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Prevalence and predictors of post-COVID-19 syndrome across SARS-CoV-2 affected Saudi individuals: From acute infection to one year after recovery

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Many patients recovering from COVID-19 report persistent symptoms that debilitate their daily activities. Post-COVID-19 syndrome (PCS) is defined as symptoms lasting more than 12 weeks after the diagnosis of SARS-CoV-2 infection. This study aimed to collect the PCS symptoms from a sample of Saudis and residents of the Kingdom. Moreover, the predictors of PCS were assessed. One-year post-recovery from acute COVID-19, a trained researcher phoned the patients to fill out a short telephone questionnaire. They were questioned regarding the symptoms they had endured for more than three months to the end of 1-year post-recovery. Ongoing symptomatic COVID-19 (OSC) symptoms and all participants' demographic and baseline clinical data were gathered via a form made on the Survey Monkey website and sent via WhatsApp to each patient's phone number (September 2020 to September 2021). Of 158 patients, 112 participants (70.9%) responded. PCS symptoms occurred in 73.2% of patients. The most frequent PCS symptoms were fatigue (37.5%), memory problems and arrhythmia (28.6%), muscle pain and hair loss (25%), sleep problems (21.4%), difficulty breathing (20.5%), headache and loss of smell (17.9%), and loss of concentration and bone pain (15.2%). The severity of the OSC increased the duration of most PCS symptoms. Furthermore, our investigation discovered that female sex, comorbidities, including diabetes and hypertension, long-term oxygen treatment after acute COVID-19, and obesity may all have an influence on PCS. In conclusion, the most common PCS symptoms were tiredness, cognitive issues, and muscular soreness. PCS predictors were female gender and adiposity.

Keywords: COVID-19, Post-COVID-2019, Severity, Gender, BMI, Oxygen therapy, Comorbidities

INTRODUCTION

In March 2020, the World Health Organisation (WHO) classified the corona virus disease 2019 (COVID-19) outbreak as a pandemic (El-Shitany et al.2021). On May 2023, following the 15th meeting of the Emergency Committee, the WHO declared that the Corona epidemic no longer constitutes a public health emergency of international concern (PHEIC)—WHO deemed COVID-19 as a long-standing and chronic health problem (WHO, 2023). The absence of a PHEIC linked with COVID-19 does not rule out the possibility that the illness is still causing considerable mortality and morbidity, especially given the widespread breakout of Omicron (House, 2023). In addition to these concerns, many patients recovering from acute COVID-19 described continuing symptoms that debilitate their daily activities. These patients are believed to have "long" or "chronic" COVID-19 disease or some form of post-acute COVID-19 syndrome (Nalbandian et al.2021).

Long COVID guides to persistent symptoms succeeding severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that doesn't relate to another diagnosis (Perego et al.2020). This includes the National Institute for Health and Care Excellence (NICE)

definitions of "ongoing symptomatic COVID-19" (OSC) (symptoms continuing 4-12 weeks) and "post-COVID-19 syndrome" (PCS) (symptoms lasting more than 12 weeks) (Sivan and Taylor, 2020), the US Centers for Disease Control and Prevention's group of "post-COVID-19 conditions" (Centers for Disease Control and Prevention (US). 2022), and the World Health Organization's "post COVID-19 condition" (Soriano et al.2022).

Acute infection with the SARS-CoV-2 causes various symptoms, including fever, generalized weakness, lower airway symptoms, and loss of smell that results from serious pulmonary damage and acute respiratory distress syndrome. It impacts numerous organs, potentially resulting in organ damage, particularly in elderly individuals and those with particular concurrent illnesses (Lake, 2020; Mehta et al.2020; Wu et al.2020). Many research and reviews have concentrated on affected organs other than the lung, such as brain, cardiac, vascular, GIT, renal, and cutaneous symptoms (Zhang et al.2020).

Apart from the acute clinical symptoms, the long-term effects of pneumonia have been informed in several research centered around persistent post-pneumonia declines in quality of life that do not return to baseline even after a year and the continued late psychological effects (Ahmed et al.2020; Denke et al. 2018; Glick et al.2021; Kapfhammer et al.2004). More than 50 symptoms of the PCS are reported in published reviews (Ahmad et al.2021; Lopez-Leon et al.2021; Michelen et al.2021; Moreno-Pérez et al.2021), many of which are incapacitating and have a significant detrimental effect on mental health and quality of life (Malik et al.2022). The most typical signs and symptoms include excessive exhaustion, shortness of breath, joint aches, brain fog, and mood fluctuations, which may continue after the acute manifestation of the illness (Saloner et al.2020). It has been shown that symptoms of the PCS might appear in clusters.

This study aimed to describe the long-COVID (> 3 months) clinical symptoms of COVID-19 survivors for a sample of Saudi persons who were infected with the SARS-CoV-2 between September 2020 and September 2021 and were tracked for one year following their initial clinical symptoms.

METHODS

Ethical approval

This study is a subset of a previous project that was authorized by the Saudi Ministry of Health (MOH) (Institutional Review Board of Research and Studies Department, Jeddah Health Affairs, Saudi Arabia). The IRB permission code is A00981.

Study persons

One hundred twelve persons who had previously contracted SARS-CoV-2 and recovered were included in the study. They were classified to 2 groups, mild (57 patients) and severe (55 patients), based on how severe their previous COVID-19 illness had been. According to the MOH categorization, patients were classified as mild when they merely required supportive treatment or monitoring and severe when they needed intervention in the intensive care unit (ICU). Patients with mild COVID-19 condition were sourced from Jeddah, Saudi Arabia's COVID-19 isolation facilities. Patients severely infected with SARS-CoV-2 have been obtained from several hospitals in Jeddah, Saudi Arabia, including the field hospital, King Fahd General Hospital, King Abdullah Hospital, and East Jeddah General Hospital. Patients were recruited between September 2020 and September 2021.

Collection of OSC patients symptoms, demographic, and baseline clinical data

In addition to the OSC symptoms, all participants' demographic and baseline clinical data (age, gender, nationality, weight, height, history of any comorbid conditions, COVID-19 vaccination doses, the number of COVID-19 infections, ICU admission, and oxygen (O2) therapy) were gathered via a form made on the SurveyMonkey website and sent via WhatsApp to each patient's phone number.

Collection of PCS symptoms

One-year post-recovery from COVID-19, the trained researchers phoned the patients with their mobile numbers and asked them several follow-up questions to fill out a short telephone questionnaire. They were questioned regarding the symptoms they had endured for more than three months up until the end of a year post-recovery. Interviews were conducted in Arabic or English patient's verbal ability. One of the researchers entered the information gathered into an Excel sheet to perform the statistics.

Inclusion criteria

Polymerase Chain Reaction (PCR)-positive patients for corona virus using either oropharyngeal or nasopharyngeal swabs participated in the research. All patients over the age of 18 were included in the study.

Exclusion criteria

Patients who reported no symptoms after three months to 1-year of COVID-19 recovery were excluded. Patients speaking languages other than Arabic or English were excluded. Those who did not answer the phone were also excluded.

Statistics

All demographic, baseline clinical data and OSC and PCS symptoms were subjected to descriptive statistics, and the results were presented as frequency (number and percentage) or mean ± SEM. The frequencies of the mild

and severe COVID-19 groups were compared using the Chi-squared test. For comparisons of means between the COVID-19 mild and severe groups, we adopted the unpaired student-t test. For comparisons of means of the same COVID-19 group OSC and PCS symptoms, we adopted the paired student-t test. The ANOVA test was used to compare the means of OSC and PCS symptoms in different blood grouping patients. Pearson correlation was also performed. GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego, California, USA, was used for statistics. The level of significance was set at $p<0.05$. Graphs were built using Microsoft EXCEL 2013. The odd ratios and 95% CI were analysed online via the Odds Ratio Calculator (gigacalculator.com).

RESULTS

Demographic and clinical data of the included COVID-19 participants

One hundred and twelve participants were included in the study. They were stratified into two strata based on how severe the COVID-19 infection is: mild (n = 57) and severe (n = 55) strata. Most participants were Saudi persons: mild cases (64.9%) and severe cases (56.4%). Male patients accounted for 75% of the study sample (90.9% of the severe COVID-19 stratum and 59.6% of the mild COVID-19 stratum; $p<0.001$, chi-square test). The mean age of the sample was 42.5 ± 1.4 years: mild cases (35.5 ± 1.9) and severe cases (49.8 ± 1.5) ($p<0.0001$, unpaired t-test). The mean BMI of the sample was 29.5 ± 0.9: mild cases (26.3 ± 0.8) and severe cases (31.8 ± 1.3) ($p<0.01$, unpaired t-test). Pre-existing comorbidities were present in 77 patients (68.8%), with diabetes being the most frequent (28.6%), followed by hypertension (19.6%), bronchial asthma (7.1%), and others (13.4%). In the mild stratum, 10.5% of the cases had diabetes, 8.8% had hypertension, and 1.8% had bronchial asthma. In the severe stratum, 47.3% of the cases had diabetes, 30.9% had hypertension, and 12.7% had bronchial asthma. The majority of the subjects had received SARS-CoV2 vaccinations (57.1% received one dose, and 38.4% received two doses). During the one-year follow-up period, most individuals (95.5%) had once been infected with SARS-CoV2.Only around one-fifth of the hospitalised individuals received treatment in the ICU (15.2%); they constituted about one-third of the severe cases (30.9%). The mean length of stay in the ICU was 4.3 ± 1.8 days. Of the study sample, 49.1% of the patients required oxygen therapy; they constituted 100% of the severe cases. The mean length of oxygen therapy was 12.02 ± 2.0 days (Table 1).

The frequency of patients with PCS symptoms

One year after the onset of COVID-19 infection, only 26.8% of the study sample was completely free of symptoms. On the other hand, 73.2% of the samples showed symptoms beyond 12 weeks after corona virus infection.

In 112 patients (sample size), the % of patients who showed PCS symptoms were as follows: 37.5% fatigue, 28.6% memory problems and arrhythmia, 25% muscle pain and hair loss, 21.4% sleep problems, 20.5% difficulty breathing, 17.9% headache and loss of smell, 15.2% loss of concentration and bone pain, 12.5% skin rash, 11.6% urine color change, 10.7% loss of taste, 6.3% constipation, 5.4% burning on urination, 4.5% mouth ulcer and hypertension, 3.6% cough and sexual health problem, 2.7% diarrhea, 1.8% sweating, dry eye, and lung fibrosis, 0.9% amenorrhea, anxiety, hyperglycemia, chest pain, kidney failure, enlarged heart, and brain stroke has (Figure. 1).

The frequencies of patients who had PCS symptoms in the mild and the severe COVID-19 groups

One year after the onset of COVID-19 infection, 21.8% of the severe COVID-19 group were completely free of symptoms compared to 31.6% of the mild COVID-19 group (12 severe (n=55) and 18 mild (n=57)). On the other hand, 78.2% of the severe COVID-19 group reported PCS symptoms compared to 68.4% of the mild group. No statistically significant differences were found concern in the frequency of patients complaining of different PCS symptoms between the severe and mild COVID-19 groups (chi-square test, $p<0.05$) (Figure. 2).

Concerning the severe COVID-19 group, the % of patients complaining PCS symptoms were as follows: fatigue (42.9 %), muscle pain (32.1%), arrhythmia (30.4%), memory problems (28.6%), sleep problems (26.8%), hair loss (25%), difficulty breathing and bone pain (21.4%), headache and loss of concentration (16.1%), skin rash and urine color change (14.3%), loss of smell (12.5%), loss of taste, constipation, and burning on urination (8.9%), hypertension and sexual health problem (7.1%), cough, and mouth ulcer (5.4%), sweating, dry eye, and lung fibrosis (3.6%), diarrhea, anxiety, kidney failure, enlarged heart, and brain stroke (1.8%) (Figure. 2).

Concerning the mild COVID-19 group, the % of patients complaining PCS symptoms were as follows: fatigue (31.6 %), memory problems (28.1%), arrhythmia (26.3%), hair loss (24.6%), loss of smell (22.8%), difficulty breathing and headache (19.3%), muscle pain (17.5%), sleep problems (15.8%), loss of concentration (14.0%), loss of taste (12.3%), skin rash (10.5%), bone pain and urine colour change (8.8%), constipation, diarrhea, and mouth ulcer (3.5%), burning on urination, hypertension, cough, chest pain, and amenorrhea (Figure. 2).

Table 1: Demographic data of the included COVID-19 participants

	Overall (n=112)	Mild Cases (n=57)	Severe Cases (n=55)	P-value
Age (year) (mean ± SEM)	42.5 ± 1.4	35.5 ± 1.9	49.8 ± 1.5	< 0.0001
Gender				
Male	84 (75%)	34 (59.6%)	50 (90.9%)	0.0002
Female	28 (25%)	23 (40.4%)	5 (9.1%)	
Nationality				
Saudi	68 (60.7%)	37 (64.9%)	31 (56.4%)	0.9882
None-Saudi	44 (39.3%)	20 (35.1%)	24 (43.6%)	
BMI (mean ± SEM)	29.5 ± 0.9	26.3 ± 0.8	31.8 ± 1.3	0.0011
Comorbidities				
Diabetes	32(28.6%)	6 (10.5%)	26 (47.3%)	0.0554
Hypertension	22 (19.6%)	5 (8.8%)	17 (30.9%)	
Bronchial asthma	8 (7.1%)	1 (1.8%)	7 (12.7%)	
Others	15 (13.4%)	8 (14.0%)	7 (12.7%)	
COVID-19 vaccination doses				
None	5 (4.5%)	2 (3.5%)	3 (5.4%)	0.8824
One	64 (57.1%)	33 (57.9%)	31 (56.4%)	
Two	43 (38.4%)	22 (38.6%)	21 (38.2%)	
The number of COVID-19 infections				
Once	107 (95.5%)	54 (94.7%)	53 (96.4%)	0.3726
Twice	4 (3.6%)	3 (5.3%)	1 (1.8%)	
Thrice	1 (0.9%)	0 (0%)	1 (1.8%)	
ICU admission				
Patients frequency	17 (15.2%)	-	17 (30.9%)	
ICU period length (day) (mean ± SEM)	4.3 ± 1.8	-	4.3 ± 1.8	
Oxygen (O2) therapy				
Patients frequency	55 (49.1%)	0 (0%)	55 (100%)	
O2 period length (day)		-	12.02 ± 2.0	

Data were presented as frequency (n) and percentage (%). Comparison between means was made by calculating unpaired student t-tests. Frequencies were compared by calculating the chi-square test. Data were considered significantly differ at $p<0.05$.

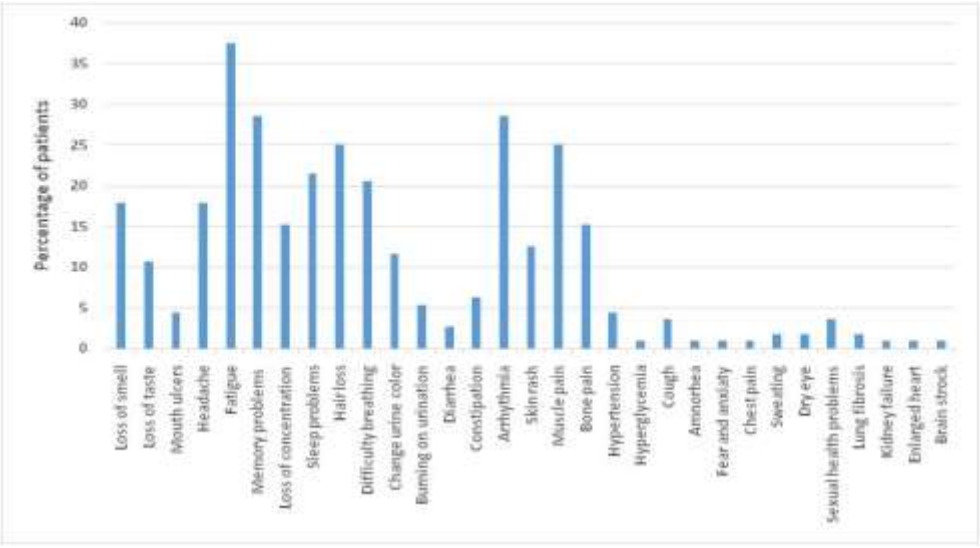

Figure 1: The frequency (%) of patients who showed post-COVID-19 syndrome (PCS) symptoms (symptoms beyond 12 weeks of coronavirus infection).

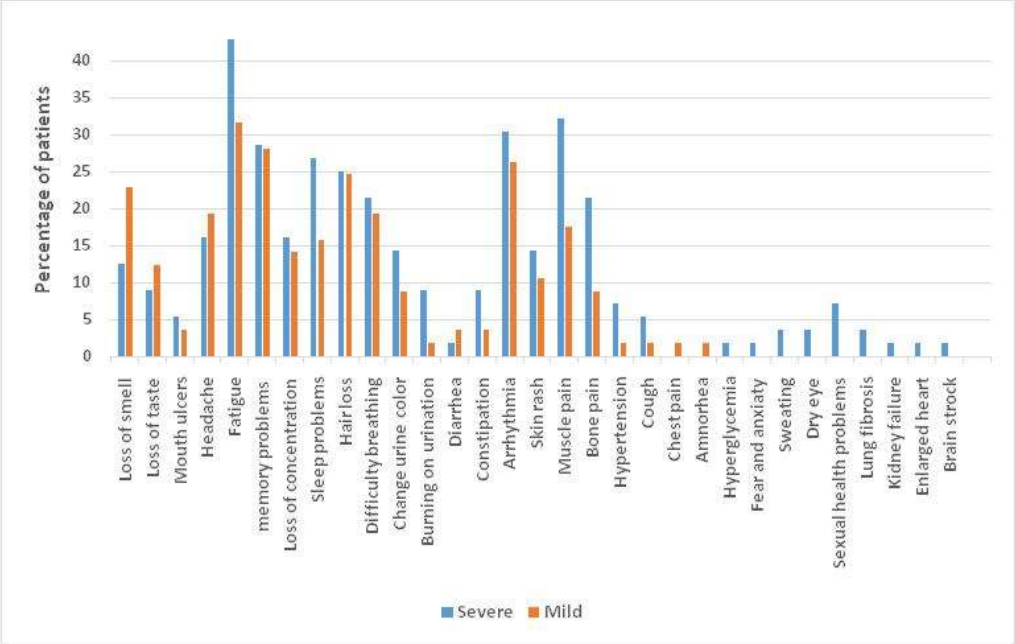

Figure 2: The frequencies of patients with post-COVID-19 syndrome (PCS) symptoms in the mild and severe COVID-19 groups.

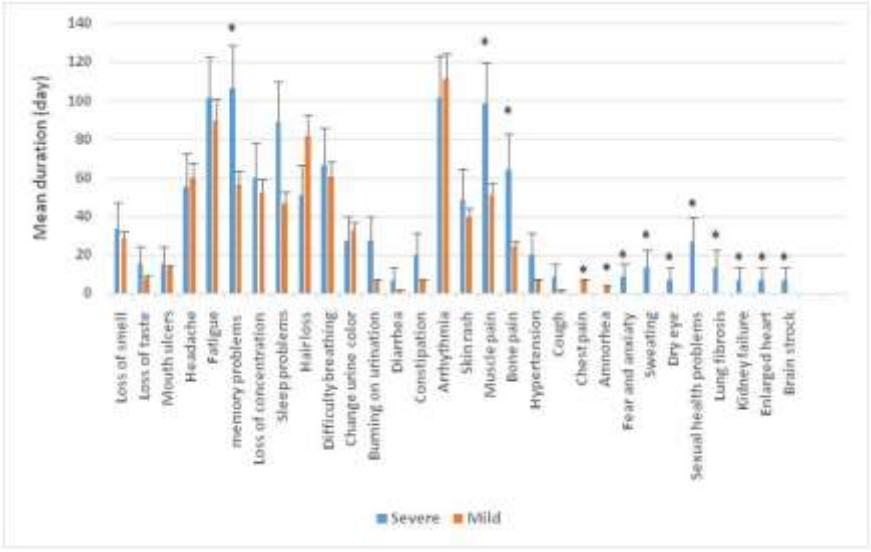

Figure 3: Mean duration (day) of post–COVID-19 (PCS) symptoms in the mild and severe groups. Patients were followed for one year post the onset of acute coronavirus infection. *significant difference from the corresponding group (unpaired t-test, $p<0.05$).

Comparison between the mean duration of PCS symptoms between the mild and the severe groups

Concerning the severe COVID-19 group, the symptoms that persisted for a mean duration of 3 months and longer were memory problems (106 days), arrhythmia and fatigue (101 days), and muscle pain (98 days) (Figure. 3).

Concerning the mild COVID-19 group, the symptoms that persisted for a mean duration of 3 months and longer were arrhythmia and fatigue (111days) (Figure. 3).

In the severe group, there were significantly longer mean durations of PCS symptoms concerning memory problems, muscle pain, bone pain (all unpaired t-test, $p<0.05$), anxiety, sweating, dry eyes, sexual health problems, lung fibrosis, kidney failure, enlarged heart, and brain stroke compared to the mild group (unpaired t-test, $p<0.0001$). While in the mild group, there were significantly longer mean durations of PCS symptoms concerning chest pain and amenorrhea compared to the severe group (unpaired t-test, $p<0.0001$) (Figure. 3).

Comparison between frequencies of the OSC and PCS symptoms in the mild and the severe groups

Figure 4 showed that in the mild COVID-19 group, the number of PCS symptoms was significantly lower than that of OSC symptoms (paired student t-test, $p<0.05$). In contrast, there were no changes in the frequency of OSC and PCS symptoms in the severe COVID-19 group (paired student t-test, $p=0.2652$).

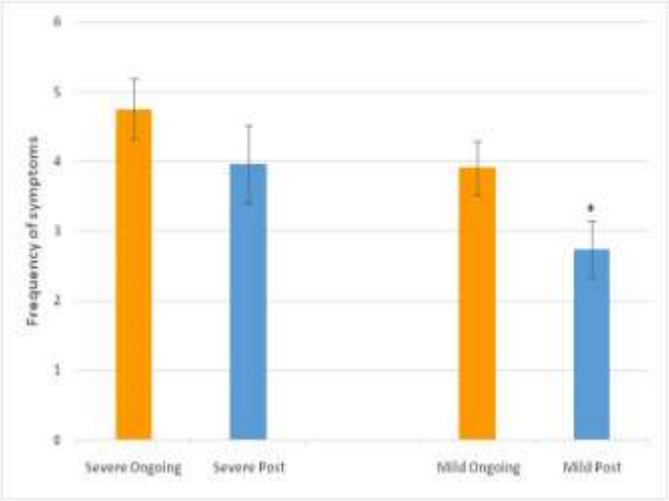

Figure 4: Comparison between frequencies of the ongoing (OSC) and post-COVID-12 (PCS) symptoms in the mild and the severe groups. Data were presented as mean ± SEM. *Significant difference between OSC and PCS symptoms of the same group (paired student t-test, $p<0.05$).

Comparison between frequencies of the OSC and PCS symptoms in male and female patients

Figure 5 demonstrated no changes in the number of COVID-19 symptoms between male and female patients concerning OCS symptoms (unpaired student t-test, $p=0.3972$). However, the frequency of PCS symptoms was significantly lower in males than in females (unpaired student t-test, $p<0.05$).

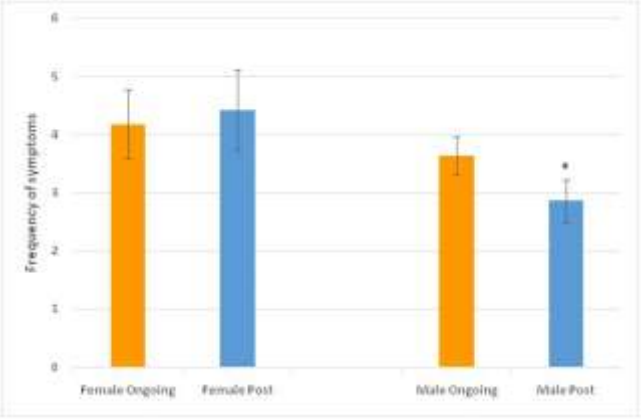

Figure 5: Comparison between frequencies of the ongoing (OSC) and post-COVID-12 (PCS) symptoms in male and female patients. Data were presented as mean ± SEM. *Significant difference between male and female PCS symptoms (unpaired student t test, $p< 0.05$).

Comparison between frequencies of the OSC and PCS symptoms in different blood grouping patients

Figure 6 demonstrated no significant difference in the frequency of OSC and PCS symptoms among the different blood groups (O, A, B, and AB) (ANOVA test, $p=0.9992$).

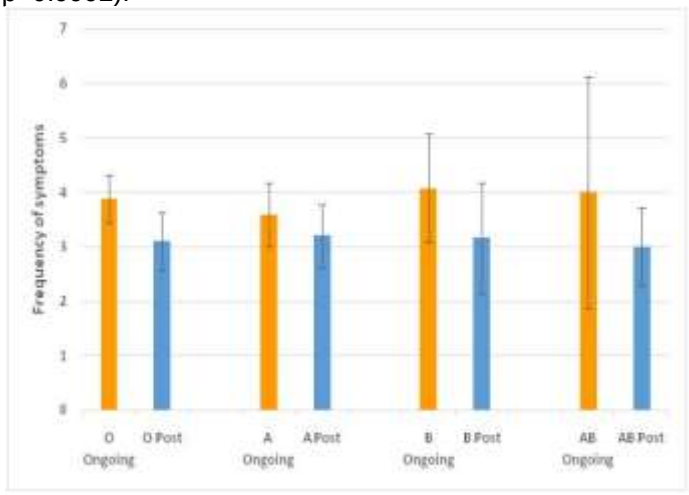

Figure 6: Comparison between frequencies of the OSC and PCS symptoms in different blood grouping patients. Data were presented as mean ± SEM.

Correlation between ages and number of PCS symptoms in the entire study population

Figure 7 demonstrated no significant correlation between ages (year) and the frequency of PCS symptoms among the entire study population (Pearson $r=0.07686$, $p=0.4164$).

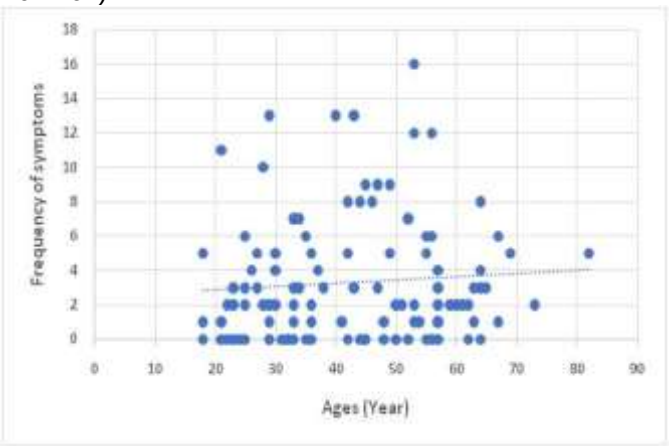

Figure 7: Correlation between ages and number of PCS symptoms in the entire study population. Pearson $r=0.07686$, $p=0.4164$.

Correlation between BMI and number of PCS symptoms in the entire study population

Figure 8 showed a significant positive relationship between BMI and the frequency of PCS symptoms among the entire study population (Pearson $r= 0.2001$, $p<0.05$).

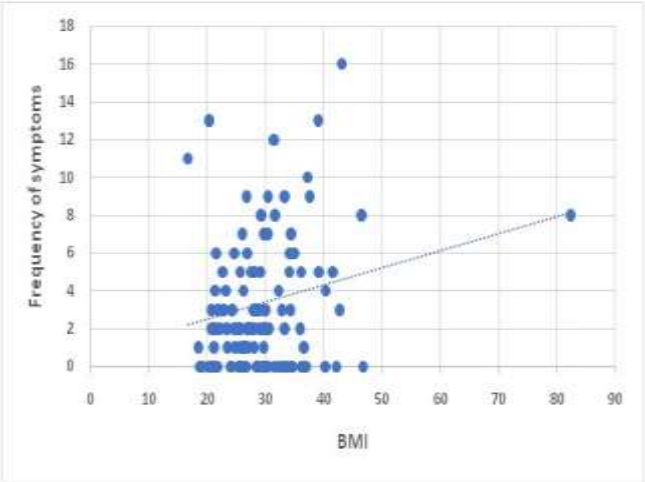

Figure 8: Correlation between BMI and number of PCS symptoms in the entire study population. Pearson r=0.2001, p<0.05. BMI: Body mass index.

Correlation between ICU period length and frequency of PCS symptoms in the severe group

Figure 9 demonstrated no significant correlation between ICU period length and the frequency of PCS symptoms among the severe COVID-19 group (Pearson r= 0.1598, p=0.2437).

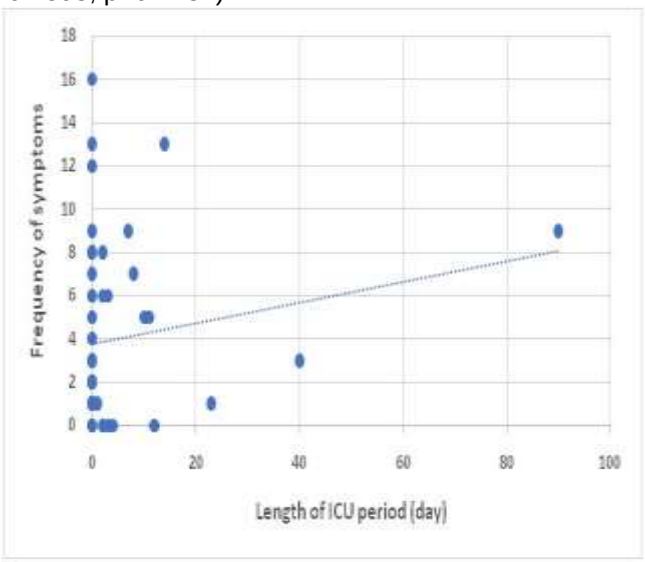

Figure 9: Correlation between ICU period length and the frequency of PCS symptoms in the severe group. Pearson r=0.1598, p=0.2437. ICU: Intensive care unit.

Correlation between O2 therapy period length and frequency of PCS symptoms in the severe group

Figure 10 demonstrated a significant positive correlation between O2 therapy period length and the frequency of PCS symptoms among the severe COVID-19 group (Pearson r= 0.3860, p<0.01).

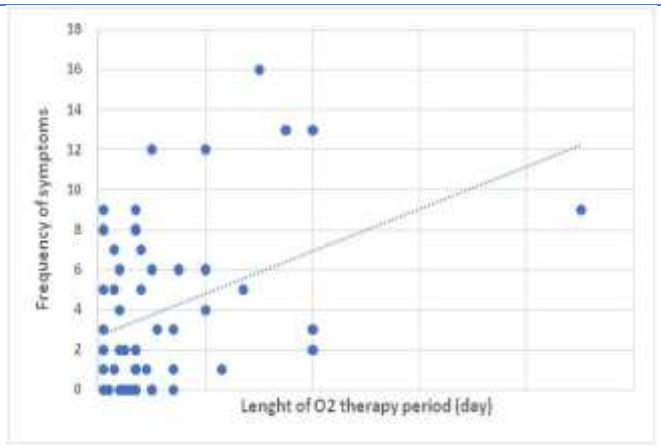

Figure 10: Correlation between O2 period length and the frequency of PCS symptoms in the severe group. Pearson r=0.3860, p=0.01. O2: Oxygen.

Predictors of PCS symptoms

The results showed that co morbidities increased the risk of PCS symptoms one year after the onset of corona virus infection (odd ratio, 2.29; 95% CI [1.005, 5.203]; p=0.024275). Diabetes increased the risk of PCS symptoms one year after the onset of corona virus infection (odd ratio, 2.35; 95% CI [0.922, 5.997]; p=0.036736). Also, hypertension increased the risk of PCS symptoms one year after the onset of corona virus infection (odd ratio, 5.4; 95% CI [1.648, 17.694]; p=0.002676). In contrast, bronchial asthma did not affect the risk of PCS symptoms one year after the onset of corona virus infection (odd ratio, 1.089744; 95% CI [0.244, 4.861]; p=0.455152).

The gender differences did not affect the risk of PCS symptoms one year after the onset of coronavirus infection (odd ratio, 0.667224; 95% CI [0.254, 1.751]; p=0.205553).

Also, the ABO blood groups did not affect the risk of PCS symptoms one year after the onset of coronavirus infection: for blood group O (odd ratio, 0.545455; 95% CI [0.226, 1.319]; p=0.089189), for blood group A, (odd ratio, 1.25; 95% CI [0.464, 3.368]; p=0.329525), for blood group B (odd ratio, 2.066667; 95% CI [0.647, +∞]; p=0.152037), and blood group AB (odd ratio, 1.941176; 95% CI [0.194, 19.461]; p=0.286387).

The severity of coronavirus infection did not affect the risk of PCS symptoms one year after the onset of coronavirus infection (odd ratio, 1.532143; 95% CI [0.696, 3.373]; p=0.144682).

Table 2: Comparison between Post-COVID-19 (PCS) symptoms gathered from several published studies

Serial	Reference	The country	Number of patients	Patients characteristics	Duration of follow up	PCS symptoms	% of patients free of PCS symptoms	Effect of gender, comorbidities, O2 therapy duration, disease severity, and ICU admission on PCS symptoms
1	**(Gautam et al. 2022)**	United Kingdom	200 patients	Severe COVID-19 infection	4–7 months from disease onset	Dyspnea (63.2%), severe tiredness (53.5%), limited mobility (37.5%), and pain (36.8%)	----------	----------
2	**(Seeble et al. 2022)**	Germany	96 patients	15 mild, 53 moderate, 24 severe, and 4 critical	5–12 months from disease onset	Impaired exercise ability (56.3%), tiredness (53.1%), breathlessness (37.5%), and difficulties with attention (39.6%), word finding (32.3%), and sleeping (26.0%)	At 12 months 22.9%	Females > male in neurocognitive symptoms
3	**(Aranda et al. 2022)**	Spain	150 patients	COVID-19 patients who had been hospitalized until 15th April 2020	12 months after hospital discharge	Breathlessness (62%), arthralgia (47%), paresthesia (42%), decline in memory (41%), and fatigue (40%)	At 12 months 20%	Female sex and COPD increase the chance of persistent dyspnea
4	**(Fernández-De-las-peñas et al. 2022)**	Spain	614 patients	201 patients infected with the Wuhan variant (Wv), 211 with the Alpha variant (Av) and 202 with Delta variant (Dv)	6 months after hospitalization	Fatigue (68% Wv, 72% Av, and 76% Dv), breathlessness (29% Wv, 14% Av, and 13% Dv); hair loss (29% Wv, 16% Av, and 36% Dv); memory loss (19% Wv, 18% Av, and 18% Dv)	----------	----------
5	**(Meije et al. 2021)**	Spain	302 patients	Patients who were discharged after hospitalization for COVID-19	7 months after discharge	Fatigue (26.5%), neurological illnesses (17.7%), anxiety (49.3%), breathing difficulties, loss of taste, and loss of smell (10% for all)	50%	----------
6	**(Fang et al. 2022)**	China	1233 patients	Older COVID-19 patients	12 months (Mar 1, 2021 and Mar 20, 2021)	Asthenia (32.4%), sweating (20.0%), breathlessness (15.8%), psychological distress (11.4%), muscle pain (9.0%), and cough (5.8%)	----------	Severity was correlated to risk of PCS symptoms
7	**(Wanga et al. 2021)**	USA	698 patients	Positive SARS-CoV-2 test result (698), and negative test result (2,437)	Symptoms lasted more than 4 weeks after COVID-19 test	Asthenia (22.5%), altered scent and dysgeusia (17.3%), breathlessness (15.5%), cough (14.5%), and headache (13.8%)	33%	----------
8	**(Kamal et al. 2021)**	Egypt	287 patients	Survivors from COVID-19	----------	Fatigue (72.8%), anxiety (38%), joints pain (31.4%), headache (28.9%), chest pain (28.9%), dementia (28.6%), depression (28.6%), and dyspnea (28.2)	10.8% of the patients	The severity of PCS symptoms depends on OSC symptoms severity

9	**(Samannodi et al. 2022)**	Saudi Arabia	7520 patients	Recovered from COVID-19	6 weeks–6 months (38.8%), and 4–6 weeks (35.5%)	Respiratory symptoms (67.0%), nervous system symptoms (28.6%), psychological problems (25.9%), and skin problems (17.5%)	64%	Age, gender, and comorbidities were linked to long-term PCS symptoms
10	**(Tleyjeh et al. 2021)**	Saudi Arabia	222 patients	Survivors from COVID-19	6 weeks–6 months post hospital discharge	Dyspnoea (40.1%), cough (27.5%) and asthenia (29.7%)	43.7%	Feminine gender, hypertension, and hospitalization length were linked to long-term PCS symptoms
11	**(Garrigues et al. 2020)**	France	120 patients	Recovered from COVID-19	> 100 days post hospital discharge	Fatigue (55%), breathlessness (42%), loss of memory (34%), concentration (28%) and sleep problems (30.8%)	----------	ICU admission didn't affect PCS symptoms

DISCUSSION

As far as we know this study is the first in Saudi Arabia that follows COVID-19 patients for a year following recovery to assess the PCS symptoms and compare them with the OSC symptoms of the acute phase of infection previously collected by our research group. It is one of the longest PCS follow-ups yet published. The study tracked the same patients from when they were infected until one year later. 73.2% of the samples had symptoms over 12 weeks after SARS-CoV-2 infection. Fatigue, memory issues, arrhythmia, muscle pain, hair loss, sleep problems, difficulty breathing, headache, loss of smell, loss of concentration, and bone pain were the main symptoms that persisted with the study participants three months to a year after COVID-19 recovery. There was no significant difference in the frequency of patients reporting PCS symptoms between severe and mild COVID-19 groups. Concerning the severe COVID-19 group, the symptoms that persisted for a mean duration of 3 months and longer were memory problems, arrhythmia, fatigue, and muscle pain compared to arrhythmia and fatigue in the mild COVID-19 group. Concerning most PCS symptoms (memory problems, muscle pain, and bone pain), the mean duration (day) was significantly rise in the severe group compared to the mild group. The number of PCS symptoms in the mild COVID-19 group was significantly lower than that of OSC symptoms. Besides, the number of PCS symptoms was significantly lower in males than in females. There was a significant positive correlation between O2 therapy period length (day) and BMI and the frequency of PCS symptoms among the entire study sample. Only the presence of comorbidities (especially diabetes and hypertension) increased could predict PCS symptoms one year after the onset of COVID-19.

Evidence suggests that 60% of COVID-19 survivors will develop post-infection symptoms at some point within the first year (Amdalet al.2021; Fernández-de-las-Peñaset al.2021). The long-term outcomes of COVID-19 survivors have been documented in numerous recent studies conducted in the United Kingdom (Gautam et al.2022), Germany (Seeble et al.2022), Spain (Aranda et al.2022; Fernández-De-las-peñas et al.2022; Meijeet al.2021), China (Fanget al.2022), USA (Wanga et al.2021), Egypt (Kamal et al.2021), Saudi Arabia (Samannodi et al.2022; Tleyjeh et al.2021), and France (Garrigues et al.2020) (Table 2). Mainly, these studies investigated PCS at earlier time points after the acute disease symptom compared to our study.

In this part, we will compare our findings to those of studies that followed COVID-19 survivors for at least three months to a year to gather PCS symptoms. Our finding (fatigue (37.5%), memory problems and arrhythmia (28.6%), muscle pain and hair loss (25%), sleep problems (21.4%), difficulty breathing (20.5%), headache and loss of smell (17.9%), loss of concentration and bone pain (15.2%), skin rash (12.5%), urine color change (11.6%), loss of taste (10.7%), constipation (6.3%), burning on urination (5.4%), mouth ulcer and hypertension (4.5%), cough and sexual health problem (3.6%), diarrhea (2.7%), sweeting, dry eye, and lung fibrosis (1.8%), amenorrhea, anxiety, hyperglycemia, chest pain, kidney failure, enlarged heart, and brain stroke (0.9%)) are more or less similar to the PCS finding of a German study carried by (Seebleet al.2022) (tiredness (53.1%), breathlessness (37.5%), and difficulties with attention (39.6%), word finding (32.3%), and sleeping (26.0%)), a Spanish study carried by (Arandaet al.2022) (breathlessness (62%), arthralgia (47%), paresthesia (42%), decline in memory (41%), and fatigue (40%)), a Spanish study carried by (Meijeet al.2021) (fatigue (26.5%), neurological illnesses (17.7%), anxiety (49.3%), breathing difficulties, loss of taste, and loss of smell (10% for all)),a Chinese study carried by (Fanget al.2022) (fatigue (32.4%), sweating (20.0%), breathlessness (15.8%), psychological distress (11.4%), muscle pain (9.0%), and cough (5.8%)), and a French study carried by (Garrigueset al.2020) (fatigue (55%), breathlessness (42%), loss of memory (34%), concentration (28%) and sleep problems (30.8%)).

Our findings revealed no statistically significant difference between the severe and mild groups in the number of patients reporting different PCS symptoms. Also, our results revealed that the risk of PCS symptoms one year after the onset of COVID-19 was unaffected by the severity of COVID-19 infection (odd ratio, 1.532143; 95% CI [0.696, 3.373]; p=0.144682). Only our results indicated that the severity of OSC symptoms may increase the mean duration of PCS symptoms. Besides, our results showed that, only in the mild COVID-19 group, the number of PCS symptoms was significantly lower than that of OSC symptoms. Conversely, the results of (Fanget al.2022) showed that COVID-19 severity during hospitalization (odd ratio, 1.46; 95% CI [1.15, 1.84]; p=0.002) was independently associated with the risk of PCS symptoms. Also, (Kamalet al.2021) showed that the severity of SARS-CoV-2 infectionwas connected to the severity of PCS symptoms. The disparity in findings between our study and (Kamalet al.2021)'s study is due to the difference in the timing of PCS symptoms collection, as the exact timing was not mentioned in (Kamalet al.2021) 's study. Likewise, (Fanget al.2022)'s study varied from our study in that it included elderly patients (above 60 years old), whereas the mean age in our sample was 42.5 ± 1.4.

Our results also reported that hair loss was noted by 25% of the patients, which is similar to (Garrigueset al.2020) findings (hair loss reported by 20% of the patients) and (Turkmenet al.2020) findings (telogen effluvium was reported by 27.9% of the patients). Hair loss might be due to telogen effluvium caused by a viral illness and/or physical and psychological stress from hospital admission and getting infected with SARS-CoV-2 (Turkmenet al.2020). Furthermore, the current findings revealed that memory issues, arrhythmia, and fatigue were the most often reported persisting symptoms after a

mean of more than 100 days. These findings were similar to (Garrigues et al.2020), which revealed that the most often reported persisting symptoms after a mean of 111 days were fatigue, breathing difficulties, loss of memory, and concentration and sleep difficulties. As a result, the care of mental health problems should be improved via a multidisciplinary strategy mixed with rehabilitation for a long time (Kamal et al.2021).

Similarly, our results PCS symptoms included more serious illnesses such as stroke, renal failure, pulmonary fibrosis (Kamal et al.2021), arrhythmia and myocardial hypertrophy. Data acquired from COVID-19 patients with heart affected indicate permanent structural and functional alteration, including chronic myocardial fibrosis and oedema. At the same time, the left ventricle is enlarged, with a lower ejection fraction and new-onset arrhythmias (Siripanthong et al.2022).

Against the findings of (Díaz-Salazaret al.2022)our findings revealed no significant variation in the prevalence of PCS symptoms between the various blood types (O, A, B, and AB) patients. Moreover, our results showed that the ABO blood groups did not affect the risk of PCS symptoms one year after the onset of COVID-19: for blood group O (odd ratio=0.545455; [95% CI: 0.226-1.319]; p=0.089189). (Díaz-Salazar et al.2022) observed that group O had a higher number of PCS symptoms compared to the non-O group. They also documented that individuals in the O group had a higher risk of PCS symptoms than non-O patients (adjusted odd ratio=6.25; [95% CI: 1.6-23]; p=0.007).

Our results presented that the number of PCS symptoms was significantly lower in men than in women. Gender differences have been connected to PCS symptoms, as previously stated (Peghin et al.2021). Consistent with prior research, the number of PCS symptoms was considerably lower in men than in womenin our sample (Pazukhina et al. 2022; Peghin et al.2021; Samannodi et al.2022).Furthermore, the number of acute COVID-19 symptoms is a risk factor for acquiring PCS disorders (Samannodiet al.2022). Our study showed similar findings in the mild COVID-19 group, as the number of PCS symptoms was significantly lower than that of OSC symptoms. In addition, there were no changes in the number of OSC and PCS symptoms in the severe COVID-19 group. There has been little research on the relationship between the number of acute symptoms of SARS-CoV-2 infection and PCS symptoms(Samannodi et al.2022).

Moreover, (Samannodi et al.2022) data showed that the length of study in the ICU is essential in developing PCS conditions, as previously reported (Halpin et al.2021; Moreno-Pérez et al.2021). Conversely, our results showed no significant correlation between ICU period length and the frequency of PCS symptoms among the severe COVID-19 group.

There was a significant positive correlation between O2 therapy period length (day) and BMI and the frequency of PCS symptoms among the entire study sample. In agree with our finding (Vimercati et al. 2021) reported that overweight patients (odd ratio=1.6; [95% CI: 1.05-2.56]; *p*=A0.029) had a higher potential for developing 35-day PCS symptoms. In addition, BMI was linked to an increased probability of acquiring PCS symptoms (relative risk=1.031; [95% CI: 1.016-1.047 for 1 kg/m^2]) (Debskiid et al.2022). Only the presence of co morbidities (especially diabetes and hypertension) increased could predict PCS symptoms one year after the onset of COVID-19. These results are consistent with those reported that participants with one or more comorbidities may have a higher chance to develop PCS symptoms (Samannodi et al.2022).Furthermore, these findings are consistent with previously established risk variables in multicentre observational research (Fernández-De-las-peñas et al.2022). Furthermore, many investigations revealed comorbidities such as hypertension, diabetes, and asthma (Asadi-Pooya et al. 2021; Pazukhina et al.2022; Thompson et al.2022). Female genders (Debskiid et al. 2022; Subramanian et al.2022), being obese, and having a wide variety of comorbidities were predictors for PCS symptoms (Subramanian et al.2022).

Study weaknesses

The limited number of patients (112) included in our study. This could be explained as this sample size was calculated as optimum for our previously published manuscript (Alwafi et al.2022) (158 COVID-19 patients). The same patients were followed for one year to collect their PCS symptoms (we couldn't communicate with 46 patients). The study also lacks the non-infected comparator group. This could result in an overestimation of PCS symptoms.

Study strength

We already have data on the patient's OSC symptoms during the acute COVID-19. The study followed the COVID-19 patients for a year following recovery to assess the PCS symptoms and compare them with the OSC symptoms of the acute phase of infection. It is one of the longest PCS follow-ups yet published. The study tracked the same patients from when they were infected until one year later.

CONCLUSION

In summary, 73.2% of our Saudi samples had symptoms more than 3 months following their acute SARS-CoV-2 infection. Fatigue, memory issues, arrhythmia, muscle pain, hair loss, sleep problems, difficulty breathing, headache, loss of smell, loss of concentration, and bone pain were the main symptoms that persisted with the study participants three months to a year after COVID-19 recovery. More serious illnesses, such as stroke, renal failure, pulmonary fibrosis, arrhythmia and myocardial hypertrophy, were also reported. The most often reported persisting symptoms

after more than 100 days were memory problems, arrhythmia, and fatigue. The severity of the acute COVID-19 condition increased the duration of most PCS symptoms, including memory problems, muscle pain, and bone pain. Moreover, our study found that female gender, co morbidities, especially diabetes and hypertension, long-term O2 therapy during acute COVID-19, and obesity may play a role in predicting PCS conditions.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

All authors contributed equally to the conception, design, data acquisition, analysis, and interpretation. They all also made article drafting and revision; agreed to submit to the current journal; gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

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