Emad *et al.*
The Egyptian Journal of Bronchology (2023) 17:51
https://doi.org/10.1186/s43168-023-00228-z

The Egyptian Journal of Bronchology

RESEARCH Open Access

Early application of continuous positive airway pressure in COVID-19 patients at risk of obstructive sleep apnea

Zeinab Emad[1], Mohammed A. Ibrahim[1*], TahaTaha Abdelgawad[1] and Abdelbaset M. Saleh[1]

Abstract

Context Respiratory support is an essential part in treating COVID-19 patients at risk for developing respiratory failure, and this become certain if associated with other comorbidities specifically obstructive sleep apnea (OSA).

Aim To evaluate the role of early use of continuous positive airway pressure (CPAP) in management of moderate to severe COVID-19 patients at risk of OSA.

Settings and design This was experimental clinical trial.

Patients and methods Eighty (80) patients with moderate to severe COVID-19 at risk of OSA were enrolled. They were simply randomized into two equal groups: non-CPAP group and CPAP group. Non-CPAP group will receive medical treatment plus oxygen therapy according to recommendation of protocol of the Egyptian Ministry of Health 2020 and CPAP group as in non-CPAP group plus using CPAP.

Results Our findings showed that there were higher percentages in hospital deaths and longer duration of hospital stay as well as increased need for invasive mechanical ventilation in non-CPAP group compared to CPAP group patients: (*P*-value = 0.03), (*P*-value = 0.04), and (*P*-value = 0.01), respectively. Also, there was a significant difference on PH, CO_2, HCO_3, and D-dimer values on both groups on admission and during follow-up with notable decrease in their values in CPAP group compared to non-CPAP group: (*P*-value = 0.04), (*P*-value = 0.003), (*P*-value = 0.001), and (*P*-value = 0.001), respectively.

Conclusion Early CPAP therapy for moderate and severe COVID-19 hospitalized patients with risk of OSA could improve patient's survival, shorten hospital stay, and decrease need for invasive mechanical ventilation.

Trial registration Clinicaltrials.gov/NCT05934916. Registered 6 July 2023 — retrospectively registered.

Keywords CPAP, OSA, COVID-19, WHO, Ventilation

Introduction

In many researches, it was reported that COVID-19 patients with OSA were more severely affected than patients without OSA, and this provides a further proof that concurrent OSA may increase the severity of COVID-19 infection, along with increased risk of mortality [1]. OSA results in ongoing low-grade inflammation, which is important because it may make individuals more susceptible to the cytokine storm, and it may perhaps help to aggravate the cytokine storm that occurs with COVID-19 pneumonia. OSA may predispose individuals to pneumonia because of frequent upper airway micro aspiration, which has been thought that is major mechanism leading to viral pneumonia. OSA may lead to deterioration

*Correspondence:
Mohammed A. Ibrahim
mohammedmansour.md@gmail.com; mohammedmansour.md@mans.edu.eg
[1] Chest Medicine Department, Faculty of Medicine, Mansoura University, Mansoura City 35511, Dakahlia Governorate, Egypt

of the symptoms of severe COVID-19, especially at night, when reduced oxygen saturation levels occur in OSA [2]. OSA lead to disturbance in renin–angiotensin–aldosterone axis, with overexpression of angiotensin-converting enzyme 2 (ACE2), a well-known entry receptor for SARS-CoV-2; taken together, there is a strong biological convincing linking OSA with higher likelihood of developing severe COVID-19 [3]. Also, insufficient sleeping enhances the inflammatory mediators, e.g., interleukin-6, interleukin-17, and tumor necrosis factor-α that promote inflammatory activity in neutrophils; these mediators have been strongly associated with severe COVID-19 and disturbed sleep and also enhance neutrophils and monocytes to invade the area of inflammation [4]. For patients with moderate to severe OSA, the mainstay of treatment is continuous positive airway pressure (CPAP). CPAP achieve variable cardiovascular and metabolic-protective effects which decrease blood viscosity, hematocrit, platelet activation, and hypercoagulability and decrease incidence of acute vascular events [5]. Acute hypoxemic respiratory failure (AHRF) is the most frequent organ failure among patients with COVID-19 leading to admission to the intensive care unit (ICU). Evidence for HFNO, CPAP, and NIV as effective treatments for AHRF is drawn from AHRF patients without COVID-19. COVID-19 is a novel disease, and extrapolating data from other causes of AHRF is not justifiable, and there is an urgent need to evaluate the effectiveness of NIV strategies in patients with COVID-19. At present, clinical practice is mainly based on personal preference, prior experience, and the local availability of resources [6].

The aim of this study was to evaluate the role of early use of continuous positive airway pressure (CPAP) in management of moderate to severe COVID-19 patients at risk of OSA.

Patients and methods

This experimental clinical trial (randomized clinical trial, parallel group trial design) was conducted on eighty (80) patients diagnosed with moderate to severe COVID-19 who were at risk for OSA. Primarily, one-hundred (100) COVID-19 patients were screened for risk factors of OSA, and six of them were excluded as they refused the research from the start, five patients were hypercapnic, seven patients were negative in PCR swab for SARS-CoV-2, and two patients were critically ill and hemodynamically unstable on admission (see Fig. 1 for flow chart of patients). The enrolled eighty patients were simply randomized into two equal groups: non-CPAP group and CPAP group using a computer-generated table of random numbers. The group allocation was concealed in sequentially numbered, sealed, and opaque envelopes. Patients were selected from isolation center in Mansoura University Hospital during the period from August 2021 to April 2022.

Inclusion criteria

Patients age above 18 years, diagnosed with moderate to severe COVID-19, and at risk of OSA as well as confirmed nasopharyngeal swab positive for SARS-CoV-2 by PCR.

Exclusion criteria

Patients were excluded from the study if their age is < 18 years, hypercapnic, unstable cardiorespiratory (shock) status or respiratory arrest, and if there are any contraindications for CPAP mask use.

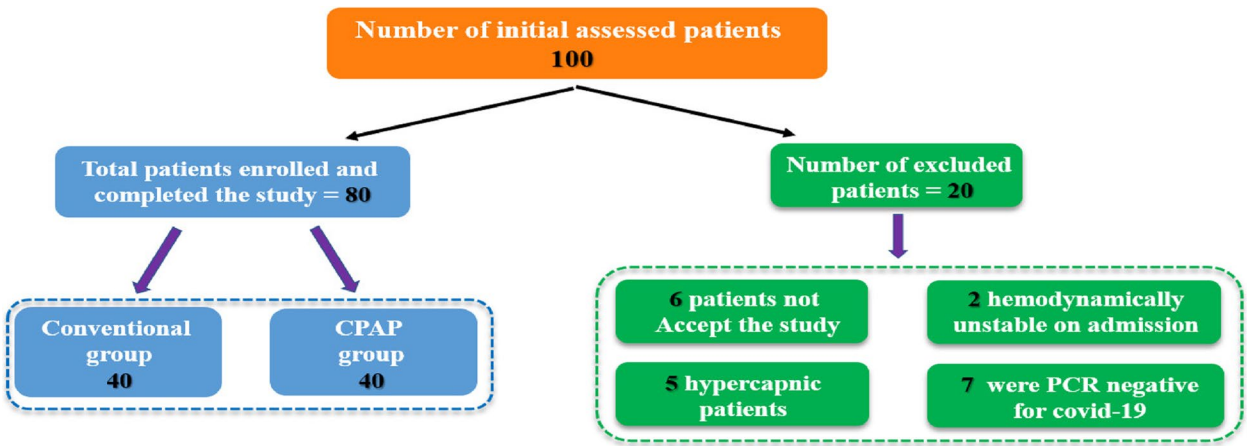

Fig. 1 Flow chart of patients included and excluded in the study

Methods

Clinical assessment

Full history taking was taken from the enrolled COVID-19 patients (including age, occupation, medical history, and special habits), COVID-19 symptoms (e.g., fever, dyspnea, fatigue, loss of smell or taste, GIT symptoms), and all OSA symptoms (e.g., snoring, insomnia, excessive daytime sleepiness, witnessed apnea. Physical examination was done with emphasis on blood pressure, pulse, respiratory rate, weight, height, body mass index (BMI), neck circumference, tonsil grades, and Mallampati score, and full cardiac and chest examination were done.

Scales and questionnaires

Epworth Sleepiness Scale (ESS)

It is designed to assess the degree of daytime sleepiness. The ESS has a maximum score of 24, and scores more than 10 are regarded as indicating excessive daytime drowsiness [7].

Berlin questionnaire

These questionnaires consist of three categories (snoring, daytime somnolence, and BMI and hypertension). Results from the first and second categories are positive if the responses demonstrate repetitive symptoms (> 3–4 times/week), whereas the third category's score is positive if there is a history of hypertension or a BMI > 30 kg/m^2. Patients who scored positively in ≥ 2 of the 3 categories are classified as being at high risk of OSA, whereas those who do not are classified as being at low risk [8, 9].

STOP-Bang questionnaire

This scoring system composed of 8 items that are graded from 0 to 8 according to yes/no responses (score: 1/0). It includes snoring, tiredness, observed apnea, high blood pressure, BMI, age, neck circumference, and male gender. Patients who score 3 or greater are considered to have a high risk of OSA, whereas those who score just under 3 are considered to have a low risk [10].

Radiological investigations

Plan chest X-ray: CXR scoring methodology total score, which varies from 0 to 18, is the sum of all the zone scores [11].

CT scan of the chest: Semiquantitative scoring system (CT- SS) total CT score, which varied from 0 (no participation) to 25 (maximum involvement), was calculated for every patient [12].

Laboratory investigations

These are blood gases, complete blood picture, C-reactive protein (CRP), lactate dehydrogenase enzyme (LDH), D-dimer, prothrombin time, INR, APTT, kidney function tests (serum creatinine) and liver function tests (serum glutamate oxaloacetate transaminase (SGOT), and serum glutamate pyruvate transaminase (SGPT), serum albumin). Follow-up of D-dimer and blood gases was done on first, 7th, and 14th days.

CPAP application

Auto-CPAP is with continuous nocturnal administration or at least 4–6 h/night and during day naps, for more than 70% of nights from the first night of admission to isolation center [13]. Regular patient's follow-up to guarantee effectiveness, toleration, and adherence of the treatment was an essential concern. We applied a suitable size of oronasal mask for each patient to ensure its fitting for every patient and allowing limited level of leak and ensuring that there was no unintentional leak. Mointoring of CPAP efficacy was done through detection hours of CPAP use and ensure that residual events (apnea/hypopnea) are within the normal range (*AHI/AI* < 5 event/h) [14]. Patients were in closely monitored environment under the supervision of medical professionals who are skilled and can perform endotracheal intubation if necessary.

Statistical analysis

Data was analyzed using SPSS (Statistical Package for Social Sciences) version 22. Qualitative data will be presented as number and percent; quantitative data will be tested for normality by Shapiro–Wilk test and then described as mean and standard deviation for normally distributed data and median and range for non-normally distributed. The appropriate statistical test will be applied according to data type with the following suggested tests: chi-square for categorical variable, Student *t*-test, and Mann–Whitney test.

Ethics approval and consent to participate

The study protocol has been approved by the Institutional Research Board, Faculty of Medicine, Mansoura University, with the proposal code: MS.21.07.1578. Precautions were used to protect participants' privacy as patients were given the option to participate or not; also, the study findings were exclusively used for scientific purpose. Personal data were hidden from any public use.

Results

Our study included 80 moderate to severe COVID-19 patients with risk of OSA, who were simply randomized into two equal groups: non-CPAP group and CPAP group. Table 1 illustrates that both study groups were homogenous without significant difference regarding demographic data of the studied patients, and there was no significant difference regarding common associated comorbidities. Baseline oxygen saturations in non-CPAP

Table 1 Demographic data and associated comorbidities in the studied patients

	Non-CPAP group (*n* = 40)	CPAP group (*n* = 40)	*p*-value
Age (mean ± SD)	60.8 ± 11.1	56.3 ± 13.09	0.1
BMI (mean ± SD)	41.7 ± 3.78	42.7 ± 4.3	0.2
Gender: male/female	17/23(42.5/57.5)	12/28 (30/70)	0.2
Smoking *n* (%)			
Current/stopped	16 (40)	17 (42.5)	0.6
Ex-smoker	6 (15)	3 (7.5)	
Nonsmokers	18 (45)	20 (50)	
Marital status *n* (%)			
Single	2 (5)	5 (12.5)	0.2
Married	38 (95)	35 (87.5)	
Hypertension *n* (%)	30 (75)	34 (85)	0.3
DM	26 (65)	23 (57.5)	0.5
COPD	11 (27.5)	6 (15)	0.2
Asthma	4 (10)	8 (20)	0.2
CKD	6 (15)	5 (12.5)	0.7
CVD	2 (5)	4 (10)	0.4
Malignancy	8 (20)	10 (25)	0.6

Data are presented as mean ± standard deviation, number (percentage)

Abbreviations: *BMI* body mass index, *n* number, *DM* Diabetes mellitus, *COPD* Chronic obstructive pulmonary disease, *CKD* Chronic kidney disease, *CVD* Cardiovascular diseases

group were 80 ± 6.1 and in CPAP group was 82 ± 4.1 with no significant difference and *P*-value of 0.06.

Figure 2 illustrates the percentage of presenting COVID-19 symptoms in the studied patients in both groups: dyspnea, bone ache, loss of sensation, and sore throat were the commonest presenting symptoms, while expectoration and GIT disorders were the least presenting symptoms in both groups.

Figure 3 illustrates the percentage of presenting OSA symptoms: snoring, excessive daytime sleepiness, and personality and mood changes were the commonest presenting symptoms, while nocturia and morning confusion were the least presenting symptoms in both studied groups.

Table 2 demonstrates radiological and laboratory findings in both studied groups; there were a statistically significant difference between both groups as regard CO2, HCO3, INR, and D-dimer. The values of D-dimer and INR were lower in the non-CPAP group than in the CPAP group, and CO2 and HCO3 were lower in the non-CPAP group than in the CPAP group. However, there is no significant difference between them in case of radiologic findings and other reported laboratory parameters.

Table 3 demonstrates blood gases and D-dimer follow-up on first, 7th, and 14th days in both studied groups. At admission, there was no significant difference between them as regard PH, while CO_2, HCO_3, and D-dimer showed significant difference with higher values in CPAP group than values in non-CPAP group. On the 7th day, there were significant differences between them as regard HCO_3 and D-dimer values with increase in CO_2, HCO_3, and D-dimer values on non-CPAP group in comparison with the first day values while decrease on HCO_3 and D-dimer values on CPAP group. At the end of 14 days, there were significant differences in PH, CO_2, HCO_3, and D-dimer values on both groups with significant increase in CO_2, HCO_3, and D-dimer values in non-CPAP group in comparison with the first- and 7th-day values while decrease on CO_2, HCO_3, and D-dimer values on CPAP group.

Figures 4 and 5 illustrate the comparison between two studied groups regarding blood gases and D-dimer analysis on the first, 7th, and 14th day during the hospital stay.

The primary and secondary outcomes of our study are presented in Table 4 in the form of the death, duration of hospital stay, and the need of invasive mechanical ventilation. The results showed that the percentage of patient's death are increased in non-CPAP group. The number of days of hospital stay increased also in the non-CPAP groups, and the need for mechanical ventilation also increased in the non-CPAP group.

Discussion

Since the start of the COVID-19 pandemic, concerns have been expressed about the possibility that OSA patients who develop COVID-19 may be more prone to increased risk of morbidity and mortality than people without OSA. Therefore, this risk could have a major influence on healthcare systems and illness outcomes due to the high prevalence of OSA and many undiagnosed cases. Since long time, CPAP is well known as the mainstay of treatment for OSA.

Our study included 80 moderate to severe COVID-19 patients with risk of OSA, who are simply randomized into two equal groups: non-CPAP group and CPAP group. Non-CPAP group was including 17 male and 23 female patients, while CPAP group was including12 male and 28 female patients. The mean age was 60.8 ± 11 year and 56 ± 13 years, and the mean value of BMI was 41.7 ± 3.7 and 42.7 ± 4.3 in non-CPAP group and CPAP group, respectively. With 16 patients are currently or stopped smoking, 6 ex-smokers, and 18 nonsmokers in non-CPAP group, while 17 patients currently or stopped smoking, 3 ex-smokers, and 20 nonsmokers in CPAP group. This finding was supported by [15] as their research indicates Covid-19 and OSA prevalence increases in older age groups.

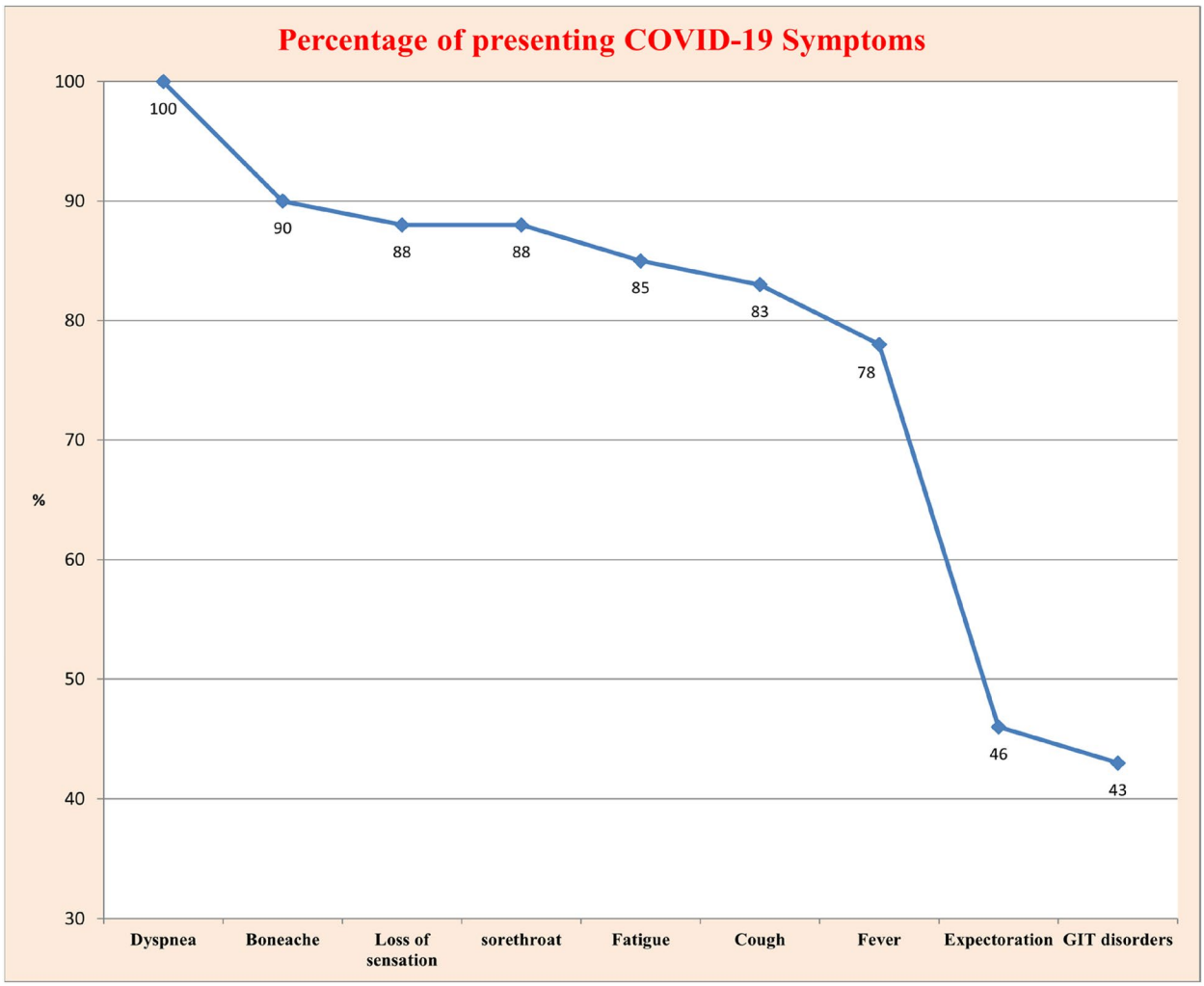

Fig. 2 Percentage of presenting COVID-19 symptoms

Our results showed that CPAP has significant impact on blood gases and D-dimer level on follow-up of patients on 7th and 14th day in CPAP group in comparison with the first day. On the 7th day, there was a decrease on HCO3 and D-dimer level on CPAP group from 26.29 ± 2 to 25.60 ± 1 mEq/L and 1.27 ± 1 to 0.95 ± 0.5 mg/L, respectively, while increase on CO2, HCO3, and D-dimer values on non-CPAP group (40.80 ± 6.7 mm Hg, 24.54 ± 3.6 mEq/L, and 1.44 ± 0.7 mg/L, respectively). By the 14th day, there were significant differences on PH, CO2, HCO3, and D-dimer values on both groups with significant increase on CO2, HCO3, and D-dimer values (42.17 ± 9 mm Hg, 27.25 ± 5 mEq/L, and 1.87 ± 0.7 mg/L, respectively) on non-CPAP group in comparison with the first- and 7th-day values while decrease on CO2, HCO3, and D-dimer values on CPAP group (37 ± 1 mm Hg, 24.06 ± 1 mEq/L, and 0.419 ± 0.26 mg/L, respectively). These agreed with the literature as CPAP reduce hypercoagulability factors in OSA patients reducing risk of thrombosis and supported with previous studies [16–18].

This study demonstrated that using CPAP early during the night and during sleep in patients with moderate to severe COVID-19 and with a high risk for OSA in comparison to the non-CPAP technique increased the incidence of survival (32 survivors in CPAP group in comparison to 23 in non-CPAP) and decreased the need for mechanical ventilation and shorten duration of hospital stay (24 patients, 15 days in CPAP group, and 34 patients and 19.5 days in non-CPAP) respectively. These all supported the literature as there are many risk factors and morbidities shared by both severe COVID-19 and

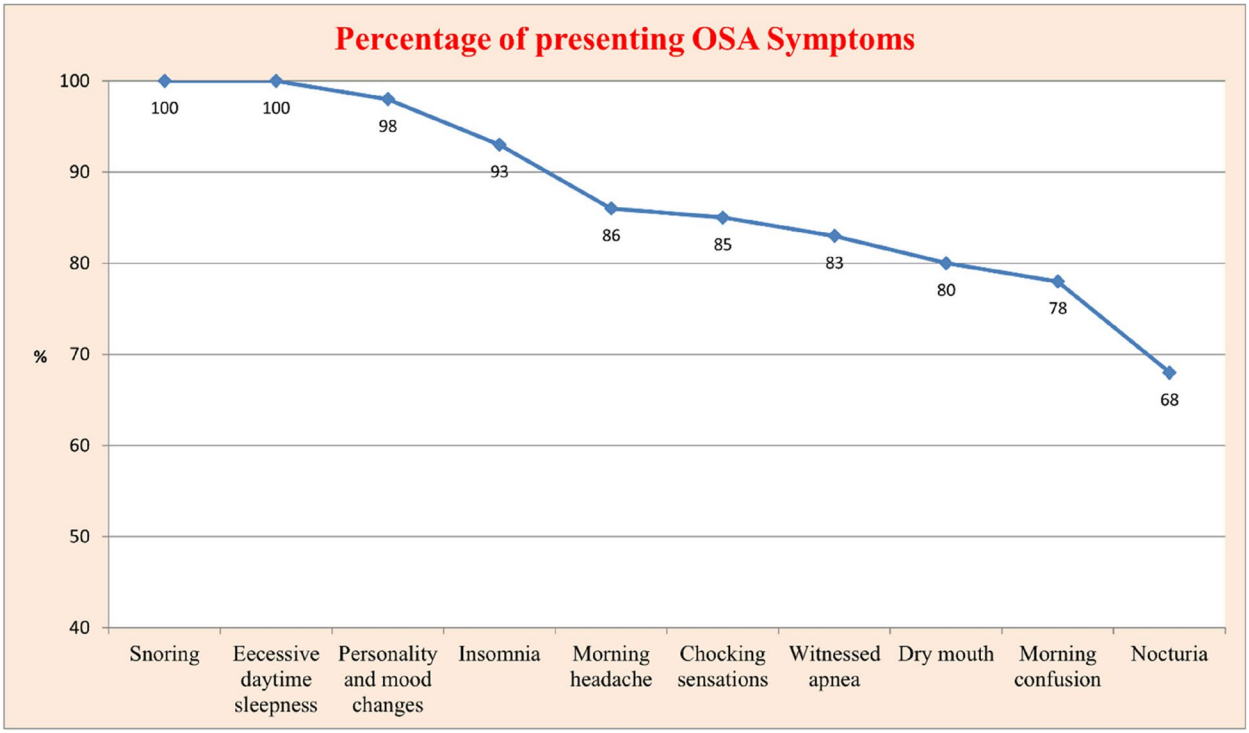

Fig. 3 Percentage of presenting OSA symptoms

Table 2 Comparison between the studied groups regarding radiological and laboratory findings

		Non-CPAP group ($n=40$)	CPAP group ($n=40$)	*p*-value
Radiology	CXR SS	14 (7–16)	12 (9–16)	0.1
	CT SS	18 (12–20)	17.5 (12–20)	0.3
Blood gases	PH	7.44 ± 0.13	7.42 ± 0.03	0.5
	CO2 level	35.75 ± 6.17	38.75 ± 4.75	0.017
	HCO3 level	23.99 ± 3.58	26.29 ± 2.09	< 0.001
Hematological parameters	Hemoglobin level	12.53 ± 2.14	12.88 ± 1.63	0.4
	Red blood cells	10.43 ± 4.57	9.5 ± 3.04	0.3
	Neutrophils	81.55 ± 8.07	82.85 ± 5.12	0.4
	Lymphocyte	10.5 (3.4–31)	10.25 (4.5–15)	0.9
	N/L ratio	8 (2–31)	7.5 (5–18)	0.9
	Platelet	232.25 ± 103.4	250.70 ± 77.48	0.4
	CRP	101.9 ± 45.39	111.3 ± 60.45	0.4
	LDH	514.05 ± 204.66	481.85 ± 139.94	0.4
	D-dimer	0.65 (0–1.6)	0.8 (0–4.2)	0.02
	INR	1.17 ± 0.24	1 ± 0.13	< 0.001
	Serum creatinine	1.15 (0.6–13.6)	0.9 (0.5–1.8)	0.1
	ALT	56.5 (23–130)	53.5 (22–323)	0.5
	AST	45 (21–88)	32.5 (4–127)	0.07
	Serum albumin	3 ± 0.42	3.13 ± 0.4	0.2

Data are presented as mean ± SD, median (range)

Abbreviations: *CXR* Chest X-ray, *SS* Scoring system, *CT* Computed tomography, *N/L* Neutrophils/lymphocyte, *CRP* C-reactive protein, *LDH* Lactate dehydrogenase, *INR* International normalized ratio, *ALT* Alanine aminotransferase, *AST* Aspartate aminotransferase

Table 3 Comparison between two studied groups regarding blood gases and D-dimer

			Non-CPAP ($n=40$)	CPAP ($n=40$)	*p*-value
First day	**Blood gases**	PH	7.44 ± 0.13	7.42 ± 0.03	0.5
		CO_2	35.75 ± 6.17	38.75 ± 4.75	0.017
		HCO_3	23.99 ± 3.58	26.29 ± 2.09	0.001
	D-dimer		0.77 ± 0.48	1.27 ± 1.03	0.001
7th day	**Blood gases**	PH	7.39 ± 0.07	7.40 ± 0.03	0.29
		CO_2	40.80 ± 6.68	39.15 ± 2.61	0.15
		HCO_3	24.54 ± 3.59	25.60 ± 1.79	0.09
	D-dimer		1.44 ± 0.65	0.950 ± 0.52	0.001
			Non-CPAP ($n=28$)	**CPAP ($n=22$)**	***p*-value**
14th day	**Blood gases**	PH	7.42 ± 0.06	7.39 ± 0.01	0.04
		CO_2	42.17 ± 9.15	37 ± 1.48	0.003
		HCO_3	27.25 ± 5.04	24.06 ± 1.27	0.001
	D-dimer		1.87 ± 0.71	0.419 ± 0.26	0.001

Data are presented as mean ± SD

OSA, and also, OSA could be an independent risk factor for poor outcomes in COVID-19 patients that cannot be explained by associated other comorbidities with two-fold increased risk of poor COVID-19 outcome [15]. Conversely, in the CPAP group, this agrees with [4] as CPAP could reduce risks for infectious complications, chronic inflammation, thrombophilia, and cardiovascular complications in OSA patients who caught COVID-19 infection. However, the results were against other studies [15, 19]. This could be explained by propelling viral particles located in the upper respiratory tract further down the respiratory tract and thus increasing the risk of viral pneumonia as in [20, 21]. In our study, the predictors of mechanical ventilation in patients with obstructive sleep apnea on CPAP were age, CO2 level, CT SS, HTN, and DM patients and the percentage of witnessed apnea. These results were in accordance with other studies that reported that older age and excessive infiltration on CT, HTN, and DM all have proved to be risky factors for poor outcomes and death in COVID-19 patients with sleep apnea [19, 22].

Also, in our study that there was no significant difference in the length of hospital stay in patients in two groups until the 28th day, after that, there were notable findings in the percentage of patients in each group with 20% and 5% of patients in the non-CPAP group and CPAP group respectively. This was in accordance with other study which reported that the presence of OSA leads to significant value in prolongation of length of hospital stay in COVID-19 patients more than 14 days [22].

Limitations

There were some limitations in our study, as it was small sample size from single isolation center and results cannot be generalized and lack of PSG to confirm the diagnosis and categorize patients according to OSA severity due to infection control measures. Also, there were strict inclusion and exclusion criteria that made selection of patients relatively difficult as patients enrolled must be with positive swab for COVID-19 PCR, so we exclude patient with typical findings but with negative PCR swab. Another limitation was about deficient studying of oxygen tension before and after CPAP therapy; this limitation is attributed to difficulty to have repeated arterial sampling from patients as most of patients were on anticoagulation therapy and risky for hematoma formation and bleeding, so we used venous samples with evaluating and tracing PH, CO2, and HCO3 as parameters for tissue oxygenation and patient improvement. Also, follow-up of patients after discharge was not involved in our work. Finally, this study cannot provide us with information about the actual incidence of OSA in patients with COVID-19 infection.

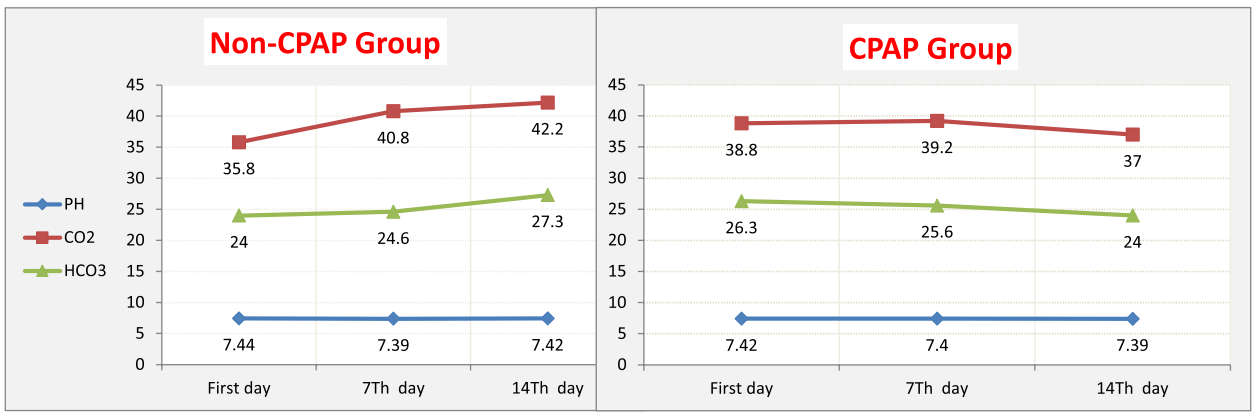

Fig. 4 Comparison between two studied groups regarding blood gases analysis on admission and follow-up

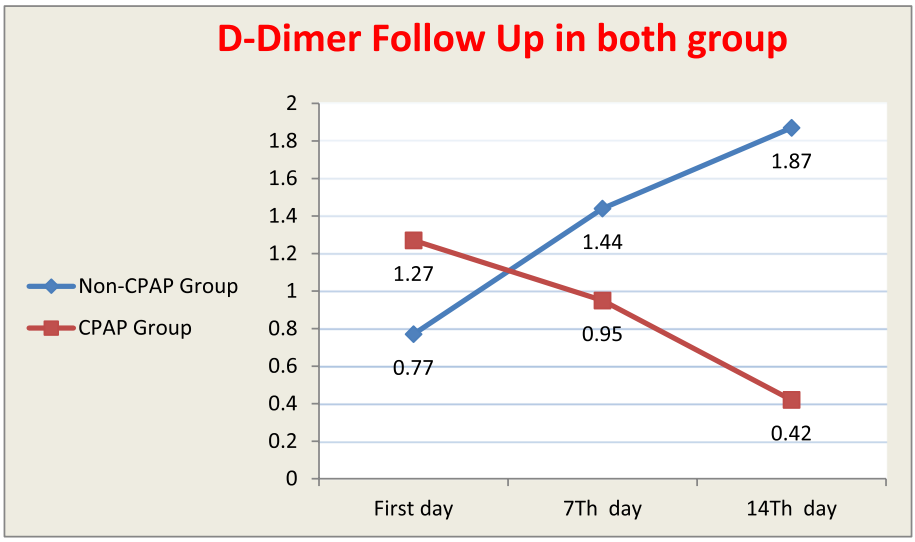

Fig. 5 Comparison between two studied groups regarding D-dimer analysis at baseline and follow-up

Table 4 Primary and secondary end point in the two studied groups

	Non-CPAP group ($n=40$)	CPAP group ($n=40$)	*p*-value
Primary end point			
Survival *n* (%)	23 (57.5)	32 (80)	0.03
Inhospital mortality *n* (%)	17 (42.5)	8 (20)	
Secondary end point			
a. Duration of hospital stay			
Total duration	19.5[a] (10–41)	15[a] (7–38)	0.04
< 14 days	12 (30%)	18 (45%)	0.09
> 14–28	20 (50%)	20 (50%)	
> 28	8 (20%)	2 (5%)	
b. Need for invasive ventilation *n* (%)	34 (85)	24 (60)	0.01

Data are presented as numbers (percentage), Median[a] (range)

Conclusion

Early CPAP therapy for moderate and severe COVID-19 hospitalized patients with risk of OSA could improve patient's survival, shorten hospital stay, and decrease need for invasive mechanical ventilation. CPAP may improve patient's outcome through decreasing hypercoagulation and oxygen requirement.

Abbreviations

COVID-19	Coronavirus disease 2019
OSA	Obstructive sleep apnea
CPAP	Continuous positive airway pressure
AHRF	Acute hypoxemic respiratory failure
ACE2	Angiotensin-converting enzyme 2
ICU	Intensive care unit
NIV	Noninvasive ventilation
HFNO	High-flow nasal oxygen
PCR	Polymerase chain reaction
BMI	Body mass index
ESS	Epworth Sleepiness Scale
CT scan	Computed tomography scan
CRP	C-reactive protein
LDH	Lactate dehydrogenase enzyme
SGOT	Serum glutamate oxaloacetate transaminase
SGPT	Serum glutamate pyruvate transaminase
AHI	Apnea/hypopnea index
DM	Diabetes mellitus
COPD	Chronic obstructive pulmonary disease
CKD	Chronic kidney disease
CVD	Cardiovascular diseases
CXR	Chest X-ray
SS	Scoring system
N/L	Neutrophils/lymphocyte
INR	International normalized ratio
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

Acknowledgements
None/not applicable.

Authors' contributions
Design and conception by AMS, TTA, and MAI; data gathering by ZE; statistical analysis by ZE, AMS, and TTA; and medical writing by TTA and MAI. The manuscript was revised by the authors. The writers reviewed the final manuscript and gave their approval.

Funding
None/not applicable.

Availability of data and materials
The author may be contacted for reasonable requests on the datasets utilized and/or analyzed in the present study.

Declarations

Ethics approval and consent to participate
The study protocol has been approved by the Institutional Research Board, Faculty of Medicine, Mansoura University, with the proposal code: MS.21.07.1578. Precautions were used to protect participants' privacy as

patients were given the option to participate or not; also, the study findings were exclusively used for scientific purpose. Personal data were hidden from any public use.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 5 June 2023 Accepted: 6 September 2023
Published online: 19 September 2023

References

1. Huang Y, Chen D, Fietze I et al (2022) Obstructive sleep apnea with COVID-19. AdvExp Med Biol 1384:281–293. https://doi.org/10.1007/978-3-031-06413-5_17
2. Jose RJ, Manuel A (2020) COVID-19 cytokine storm: the interplay between inflammation and coagulation. Lancet Respir Med 8(6):e46–e47. https://doi.org/10.1016/S2213-2600(20)30216-2
3. Salles C, Mascarenhas BH (2020) COVID-19 and obstructive sleep apnea. J Clin Sleep Med 16(9):1647. https://doi.org/10.5664/jcsm.8606
4. Mutti C, Azzi N, Soglia M, Pollara I et al (2020) Obstructive sleep apnea, cpap and COVID-19: a brief review. Acta Biomed 91(4):e2020196. https://doi.org/10.23750/abmv91i4.10941
5. Cross MD, Mills NL, Al-abri M et al (2008) Continuous positive airway pressure improves vascular function in obstructive sleep apnea hypopnea syndrome: a randomized controlled trial. Thorax 63(7):578–583. https://doi.org/10.1136/thx.2007.081877
6. Jain P (2022) Noninvasive ventilation by helmet vs face mask in COVID-19 pneumonia: emerging evidence and need of the hour. Indian J Crit Care Med 26(3):256–258. https://doi.org/10.5005/jp-journals-10071-24159
7. Guo Q, Song Wd, Li W et al (2020) Weighted Epworth Sleepiness Scale predicted the apnea-hypopnea index better. Respir Res 21:147. https://doi.org/10.1186/s12931-020-01417-w
8. Netzer NC, Stoohs RA, Netzer CM et al (1999) Using the Berlin questionnaire to identify patients at risk for sleep apnea syndrome. Ann Intern Med 131(7):485–491. https://doi.org/10.7326/0003-4819-131-7-199910050-00002
9. Saleh AB, Ahmad MA, Awadalla NJ (2011) Development of Arabic version of Berlin questionnaire to identify obstructive sleep apnea at risk patients. Ann Thorac Med 6(4):212–216. https://doi.org/10.4103/1817-1737.84775
10. Nagappa M, Liao P, Wong J et al (2015) Validation of the STOP-Bang questionnaire as a screening tool for obstructive sleep apnea among different populations: a systematic review and meta-analysis. PLoS One 10(12):e0143697. https://doi.org/10.1371/journal.pone.0143697.
11. Borghesi A, Maroldi R (2020) COVID-19 outbreak in Italy: experimental chest X-ray scoring system for quantifying and monitoring disease progression. Radiol Med 125(5):509–513. https://doi.org/10.1007/s11547-020-01200-3
12. Francone M, Iafrate F, Masci GM et al (2020) Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur-Radiol 30(12):6808–6817. https://doi.org/10.1007/s00330-020-07033-y
13. Huang HCC, Hillman DR, McArdle N (2012) Control of OSA during automatic positive airway pressure titration in a clinical case series: predictors and accuracy of device download data. Sleep 35(9):1277–1283
14. Schwab RJ, Badr SM, Epstein LJ et al (2013) ATS subcommittee on CPAP adherence tracking systems. An official American Thoracic Society statement: continuous positive airway pressure adherence tracking systems. The optimal monitoring strategies and outcome measures in adults. Am J RespirCrit Care Med 188(5):613–20. https://doi.org/10.1164/rccm.201307-1282ST
15. Rögnvaldsson KG, Eyþórsson ES, Emilsson Öl et al (2022) Obstructive sleep apnea is an independent risk factor for severe COVID-19: a population-based study. Sleep 45(3):zsab272. https://doi.org/10.1093/sleep/zsab272
16. Schreiber A, Surbone S, Malovini A et al (2018) The effect of continuous positive airway pressure on pulmonary function may depend on the basal level of forced expiratory volume in 1 second. J Thorac Dis 10(12):6819–6827. https://doi.org/10.21037/jtd.2018.10.103
17. SowhoM SH, Jun J et al (2022) D-dimer in Marfan syndrome: effect of obstructive sleep apnea induced blood pressure surges. Am J Physiol Heart CircPhysiol 322(5):H742–H748. https://doi.org/10.1152/ajpheart.00004.2022
18. LiakC FM (2011) Coagulability in obstructive sleep apnea. Can Respir J 18(6):338–348. https://doi.org/10.1155/2011/924629
19. Cade BE, Dashti HS, Hassan SM et al (2020) Sleep apnea and COVID-19 mortality and hospitalization. Am J RespirCrit Care Med 202(10):1462–1464. https://doi.org/10.1164/rccm.202006-2252LE
20. Su VY, Liu CJ, Wang HK et al (2014) Sleep apnea and risk of pneumonia: a nationwide population-based study. CMAJ 186(6):415–421. https://doi.org/10.1503/cmaj.131547
21. Mercieca L, Pullicino R, Camilleri K et al (2017) Continuous positive airway pressure: is it a route for infection in those with obstructive sleep apnoea? Sleep Sci 10(1):28–34. https://doi.org/10.5935/1984-0063.20170005
22. Mashaqi S, Lee-Iannotti J, Rangan P et al (2021) Obstructive sleep apnea and COVID-19 clinical outcomes during hospitalization: a cohort study. J Clin Sleep Med 17(11):2197–2204. https://doi.org/10.5664/jcsm.9424

Publisher's Note