Persistence of Symptoms Following Hospitalization for COVID-19 in Oman: A Bidirectional Observational Study

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Abstract

Objectives: This study sought to assess the prevalence persistent COVID-19 related symptoms in patients with mild, severe, and critical disease. **Methods:** We conducted a bidirectional cohort observational study that included all adult patients 18 years and above, admitted to Armed Forced Hospital Muscat between July 2020 and June 2022, with COVID-19 infection and discharged alive. Patients were requested to attend outpatient clinic at weeks 6 and 12 post-discharge, where they filled out a questionnaire and underwent a chest X-ray. Additionally tests, such as blood tests, were performed if necessary. Health care workers with mild infection were also requested to fill out a questionnaire about their initial symptoms, persistent symptoms, and comorbidities. **Results:** The study included 468 patients, comprising 261 hospitalized patients and 207 health care workers. On follow up, 39.7% of patients presented with residual symptoms, such as cough, breathlessness, and joint pain. These symptoms were more common in patients with medical comorbidities, particularly hypertension, diabetes, and dyslipidemia. Notably, these symptoms were also observed in patients with mild disease. Post COVID-19 pulmonary fibrosis was observed in 21 patients, mainly among those admitted to the ICU or requiring prolonged hospitalization. **Conclusions:** This study highlights the persistence of symptoms and the prevalence of post-COVID-19 syndrome at two months post discharge, especially among patients with severe and critical disease during the acute phase. Various predictors of post-COVID-19 syndrome were identified, including female gender, older age, presence of co-morbidities, disease severity, and hypertension. Therefore, patients in these categories require thorough evaluation and long-term follow-up to manage residual symptoms.

Keywords: COVID-19 Pandemic; Post-COVID-19 Syndrome; Long COVID; Oman.

Introduction

In March 2020, the World Health Organization (WHO) declared the SARS-CoV-2 virus as a pandemic infection, leading to COVID-19.[1-3] As of 5 June 2023 over 767 million people worldwide have been infected, with more than 6.9 million deaths reported.[1] Oman has seen a total of 399 449 COVID-19 cases and over have 4600 confirmed deaths.[1] The clinical features of the disease are well-established, including fever, headache, body ache, cough, shortness of breath, loss of smell and taste, and gastrointestinal symptoms such as diarrhea and vomiting.[4] Additionally, various complications have been reported, such as respiratory failure, cardiac issues, renal problems, neurological manifestations, thrombotic events, and hepatic complications.[5-8] Post COVID-19 syndrome, also known as long COVID, typically refers to persistent symptoms that last beyond four weeks of disease onset.[9-11] Recently, WHO defined long COVID as persistent symptoms beyond three months from the onset of COVID-19 that persist for two months and cannot be explained by another diagnosis in patients who had probable or confirmed COVID-19.[12] The epidemiology of long COVID has been described in many studies from various parts

of the world with variable results due to variation in methodology, patients included, and follow-up period.[9,10] The incidence of post COVID symptoms in American and European studies ranges from 30 to 90% at six months.[13-15] Although common residual symptoms including fatigue (40%), shortness of breath (36%), atypical chest pain (13.1%), a persistent cough (16.9%), and anosmia (11%) have been described in several studies,[16-18] there are no studies on the prevalence of post COVID symptoms in Oman. This study aims to assess the incidence of COVID-19 related symptoms in patients with mild, severe, and critical disease in Oman.

Methods

This is a bidirectional observational cohort study included adult patients aged 18 years and above admitted to the Armed Forces Hospital (AFH) with SARS-CoV-2 infection confirmed by RT-PCR between July 2020 and June 2022. Patients were admitted to COVID ward if they had bilateral lung infiltrates and oxygen desaturation below 93% or required oxygen for other indications related to severe COVID-19. Patients admitted to the ICU, or transferred from the COVID ward to ICU if they had critical disease as per WHO guidelines were also included.[19] Healthcare workers (HCWs) with mild disease were included as a comparative group. HCWs were requested to complete an online questionnaire and the admitted patients were asked to attend post COVID follow-up clinics at weeks six and 12 post-discharge, during which patients answered questionnaires that included demographic data, past medical history, presenting symptoms that led to hospital admission and residual symptoms. Chest X-rays and abnormal blood investigations were repeated as clinically indicated. Other investigations such as ECG, echocardiography, and chest CT were performed according to clinical indications.

Patients who died, those who were aphasic or had poor mental status, patients who were bedridden and could not be followed at an outpatient clinic, and those who did not attend the follow-up appointment were excluded from the study.

A scoring system modified from I Galal et al,[20] was created based on 18 symptoms during the acute and post-COVID-19 stages. A scale of (0–1) was used for each symptom (0 = absent, 1 = present). The range of the overall score was 0–18, with a high score indicating more severe symptoms.

Statistical analyses were performed using STATA 14 (College Station, TX, USA) software. Categorical data were presented as numbers and percentages, while continuous data were reported as means ± SD and/or median (interquartile range) and tested for normality using the Shapiro-Wilkes test. Continuous variables were analyzed using either Students' t-test or Mann-Whitney test for comparison of two groups whenever appropriate. Chi-squared test was used for comparison of binary variables. Spearman's correlation was used to find the correlation between symptom score in acute and post-COVID-19 stages. Univariate and multivariate adjusted logistic regression analyses were performed to identify baseline determinants of persistent post COVID symptoms. In all statistical tests, a p-value < 0.05 was considered statistically significant.

The study was approved by the ethical committee of Armed Forces Hospital, Oman (IRB number: FMS-MREC 027/2020). Verbal informed consent was taken from all patients at the clinic.

Results

Our study included a total of 468 patients diagnosed with COVID-19 followed up at the post-COVID clinic. The mean age of the enrolled participants was 48.4 years, with 209 (44.7%) males and 259 (55.3%) females [Table 1].

Table 1: Baseline demographics and clinical data, n = 468. Baseline demographics and clinical data of the study participants (n = 468), categorized into three groups based on the severity of COVID-19 disease. Numeric values are presented as means ± standard deviations, and categorical values are expressed as frequencies (percentages).

Variables	Mild disease (HCW) n = 207	Non-ICU n = 208	ICU n = 53
Age, years	41.9±18.8	54.6±14.1	49.3±11.8
Male gender	35 (16.9)	140 (67.3)	34 (64.1)
BMI	25.9±4.2	30.5±6.6	30.5±4.8
Vaccination status, Y	No available data	10 (4.8)	5 (9.4)
How many doses	No available data	6 (2.9)	4 (7.5)
One dose		4 (1.9)	1 (1.9)

Two doses			
Oxygen requirements:	None	22 (10.6)	0 (0.0)
None		118 (56.3)	6 (11.3)
2–5		40 (19.2)	4 (7.5)
5–10		26 (12.5)	43 (81.1)
15			
Persistent COVID	55 (26.6)	102 (49.0)	29 (54.7)
Medical background			
Diabetes mellitus, Y	11 (5.3)	95 (45.7)	16 (30.2)
Hypertension, Y	9 (4.3)	99 (47.6)	23 (43.4)
Heart disease	1 (0.5)	26 (12.5)	6(11.3)
Dyslipidemia, Y	0 (0.0)	80 (38.5)	18 (34.0)
Chronic lung disease	1 (0.5)	13 (6.3)	6 (11.3)
Smoking	1 (0.5)	0 (0.0)	0 (0.0)
Renal failure	2 (1.0)	5 (2.4)	4 (7.5)
Liver disease	0 (0.0)	2 (1.0)	0 (0.0)
CVA	0 (0.0)	2 (1.0)	1 (1.9)
Thyroid disease	3 (1.4)	5 (2.4)	0 (0.0)

A majority of patients, 445 out of 468 (95.1%), did not receive COVID-19 vaccination. Among the hospitalized patients, 131 patients (28.0%) had hypertension, 122 (45.6%) had diabetes, and 98 (20.9%) had dyslipidemia. Among all included patients, 44.2% (n = 207) experienced mild disease that did not require hospitalization, while 261 (55.8%) were admitted. Among the admitted patients, 53 (11.3%) required ICU admission.

The most common presenting symptoms of acute COVID-19 for both admitted and HCWs during the acute phase were fever (385/468, 8.32%), fatigue (336/468, 71.8%), and cough (303/468, 64.7%). The mean duration from symptom onset to the follow-up visit was 68.0 days. The mean total score of acute stage symptoms was 8.0±3.5, whereas the post-COVID-19 symptom score was 1 ($p < 0.001$) as shown in Table 2.

Table 2: Comparison of baseline symptoms according to patients' groups.

	Mild disease (HCW) n = 207		**Non-ICU n = 208**		**ICU n = 53**	
	Baseline	**Follow-up**	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**
Fever 385/8	156 (75.4)	2 (1.0	180 (86.5)	5 (2.4)	49 (92.5)	1 (1.9)
Cough 303/68	112 (54.1)	14 (6.8)	149 (71.6)	39 (18.8)	42 (79.2)	15 (28.3)
Sputum 167/44	48 (23.2)	7 (3.4)	92 (44.2)	25 (12.0)	27 (50.9)	12 (22.6)
Shortness of breath 271/75	48 (23.2)	7 (3.4)	179 (86.1)	48 (23.1)	44 (83.0)	20 (37.7)
Chest pain 200/49	42 (20.3)	7 (3.4)	127 (61.1)	31 (14.9)	31 (58.5)	11 (20.8)
Loss of smell 230/ 22	131 (63.3)	12 (5.8)	78 (37.5)	8(3.8)	21 (39.6)	2 (3.8)
Loss of taste 233/17	126 (60.9)	9 (4.3)	85 (40.9)	5 (2.4)	22 (41.5)	3 (5.7)
Rhinitis 134/14	79 (38.2)	3 (1.4)	45 (21.6)	10 (4.8)	10 (18.9)	1 (1.9)

Red eye 53/7	22 (10.6)	0 (0.0)	27 (13.0)	7 (3.4)	4 (7.5)	0 (0.0)
Diarrhea 116/8	52 (25.1)	1 (0.5)	48 (23.1)	6 (2.9)	16 (30.19)	1 (1.9)
Nausea 121/1	46 (22.2)	3 (1.4)	62 (29.8)	10 (4.8)	13 (24.5)	0 (0.0)
Vomiting 68/4	28 (13.5)	0 (0.0)	33 (15.9)	4 (1.9)	7 (13.2)	0 (0.0)
Fatigue 336/54	148 (71.5)	13 (6.3)	150 (72.1)	29 (13.9)	38 (71.7)	12 (22.6)
Vertigo 150/26	57 (27.5)	11 (5.3)	75 (36.1)	12 (5.8)	18 (334.0)	3 (5.7)
Headache 264/33	148 (71.5)	12 (5.8)	91 (43.8)	18 (8.7)	25 (47.0)	3 (5.7)
Weakness 53/17	1 (0.5)	0 (0.0)	45 (21.6)	10 (4.8)	7 (13.2)	7 (13.2)
Joints pain 271/60	128 (61.8)	9 (4.3)	113 (54.3)	36 (17.3)	30 (56.6)	15 (28.3)
Myalgia 285/1	144 (69.6)	12 (5.8)	113 (54.3)	33 (15.9)	28 (52.8)	14 (26.4)

At the follow-up time point, 60.3% of the patients (n = 282 out of 468) had symptom score of 0, indicating the absence of persistent symptoms. On the other hand, 39.7% of the patients (n = 186) had a symptom score of at least 1, indicating the presence of persistent symptoms. The most commonly reported persistent symptoms during the follow-up visit were shortness of breath reported by 75 patients (16.0%), followed by cough (n = 68, 14.5%), and joints pain (n= 60/468, 12.8%). A strong positive correlation was observed between the symptom score during the acute attack and post-COVID-19 stage ($p < 0.001$, r = 0.20) as illustrated in Figure 1. There was significant reduction in baseline symptoms scores at the follow-up time point across different patient subgroups including age, gender, BMI, and severity of baseline illness, as shown in Table 3. The most frequent pre-existing comorbidities associated with persistent post-COVID-19 symptoms and symptom scores among the study population were hypertension ($p = 0.003$) followed by chronic pulmonary disorders ($p = 0.004$), dyslipidemia ($p = 0.010$) and cardiac diseases that include ischemic heart disease (IHD), AF, and HF ($p = 0.040$) as shown in Table 4.

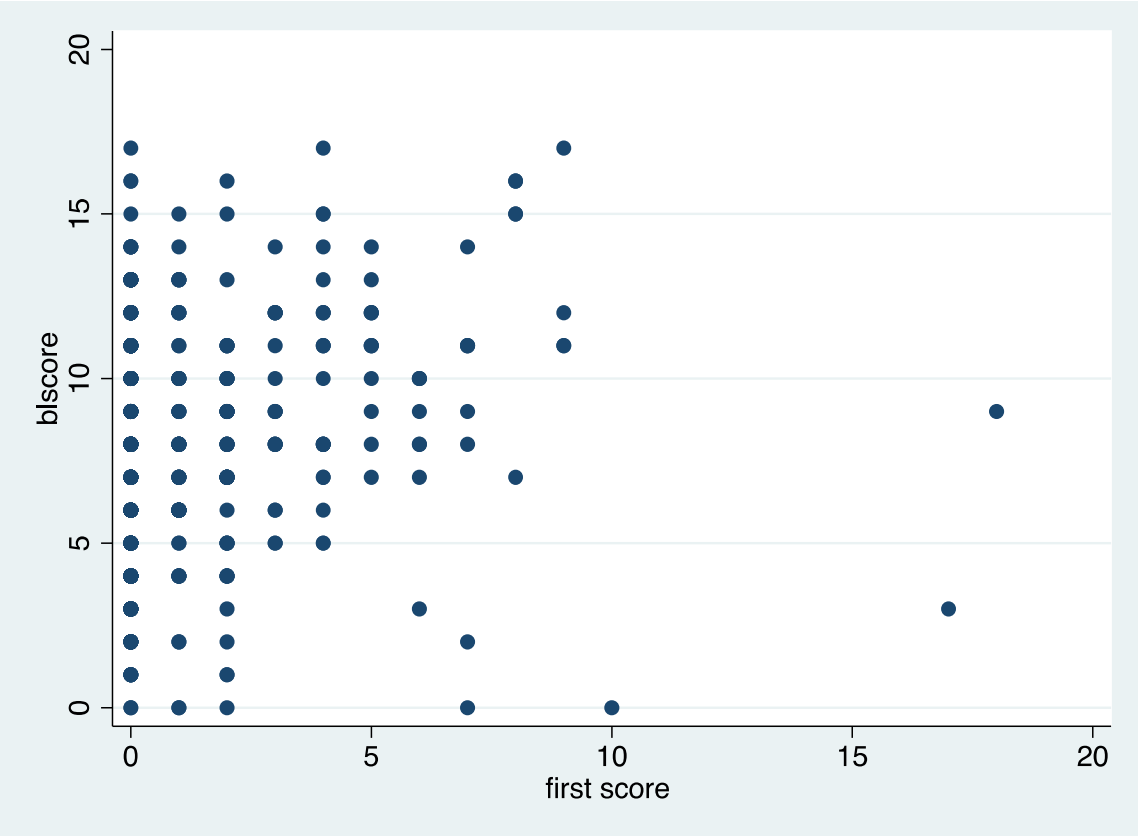

Figure 1: Correlation between symptom score during acute and post-COVID-19 stage.

Table 3: Comparison of baseline symptoms scores among different patient groups at follow-up (n = 468).

Variables	n (%)	Baseline mean score	Follow-up	*p*-value
Age, years	16 (3.4)	8.1±3.2	0 (0,3.5)	< 0.001*
< 25	285(60.9)	7.9±3.6	0 (0,1)	
25–50	172 (36.8)	7.5±3.5	0 (0,2)	
> 50				
Gender	259 (55.3)	7.9±3.7	0 (0,1)	< 0.001 *
Male	209 (44.7)	7.5±3.3	0 (0,2)	
Female				
BMI^	6 (1.3)	9.6±3.9	0 (0,2)	(0.030, < 0.001, <
Underweight	105 (22.4)	7.3±3.5	0 (0,1)	0.001, < 0.001) *
Normal	184 (39.3)	7.9±3.7	0 (0,1.5)	
Overweight	113 (24.1)	7.0±3.1	0 (0,2)	
Obese				
Severity of illness	207 (22.2)	7.3±3.6	0 (0, 1)	< 0.001
Mild (HCW)	208 (44.4)	8.1±3.5	0 (0,2)	
Moderate (non-ICU)	53 (11.3)	8.1±3.3	2 (0,4)	
Severe (ICU)				
Baseline symptoms score	128 (27.4)	3.3±1.4	0 (0, 1)	< 0.001
< 5 (n = 128)	231 (49.4)	6.9±1.3	0 (0, 2)	
5–10 (n = 231)	109 (23.3)	12.5±1.6	1 (0, 4)	
> 10 (n = 109)				

**Compare baseline to first follow-up score.*
^Missing for 60 patients.
Note: Numeric values are presented as means ± standard deviations, and categorical values are expressed as frequencies (percentages). The p-values indicate the significance of the changes in symptom scores from baseline to follow-up within each patient group.

Table 4: Median post-COVID-19 symptom score in patients according to comorbidities (n = 468).

Variables	No	Yes	*p*-value
Diabetes mellitus	0 (0, 1) n = 346	0 (0,2) n = 122	0.180
Hypertension	0 (0,1) n = 337	1 (0, 2) n = 131	**0.003**
Cardiac (IHD, CCF, AF)	0 (0, 2) n = 436	1 (0, 3.5) n = 32	**0.040**
DLP	0 (0,1) n = 370	0 (0,2) n = 98	**0.010**
Chest disease	0 (0, 2) n = 448	2 (0,5) n = 20	**0.004**
Renal failure	0 (0, 2) n = 457	0 (0,0) n = 11	0.140
Liver disease	0 (0, 2) n = 466	1.5 (0, 3) n = 2	0.680
CVA	0 (0,2) n = 465	0 (0,0) n = 3	0.180
Thyroid disease	0 (0, 3) n = 460	0.5 (0, 1.5) n = 8	0.690
IS therapy	0 (0, 2)	0 (0, 0)	**0.080**

IHD: ischemic heart disease; CCF: congestive cardiac failure; IS: immunosuppressant.

Univariate logistic regression analyses revealed that age older than 50 years (OR: 1.51, 95% CI: 1.03–2.20, $p = 0.037$), higher baseline symptom score (OR: 1.10, 95% CI: 1.04–1.16, $p < 0.001$), severe disease (OR: 2.66, 95% CI: 1.76–4.01, $p < 0.001$), and critical disease (OR: 3.33, 95% CI: 1.79–6.22, $p < 0.001$) were significantly associated with persistent COVID-19 symptoms. Additionally, hypertension (OR: 1.8, 95% CI: 1.22–2.76, $p = 0.004$) showed a significant association with persistent symptoms. The multivariate adjusted logistic regression model showed that higher baseline symptom score (OR: 1.10, 95% CI: 1.04–1.17, $p = 0.001$) and hypertension (OR: 1.71, 95% CI: 1.00–2.91, $p = 0.050$) were independent determinants for persistent COVID-19 symptoms, as demonstrated in Table 5.

Table 5: Logistic regression model for predictors of persistent COVID-19 (n = 468).

	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value
Age, > 50 years	1.51 (1.03–2.20)	**0.037**	1.21 (0.75–1.95)	0.440
Male ender	1.38 (0.95–2.00)	0.090	1.37 (0.93–2.04)	0.110
Baseline symptom score	1.10 (1.04–1.16)	**< 0.001**	1.10 (1.04–1.17)	**0.001**
Disease severity at baseline	Ref	**Ref**	NA	NA
Mild	2.66 (1.76–4.01)	**< 0.001**		
Moderate	3.33 (1.79–6.22)	**< 0.001**		
Severe				
Diabetes mellitus	1.29 (0.84–1.96)	0.240	0.81 (0.47–1.38)	0.430
Hypertension	1.8 (1.22–2.76)	**0.004**	1.71 (1.00–2.91)	**0.050**
Chest disease	2.36 (0.95–5.89)	**0.065**	1.52 (0.58–4.03)	0.400
Cardiac disease	1.79 (0.87–3.68)	0.110	1.07 (0.49–2.31)	0.870

Univariate logistic regression revealed that female gender (OR: 1.56, 95% CI: 1.12–1.31, $p = 0.040$) and higher baseline symptoms score (OR: 1.21, 95% CI: 1.02–1.31, $p < 0.001$) were positively associated with persistent COVID-19. Multivariate adjusted logistic regression model showed that a higher baseline symptoms score (OR: 1.20, 95% CI: 1.09–1.31, $p < 0.001$), absence of diabetes (OR: 2.14, 95% CI: 1.05–4.33, $p = 0.040$) were independent determinants for persistent COVID-19 [Table 6].

Among the hospitalized patients, 42 developed COVID-19 related complications. The most encountered post-COVID complications were pulmonary embolism (7.7%), denovo diabetes mellitus (1.9%), and lung fibrosis (8.0%).

Table 6: Logistic regression model for predictors of persistent covid among admitted patients (n = 261).

	OR (95%CI)	***p*-value**	**OR (95%CI)**	***p*-value**
Age, > 50	0.98 (0.60–1.60)	0.9400	1.54 (0.77–3.06)	0.220
Male gender	0.52 (0.31–0.88)	**0.02**	0.67 (0.34–1.33)	0.250
Baseline symptom score	1.21 (1.12–1.31)	**< 0.001**	1.20 (1.09–1.31)	**< 0.001**
Severe disease at baseline	1.26 (0.69–2.30)	0.460	Na	Na
Diabetes mellitus	0.66 (0.40–1.07)	0.090	0.47 (0.23–0.95)	**0.040**
Hypertension	1.11 (0.69–1.81)	0.660	1.42 (0.70–2.87)	0.330
Chest disease	1.77 (0.67–4.65)	0.250	0.67 (0.20–2.32)	0.530
Cardiac disease	1.14 (0.54–2.40)	0.720	1.21 (0.44–3.30)	0.710
CRP	0.99 (0.99–1.00)	0.190	0.99 (0.99–1.00)	0.320
Ferritin	0.99(0.99–1.00)	0.900	0.99 (0.99–1.00)	0.680
D dimer	1.00 (0.99–1.01)	0.470	1.00 (0.99–1.00)	0.970
LDH	0.99 (0.99–1.00)	0.560	1.00 (0.98–1.04)	0.510
Lymphocytes	1.03 (0.67–1.59)	0.890	1.01 (0.55–1.87)	0.970

Discussion

The definition of long COVID has evolved over the course of the COVID-19 pandemic.[21] Initially, studies observed symptoms persisting beyond four weeks in 13.3% of patients,[10] but later investigations explored symptoms persisting beyond one year.[17] This study presents the first detailed examination of the long-term consequences of COVID-19 infection in a large group of Omani patients, including those who were hospitalized with severe and critical disease and HCWs with mild disease. Our study showed that 40% of patients experienced at least one residual symptom, with breathlessness, cough, and joint pain being the most common at two months from the onset of symptoms. A study from Saudi Arabia showed that the incidence of post-COVID-19 syndrome was 45% which is comparable to our findings.[22] Another study from Saudi Arabia demonstrated a lower incidence of 22%.[23] Patients who had severe and critical disease had more residual symptoms, aligning with other international studies.[16,24,25] Fatigue was a common residual symptom in many studies and ranged from 13% to 77% depending on study inclusions and follow up period.[26,27] This was not the case in our study as fatigue was a common presenting symptom during the acute illness (71.8%) but not in the post-COVID period. The same observations have been noted in the studies from Saudi Arabia, with fatigue being reported in 11.5% in one study and 19% in the other.[22,23] This could be explained by the cultural background of our patients who always try to underreport non-physical symptoms such as fatigue.

The most prevalent co-morbidities in the study cohort were diabetes, hypertension, and dyslipidemia, consistent with observations from other studies in the region.[22,23,28] Post-COVID-19 syndrome has been related to older age, diabetes, hypertension, dyslipidemia, and cardiovascular disease which is similar to our findings.[29] Post-COVID-19 symptoms were also seen in HCWs with mild disease, impacting their work performance and return to normal duties.[30] Although, previous studies have shown that HCWs had more residual symptoms compared to non-healthcare patients,[29] however, this was not apparent in our study, probably due to the fact that HCWs are of younger age at our institution and very few had co-morbidities.

Moreover, 21 patients developed post-COVID-19 pulmonary fibrosis (PCPF), primarily in severe and critical disease, and those who spent extended days in hospital with an average of 37 days. Similar risk factors for PCPF have been reported in many other studies.[31,32] In a recent metanalysis study, the authors have shown that the prevalence of PCPF was 44.9% for COVID-19 survivors.[33] They reported that COPD was the only comorbidity associated with PCPF. Although some laboratory blood results (pre-discharge) were abnormal in many patients, however, most had normal results during follow-up visits, which is in line with prior research.[34,35]

The number of newly diagnosed diabetes post-COVID-19 in our cohort was small (1.9%) compared to (14%), reported by a large metanalysis of eight studies that investigated newly diagnosed diabetes in admitted Covid patients.[36]

Furthermore, our study included patients with mild, severe, and critical disease, which covered various severity grades of COVID-19 infection. In addition, one of the strengths of our study is that our patients were interviewed and clinically evaluated, unlike other studies that mainly relied on administering questionnaires to patients over the phone or conveyed through social media tools.[37]

The limitations of our study include the relatively small number of patients attending follow-up clinics despite multiple reminders and calls. In addition, we also did not carry out lung function test in patients who reported persistent respiratory symptoms because the lung function lab was not functioning during the study period due to COVID restrictions. Moreover, there might be a recall bias in the HCWs group with mild disease. Also, there was no systematic assessment of the breathlessness severity using a known index. We also did not include sleep related and mental health-related sequelae.

Conclusion

This is the first comprehensive study of post-COVID-19 syndrome in the Omani population. The study sheds light on the significant percentage of residual symptoms in patients two months after discharge and underscores the need for systematic follow-up and management of individuals recovering from acute COVID-19. Predictors of post-COVID-19 syndrome include female gender, older age, severe disease, and hypertension. HCWs who have significant residual symptoms also require support to help them go back to work and to identify those who require modification of their work environment to be able to cope with their work challenges.

Disclosure

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