmonary parenchymal or pulmonary vasculature involvement, are at higher risk of mortality.[5] Consistent with this, in our study, we found median SpO_2 at presentation in the emergency department to be higher in those with HFNC success than in those with failure (80 vs 70%, $p = 0.036$).

HFNC use in out-ICU-setting was found to be successful in managing more than two-thirds of severe COVID-19 patients failing standard oxygen therapy in our cohort. Future studies are required to further confirm the findings of our study as well to explore other relevant aspects of out-of-ICU HFNC use.
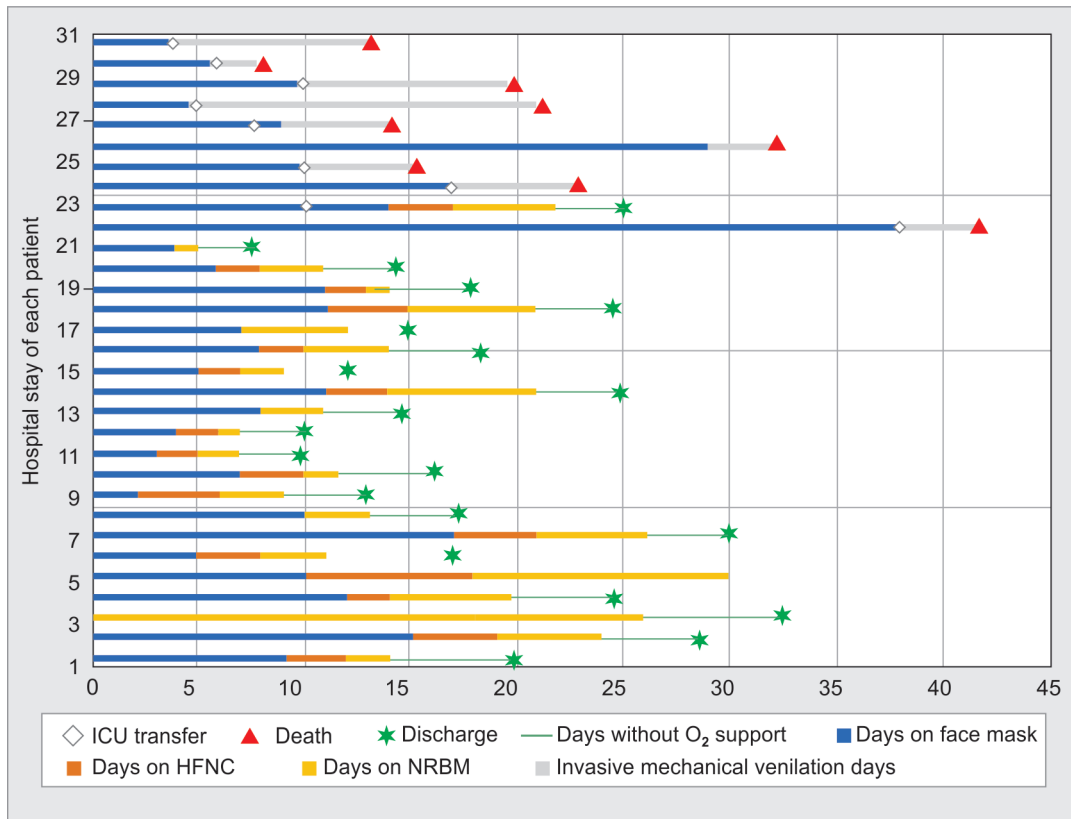
Fig. 1: Patient outcomes and events during hospital stay

Table 1: Patient details, management, and outcomes

Patient characteristics	Total	HFNC success n = 21 (%)	HFNC failure n = 10 (%)	p value
Age (years), median (IQR)	62 (50–69)	60 (50–68)	64.5 (53–72)	0.41
Male, n (%)	24 (77.4)	16 (76)	8 (80)	0.81
Comorbidities, n (%)				
No comorbidities	10 (32%)	9 (42%)	1 (10%)	0.1
Hypertension	15 (48.4)	9 (42.3)	6 (60)	
Diabetes	16 (51.6)	10 (47.6)	6 (60)	
Coronary artery disease	6 (19.3)	3 (14.3)	3 (30)	
Chronic lung disease	2 (6.6)	1 (4.7)	1 (10)	
Malignancy	5 (16.1)	3 (14.3)	2 (20)	
Posttransplant	1 (3)	1 (4.7)	0 (0)	
Chronic kidney disease	1 (3)	1 (4.7)	2 (20)	
Initial SpO_2 (%), median (IQR)	75 (67–84)	80 (70–84)	70 (65–74)	0.036
SpO_2/FiO_2 ratio (%), median (IQR)	192 (172–217)	196 (188–217)	182 (170–211)	0.25
Chest radiograph severity score, median (IQR)	9 (5–12)	11 (8–15)	10.5 (8–16)	0.78
Initial inflammatory markers				
CRP (mg/dL), median (IQR)	10.37 (1.76–13.85)	10.81 (2.56–13.85)	8.96 (0.74–12)	0.52
Ferritin (ng/mL), median (IQR)	552.8 (338.1–1056.4)	605.4 (339.6–1061.3)	502.95 (219.4–844.3)	0.29
IL-6 (IU/mL), median (IQR)	30.3 (14.23–87.59)	33.69 (14.41–103.6)	22.31 (14.18–49.96)	0.31
D-dimer (mg/L), median (IQR)	0.8 (0.41–2.13)	0.6 (0.4–0.9)	2.175 (1.7–3)	0.0014
Remdesivir use, n (%)	16 (51.6%)	12 (57.1%)	4 (40%)	0.44
Methylprednisolone dose per day (mg), median (IQR)	80 (80–120)	81 (80–80)	82 (80–120)	0.38
HFNC duration, median days (IQR)	9 (5–12)	8 (5–11)	10 (6–17)	0.25
Required mechanical ventilation, n (%)		—	9 (90%)	
Duration of mechanical ventilation, n (%)		—	5 (3–9)	

(Contd...)

Table 1: (*Contd...*)

Patient characteristics	Total	HFNC success n = 21 (%)	HFNC failure n = 10 (%)	p value
Total days on oxygen therapy, median days (IQR)	14 (11–22)	14 (11–21)	20.5 (14–23)	0.08
Duration of hospital stay, median days (IQR)	17 (14–25)	16 (14–25)	19.5 (14–26)	0.56
Mortality, *n* (%)	9 (29%)	0	9 (90%)	<0.001
Discharged, *n* (%)	22 (71%)	21 (100%)	1 (10%)	

Highlights

Ours is the first study from India, describing the outcomes of HFNC use in a non-ICU setting among COVID-19 patients. HFNC use outside ICU settings was found to be feasible, with a failure rate of approximately 32% in patients with severe COVID-19 pneumonia. HFNC failure was predicted most reliably by D-dimer at presentation, with a cutoff of 1.7 mg/L having a positive predictive value of 80%.

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