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ORIGINAL ARTICLE

Respiratory outcomes after twelve weeks in patients recovered from COVID-19 managed with non-invasive positive pressure ventilation

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ABSTRACT

Aim: To assess the respiratory outcomes twelve weeks after the management with non-invasive positive pressure ventilation (NIPPV) in patients recovered from severe corona virus disease 2019 (COVID-19).
Methodology: The cross-sectional analytical study was conducted in the Department of Pulmonology, Sir Ganga Ram Hospital Lahore between October 2020 and March 2021. Total 124 patients visiting the hospital twelve weeks after recovery from COVID-19 were enrolled using convenience sampling. After excluding patients with a history of previous respiratory symptoms before the development of COVID-19, data from 87 patients who required oxygen >15 L/minute and NIPPV support were subjected to final analysis.
Results: The proportion of middle-aged adults was 52.9%, males 64.4% and smokers 49.4%. Twelve weeks after treatment with NIPPV, O_2 saturation <97.0% at rest was found in 97.7% patients, PR >100 at rest in 16.1% patients, severe dyspnea in 65.5% patients, O_2 dependency >5 L/min in 2.3% patients, severe CXR abnormalities in 20.7% patients and lung fibrosis in 27.6% patients. The distribution of SpO_2, PR, and dyspnea status twelve weeks after recovery from severe COVID-19 were not significantly different between NIPPV duration groups (p-value >0.05). However, the number of patients with O_2 dependency, severe CXR abnormality, and lung fibrosis were significantly different between NIPPV duration groups (all p-values <0.05).
Conclusion: Oxygen desaturation, severe dyspnea and severe CXR abnormalities twelve weeks after the treatment with NIPPV were common among patients recovered from COVID-19. Severe CXR abnormality, lung fibrosis, and O_2 dependency were significantly associated with prolonged duration of NIPPV.
Keywords: COVID-19, Dyspnea, Pulmonary fibrosis, SARS-CoV-2, NIPPV.

INTRODUCTION

Corona virus disease 2019 (COVID-19) is a term described by the World Health Organization (WHO) as a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), manifested as a worldwide pandemic in 2019[1]. It is associated with a large number of death due to acute respiratory distress syndrome (ARDS), which is sequelae of COVID-19[2,3]. ARDS secondary to COVID-19 is different from other etiologies as lung compliance is preserved but there is wide ventilation/perfusion mismatch and severe hypoxemia leading to characteristic happy hypoxia in the initial stage[4]. On the other hand, histopathological features are a bit different characterized by microvascular endothelial dysfunction, massive intraalveolar fibrin deposition instead of hyaline membrane formation[5]. Treatment of ARDS and resultant respiratory failure was a challenge for healthcare professionals. Initially, patients were treated by invasive positive pressure ventilation through an endotracheal tube. This created a shortage of ventilators all over the world and then even more than one patient were given ventilation support through a single ventilator[6]. Then health professionals started ventilator support via special mask rather than endotracheal tube known as non-invasive positive pressure ventilation (NIPPV). This reduced the complications of invasive ventilation and the cost of treatment[7]. On the other hand role of dexamethasone was established in the treatment of COVID-19 pneumonia and ARDS in the recovery trial which reduced the mortality[8]. This is now a rule to treat every patient with severe COVID-19 pneumonia with high-dose steroids. The patients who survived after ARDS developed different pulmonary and extra-pulmonary complications.[9] because the patients who were treated with NIPPV were in severe COVID-19 pneumonia, it is important to follow these patients to monitor respiratory reserve and complications.

Therefore, the present study aimed to assess the respiratory outcomes twelve weeks after management with NIPPV in patients who recovered from severe COVID-19.

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SUBJECTS AND METHODS

Ethical approval: The study was approved by the COVID-19 Research Committee of Fatima Jinnah Medical University Lahore Pakistan vide letter No.5679-89/F.J. dated 18th September 2020. Written informed consent was taken from all patients.
Study design, duration & settings: The cross-sectional analytical study was carried out at the Department of Pulmonology, Sir Ganga Ram Hospital Lahore Pakistan between October 2020 and March 2021.
Sample size, sampling technique, study population: Total 124 patients of age 14-90 years, gender male and female, and visiting hospital outdoor department twelve weeks after recovery from severe COVID-19 were enrolled by convenience sampling. After excluding patients (n=37) with a previous history of respiratory symptoms before the development of COVID-19, data from 87 patients who required more than 15 L/minutes oxygen and NIPPV support was subjected to final analysis.
Operational definitions: Reverse transcription-polymerase chain reaction (RT-PCR) positive result on nasopharyngeal swab sample defined as COVID-19.[10] According to the WHO criteria, severe COVID-19 is described as patient required more than 15L/minutes oxygen and invasive or noninvasive positive pressure ventilator support.[10] Two consecutive RT-PCR negative results or remained afebrile for at least three days defined as COVID-19 survivor.[11] SpO_2 <97.0% at rest defined as oxygen desaturation. The MRC dyspnea scale was used to calculate dyspnea scores. MRC dyspnea score 1 categorized as mild, 2-3 as moderate, and 4-5 as severe[12]. Brixia CXR score was calculated to assess radiological severity of disease at the time of COVID illness by dividing each lung into three zones and counting score in each zone 0-3 depending upon the area of ground-glass opacity. Radiologic score 0 categorized as normal, 1-6 as mild, 7-12 as moderate, and 13-18 as severe[13]. Lung fibrosis labelled radiologically as sequelae of COVID-19 pneumonia leading to persistent parenchymal changes (ground-glass opacities, reticular opacities, traction bronchiectasis) predominantly in the middle and lower radiological zone. It is manifested as impaired oxygen transfer in the lungs leading to permanent hypoxia documented by O2 desaturation on pulse-oximeter.[14] We used a score for assessment of lung fibrosis after

COVID-19 by dividing each lung into three equal zones and count score in each zone as follows: a score 0 as no lung abnormalities, 1 as ground-glass opacities, 2 as ground-glass opacities, and reticular opacities, and 3 as ground-glass opacities, reticular opacities, and traction bronchiectasis[15,16].

Data collection procedure: Baseline data collected upon enrollment in the study included age, gender, smoking status, O_2 dependency, radiological abnormalities, and duration of NIPPV at the time of COVID-19. Outcome data collected twelve weeks after recovery from COVID-19 included oxygen saturation (SpO_2) at rest, pulse rate (PR) at rest, Medical Research Council (MRC) dyspnea score, and O_2 dependency. CXR abnormalities at the time of COVID-19 and after twelve weeks were noted.

Statistical analysis procedure: SPSS version 26 was used for data entry and analysis. Categorical variables including gender, smoking status, and presence of lung fibrosis were reported using frequency (percent). Continuous variables including age, SpO_2, pulse rate, MRC dyspnea score, O_2 dependency, and duration of NIPPV were categorized into groups and reported using frequency (percent). Chi-square test was used to compare the frequencies between groups. P-value ≤ 0.05 was considered significant.

RESULTS

Among severe COVID-19 patients treated with NIPPV (n=87), the participation of middle-aged adults (52.9%) was higher than older (41.4%) and young adults (5.7%). The proportion of males (64.4%) was higher than females (35.6%). The frequency of cigarette smokers was 49.4%. About radiological severity of disease, 79.3% patients had severe Brixia CXR score (13-18), while 19.5% of patients had moderate scores (7-12) (Table 1).

Twelve weeks after treatment with NIPPV, O_2 saturation <97.0% at rest was found in 97.7% of patients and PR>100 at rest in 16.1% of patients. Severe dyspnea was present in 65.5% of patients and moderate dyspnea in 29.9% of patients. O_2 dependency >5L/min was found in 2.3% patients, 3-5L/min in 16.1% and 1-2L/min in 52.9 % patients. About post-COVID illness radiological severity, 79.3% had moderate CXR abnormalities, while 20.7% had severe abnormalities. Lung fibrosis was seen in 27.6% of the patients, (Table 2).

The distribution of age groups, gender, and smokers at the time of COVID-19 was not significantly different between NIPPV duration groups (p-value>0.05). However, Brixia CXR score at the time of COVID-19 showed significant association with the duration of NIPPV support. The numbers of patients with moderate and severe Brixia CXR scores were significantly different between NIPPV duration groups (p-value<0.001). The number of patients with O_2 dependency, severe CXR abnormality, and lung fibrosis were significantly different between NIPPV duration groups (all p-values <0.05) (Table 3).

Table 1: Characteristics of patients at the time of COVID-19 (n=87)

		n	%
Age(years)	≤35(young)	05	5.7
	36-55(middle-aged)	46	52.9
	≥56(older)	36	41.4
Gender	Male	56	64.4
	Female	31	35.6
Smoking	No	44	50.6
	Yes	43	49.4
Brixia CXR score	1-6(mild)	01	1.1
	7-12(moderate)	17	19.5
	13-18(severe)	69	79.3

Table 2: Characteristics of NIPPV patients at twelve weeks follow up (n=87)

		n	%
SpO_2 at rest(%)	<97.0	85	97.7
	≥97.0	02	2.3
PR at rest(BPM)	≤100(normal)	73	83.9
	>100(tachycardia)	14	16.1
MRC dyspnea score	1(mild)	04	4.6
	2-3(moderate)	26	29.9
	4-5(severe)	57	65.5
O_2 dependency (L/min)	0	25	28.7
	1-2	46	52.9
	3-5	14	16.1
	6-10	02	2.3
	>10	0	0.0
CXR score	0(normal)	01	1.1
	1-6(mild)	62	71.3
	7-12(moderate)	21	24.1
	13-18(severe)	03	3.4
Lung fibrosis	No	63	72.4
	Yes	24	27.6

Table 3: Comparison between NIPPV duration groups (n=87)

			Duration of NIPPV (days)						
			≤ 3		4-5		> 5		
			n	%	n	%	n	%	p-value
At the time of COVID-19	Age(years)	≤35	0	0.0	01	20.0	04	80.0	0.373
		36-55	10	21.7	20	43.5	16	34.8	
		≥56	06	16.7	16	44.4	14	38.9	
	Gender	Female	03	9.7	16	51.6	12	38.7	0.232
		Male	13	23.2	21	37.5	22	39.3	
	Smoking	No	07	15.9	18	40.9	19	43.2	0.692
		Yes	09	20.9	19	44.2	15	34.9	
	Brixia CXR score	1-6(mild)	01	100.0	0	0.0	0	0.0	0.001
		7-12(moderate)	05	29.4	12	70.6	0	0.0	
		13-18(severe)	10	14.5	25	36.2	34	49.3	
12 weeks after treatment with NIPPV	SpO_2 at rest(%)	<97	16	18.8	36	42.4	33	38.8	0.792
		≥97	0	0.0	01	50.0	01	50.0	
	PR at rest (BPM)	≤100	13	17.8	32	43.8	28	38.4	0.849
		>100	03	21.4	05	35.7	06	42.9	
	MRC dyspnea score	1	0	0.0	03	75.0	01	25.0	0.281
		2-3	07	26.9	12	46.2	07	26.9	
		4-5	09	15.8	22	38.6	26	45.6	
	O_2 dependency	0	07	28.0	14	56.0	04	16.0	0.001
		1-2	09	19.6	21	45.7	16	34.8	
		3-5	0	0.0	02	14.3	12	85.7	
		6-10	0	0.0	0	0.0	02	100.0	
		>10	0	0.0	0	0.0	0	0.0	
	CXR Abnormalities score at twelve weeks	0(normal)	01	100.0	0	0.0	0	0.0	0.002
		1-6(mild)	15	24.2	30	48.4	17	27.4	
		7-12(moderate)	0	0.0	07	33.3	14	66.7	
		13-18(severe)	0	0.0	0	0.0	03	100.0	
	Lung fibrosis	Yes	0	0.0	07	29.2	17	70.8	<0.001
		No	16	25.4	30	47.6	17	27.0	

DISCUSSION

COVID-19 pneumonia leading to ARDS is a serious complication of COVID-19, labelled as severe COVID-19.[3] Earlier, the patients of severe COVID-19 had been treated with invasive ventilation support. However, the patients included in this study were managed with NIPPV and high flow O_2 in the present study. Thus, we aimed to assess the respiratory outcomes twelve weeks after management with NIPPV in patients who recovered from severe COVID-19. Our study revealed that this strategy reduces the complications associated with invasive ventilation. However, despite survival from ARDS these patients still have inadequate respiratory reserve and marked impairment of lung function evident in a respiratory follow-up study published earlier by Shah et al.[17]

In the present study, we found that as the duration of NIPPV increased during COVID-19 illness, the severity of dyspnea after twelve weeks also increased. 45.6% of patients who were on NIPPV for >5days had severe dyspnea score grade 4-5. As we know patients on the dyspnea scale 5 become short of breath while removing their clothes, so these patients have limited activity and are dependent on family for daily life activities.

Similarly, a considerable number of patients are at home on oxygen showing deterioration of lung function as a sequelae of ARDS and lung fibrosis after twelve weeks of recovery.

Shah et al demonstrated in their study that there was no correlation between the number of days on oxygen during acute disease and dyspnea score at twelve weeks on follow up but they did not elaborate patients who required positive pressure ventilator support. On the other hand, Shah et al. pointed out the association of severity of disease with markedly reduced lung function after twelve weeks[15]. This is close to our study findings that patients had markedly reduced lung function and faced great difficulty in maintaining normal SPO2 on room air.

Faverio et al in their follow up study divide patients into three groups to assess physiological impairment of lungs. In oxygen group it was 40(58%) who received invasive ventilator support 52(54%) and in CPAP group 50(36%)[18]. However “IMV” group and “CPAP” group have moderate to severe physiological impairment showing extensive deterioration of lung function in patients managed on ventilator support which is closed to our study. With regard to chest x-ray, the abnormalities are close to our study as 21% in the CPAP group and 26% in IMV have reticular opacities which is 24.1% in our study.

Bellan et al found 51.6% of patients with respiratory impairment and 15.5% patients with severe respiratory impairment. The risk factor associated with severe respiratory impairment is female sex and ICU admission during the hospital stay[19]. Although they do not elaborate the ventilator support invasive or noninvasive in ICU admission but most of the patients stayed in ICU for ventilator support so their findings are closed to our study.

CONCLUSIONS

Oxygen desaturation, severe dyspnea and severe CXR abnormalities twelve weeks after treatment with NIPPV were common among patients recovered from COVID-19. Severe CXR abnormality, lung fibrosis and O_2 dependency were significantly associated with prolonged duration of NIPPV.

Limitations: We did not perform spirometry test to avoid reinfection as new strains of COVID-19 are emerging.

Authors Contribution: MMAB designed the study, wrote the original draft, critically reviewed the manuscript; approved the final version to be published; takes responsibility for the content and similarity index of the manuscript. **MA** performed analysis and interpretation of data, critically reviewed and revised the manuscript; approved the final version to be published; takes responsibility for the content and similarity index of the manuscript. **ZR** performed collection of data, critically reviewed the manuscript; approved the final version to be published; takes responsibility for the content and similarity index of the manuscript. **MUB** performed collection of data, critically reviewed the manuscript; approved the final version to be published; takes responsibility for the content and similarity index of the manuscript. **FZ** performed collection of data, AND critically reviewed the manuscript; approved the final version to be published; takes responsibility for the content and similarity index of the manuscript.

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