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Original article

Post-acute COVID-19 condition in Saudi Arabia: A national representative study



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ABSTRACT

Background: Many survivors of COVID-19 have developed symptoms and diseases similar to those observed after severe acute respiratory syndrome (SARS). Therefore, this study aimed to characterize the symptoms that appear after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been eradicated and to determine their relationship with COVID-19 severity.

Methods: This multicenter, retrospective cross-sectional study was conducted in all eligible confirmed cases of SARS-CoV-2 infection from Saudi Arabia. Study participants were randomly selected using computerized random sampling from a population of 314,821 patients. Descriptive statistics were used to describe baseline demographic data and clinical characteristics. Categorical variables were presented as counts and percentages, while continuous variables were presented as means and standard deviations.

Results: Approximately 70% of patients were found to have five or fewer symptoms simultaneously. Late symptoms (in the ongoing symptomatic COVID-19) occurred in 225 (22-5%) patients with the most common late symptoms being loss of smell, loss of taste, fatigue, shortness of breath, and cough (52-4%, 31-1%, 11-5%, 10-2%, and 8-9% of patients with late symptoms, respectively). We also found that the presence of acute symptoms of COVID-19 and admission to the hospital were significant independent predictors of the post-COVID-19 condition.

Conclusion: Saudi patients with COVID-19 develop a wide range of symptoms, similar to those observed and reported in other countries. The loss of smell, the loss of taste, shortness of breath, and fatigue were the

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main persistent symptoms. Regular follow-up of COVID-19 survivors is highly recommended to minimize the burden of the post-acute COVID-19 condition and improve the quality of life of patients. © 2022 The Author(s). Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health

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Introduction

The novel coronavirus disease 2019 (COVID-19) is a serious respiratory disease that results from infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been declared as a global pandemic by the World Health Organization (WHO) [1-3]. At the beginning of 2022, approximately 304,513,000 individuals were infected with SARS-CoV-2, and 5483,562 lives have been lost worldwide(1). The disease affects the physical and mental health of individuals who become infected. Economic and social difficulties markedly increase every day due to the distress and fear faced by combating this rampant virus [4].

Saudi Arabia is one of the countries that battled the pandemic in its early phases [5]. The first case of COVID-19 was discovered in March 2020, and once the first wave of COVID-19 had ended, 557,082 individuals had been infected with SARS-CoV-2 and 8878 deaths were reported at the end of 2021(1). The second COVID-19 wave is currently in its early stages in Saudi Arabia, while the fourth wave has already started in some countries. This rapid progression has been driven by emerging variants of the virus, which have required new preventive and corrective measures to combat the emergence of each variant [6]. According to the WHO, COVID-19 has many variants; the variants of concern (VOCs) are Alpha, Beta, Gamma, Delta, and Omicron, and the variants of interest (VOIs) are Lamda and Mu [7]. ⁷ VOCs may be associated with any of the following: increased transmissibility; increased virulence; detrimental changes in the epidemiology or presentation of COVID-19; and decreased effectiveness of preventive measures, diagnostics, vaccines, or therapeutics. VOIs are also associated with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, and immune, diagnostic or therapeutic escape [7.8].

Patients present with symptoms such as fever, dry cough, and fatigue, which are moderate in around 80% of cases, but severe cases of the disease might proceed to respiratory distress, respiratory failure, or multi-organ failure (MOF), necessitating admission to an intensive care unit (ICU) [9,10]. The long-term effects of acquiring SARS-CoV-2 remain unclear given the novelty of the outbreak. Most individuals infected with COVID-19 recover completely; however, a small percentage of patients infected with SARS-CoV-2 experience recurring difficulties years later, and exhibit symptoms associated with the so-called "post-COVID-19 syndrome" or "post-COVID-19 condition" [11].

The post-acute COVID-19 condition is characterized by a wide range of new, returning, or chronic health problems that present 4 weeks or more after being infected with SARS-COV-2 [12]. The post-acute COVID-19 condition consists of subacute/ongoing COVID-19 and chronic or post-COVID-19 syndrome. Subacute/ongoing COVID-19 includes symptoms that appear 4–12 weeks after the onset of acute COVID-19, while chronic or post-COVID-19 syndrome includes symptoms that persist or appear beyond 12 weeks after the onset of acute COVID-19 and are not attributable to other diagnoses [13,14]. Individuals often report experiencing different combinations of the following symptoms: rash, fever, diarrhea, sleep disorders, dizziness, cough, chest or stomach pain, tiredness or fatigue, difficulty

breathing, difficulty thinking or concentrating, mood changes, changes in menstrual period cycles, and changes in smell or taste [15]. Furthermore, post-acute COVID-19 conditions can be associated with MOF, including cardiovascular, pulmonary, renal, and neuropsychiatric organ systems [16]. Although extremely rare, some patients, especially children, develop multisystem inflammatory syndrome (MIS) during or shortly after contracting COVID-19 [17]. Various areas of the body can become inflamed due to MIS, which may eventually lead to MOF. Therefore, this study aimed to investigate and characterize the post-acute COVID-19 condition and its relationship with the severity of the disease.

Methods

Study design

This national cross-sectional study was conducted over a sixmonth period from March 2020 to August 2020, as authors collaborated from the Saudi Ministry of Health and Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia. The study participants were randomly selected from a population of 314,821 patients registered at the Ministry of Health Database. All participants were informed about their enrollment in the study and oral consents were obtained through phone interviews. During the collection, handling, and storage of data, the ethical standards of the Declaration of Helsinki were followed, and all precautions were taken to ensure participant confidentiality. The study protocol was approved by the Institutional Review Board (IRB) of Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia (No: 21–0172).

Inclusion and exclusion criteria

The study included all patients diagnosed with COVID-19 who were at least 18 years old. We excluded patients who died during acute illness and patients who refused to consent for participation and provide all requested information.

Sample size calculation

Raosoft * software was used to determine the sample size calculation; to obtain a 95% confidence interval, a response distribution of 50%, and a 5% margin of error, the target sample size was estimated to be 371 participants. Adjusting the calculation for the projected 10% attrition, the final sample size was estimated to be 415 participants.

Data collection

Two public health specialists and two family physicians evaluated the questionnaire before and after it was translated into Arabic. Eight health practitioners (trained by the experts in the field), interviewed all participants and recorded all information using a designated data collection form. Oral consents and interviews were obtained by phone through the "937" Ministry of Health call center.

The demographic dat	a of the entire study	population (n	= 1000 patients).
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Characteristic	n	%
Age (range 21–81), years	36.9	+11.9
< 30	368	36.8
31-40	311	31.1
41-50	180	18.0
51-60	99	9.9
> 60	42	4.2
Sex		
Female	395	39.5
Male	605	60.5
Occupation		
Employed	565	56.5
Not working	292	29.2
Retired	67	6.7
Healthcare employed	52	5.2
Student	24	2.4
Smoking		
Never	719	71.9
Current	201	20.1
Past	79	7.9

An independent reviewer resolved any discrepancies between the collected data and medical records. The questionnaire included sociodemographic data such as age; sex and occupation; questions about the medical history related to COVID-19, including a history of medical illness, hospital or ICU admission; history of smoking; questions about the ongoing symptomatic COVID-19; and questions about the post-COVID-19 condition. Acute SARS-CoV-2 infection was defined as signs and symptoms of COVID-19 lasting for up to 4 weeks. Ongoing symptomatic COVID-19 was defined as signs and symptoms of COVID-19 condition was defined as signs and symptoms that developed during or after an infection consistent with COVID-19, continuing for more than 12 weeks, and not explained by an alternative diagnosis. ¹⁵.

Statistical analysis

Descriptive statistics were used to describe the baseline demographic data and clinical characteristics. Categorical variables were presented as counts and percentages, whereas continuous variables were presented as means and standard deviations (SDs). The t-test was used for continuous variables, and the chi-squared test was used for categorical variables. Simple and multiple logistic regression analyses were performed to identify factors associated with the appearance of COVID-19 symptoms 4 weeks after the diagnosis; odds ratios (OR), adjusted odds ratios (aORs) and 95% confidence intervals (CI) were calculated. A p-value of less than 0.05 was considered significant. Statistical analyses were performed using the Statistical Package of Social Science (SPSS vers. 24; IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics of the study population

A total of 1000 participants with confirmed SARS-CoV-2 infection were included in the study, with a mean age of 36.9 ± 11.9 years. Most of the participants (85.9%) were < 50 years of age. The male to female ratio was 1-5:1. More than half of the participants were workers (56.5%), while 29.2% were unemployed, 6.7% were retired, and 2.4% were students. Regarding smoking status, 20.1% currently smoked, and 7.9% formally smoked, and 71.9% had never smoked (Table 1). Comorbid conditions were prevalent in 247 (24.7%) participants (Fig. 1). In terms of associated comorbidities, 24.7% of the participants had comorbidities; of these, 16.3% had one comorbidity and 8.2% had two or more comorbidities. The most prevalent comorbidity was diabetes (9.7%), followed by hypertension (7.9%), asthma (5.7%), hyperparathyroidism (2.3%), and allergic disorders (1.8%). Fig. 1 summarizes the recorded comorbidities.

Acute COVID-19 symptoms

Of the participants included in the study, 948 (94.8%) experienced acute COVID-19 symptoms. Of these, 74.7% had fewer than six symptoms. The most common symptoms were fever (68.5%), loss of smell (58%), loss of taste (51.7%), headache (44.7%), and fatigue (40.1%). Table 2 shows the distribution of symptoms of acute SARS-CoV-2 infection.



Fig. 1. Distribution of comorbid conditions among the entire study cohort (N = 1000) Any comorbidity= 247 (24.7%), 1 morbidity= 163 (16.3%), 2 or more comorbidities= 82 (8.2%).

The	distribution	of acut	e SARS-CoV-	2 infection	symptoms	(N = 1000.
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	COVID-19 symptoms within 4 weeks of the			
	diagnosis			
	Counts	% of Total	% of Symptomatic	
At least one symptom	948	94-8		
Number of symptoms:				
1 to <6	708	70.8	74.7	
>6	240	24	25.3	
Fever	649	64.9	68.5	
Loss of smell	550	55	58.0	
Loss of taste	490	49	51.7	
Headache	424	42.4	44.7	
Fatigue	380	38	40.1	
Joint pain	256	25.6	27.0	
Shortness of breath	226	22.6	23.8	
Cough	217	21.7	22.9	
Myalgia	173	17.3	18.2	
Sore throat	110	11	11.6	
Diarrhea	80	8	8.4	
Loss of appetite	55	5.5	5.8	
Dizziness	51	5.1	5.4	
Sneezing	49	4.9	5.2	
Nausea	43	4.3	4.5	
Chest pain	36	3.6	3.8	
Runny nose	35	3.5	3.7	
Vomiting	33	3.3	3.5	
Abdominal pain	22	2.2	2.3	
Low mood	17	1.7	1.8	
Change of taste	15	1.5	1.6	
Sweating	15	1.5	1.6	
Back pain	12	1.2	1.3	
Hypersonnia	11	1.1	1.2	
Insomnia	10	1	1.1	
Nasal congestion	9	0.9	0.9	
Red-eye	/	0.7	0.7	
Sputum	7	0.7	0.7	
Weight loss	6	0.6	0.6	
Vertigo	6	0.6	0.6	
Hair loss	6	0.6	0.6	
Numbness	4	0.4	0.4	
Orticaria	3	0.3	0.3	
Allxiely	3	0.3	0.3	
Skin rach	∠ 2	0.2	0.2	
JRIII [d5]] Enjetavje	2	0.2	0.2	
Otalgia	2 2	0.2	0.2	
High blood pressure	2	0.2	0.2	

Post-acute COVID-19 condition

Ongoing COVID-19 symptoms were experienced by 22.5% of the participants with a median (IQR) of 16.3 duration (10.1-32.1) days, including loss of smell (52.4%), loss of taste (31.1%), fatigue (11.5%), shortness of breath (10.2%), cough (8.9%), and joint pain (8.4%). Of 92 (9.2%) participants with the post-COVID-19 condition, the following symptoms were reported: loss of smell (38%), loss of taste (16.3%), fatigue (7.6%), shortness of breath (5.4%), fever (5.4%), joint pain (4.3%), and headache (3.3%) (Table 3). The most commonly used treatments for relieving symptoms were analgesics or antipyretics (7.5%), vitamins (6.2%), herbal preparations (2.6%), zinc (2.3%), cough syrup/expectorants (2.3%), and strong odors (1.6%). The most aggravating factors were changes in physical activity (2.6%), smoking (1.0%), and cough (0.6%). Similar symptoms were observed in family members in 19.1% of cases. In 31% of participants, the symptoms influenced social and work-related activities. Hospital admission for COVID-19 was reported in 6.4% of participants with a mean length of hospital stay of 8.0 ± 7.9 days, while admission to ICU was reported

in 0.9% of participants. Only four deaths (0.4%) occurred subsequent to the acute SARS-CoV-2 infection (Table 4).

Predictors of the post-COVID-19 condition

Univariate logistic regression analysis showed that many factors were associated with an increased risk of the post-COVID-19 condition, including history of acute COVID-19 condition (OR=6.8, 95% CI 2.5–18.8; p < 0.0001), and hospital admission (OR=2.33, 95% CI 1.4–4.0; p = 0.001). Multivariate logistic regression analysis demonstrated that the presence of acute symptoms of COVID-19 and hospital admission were significant independent predictors of post-COVID-19 condition (aOR= 15.0, 95% CI 2.1–109-4; p = 0.008 and aOR= 2.3, 95% CI 1.3–3.9), p = 0.002), respectively (Table 5).

Discussion

Persistent post-COVID-19 symptoms have a negative impact on health-related quality of life and exert increased burden on health systems [18,19]. The extent of those symptoms, their predictors, and possible alleviating and aggravating factors were not studied and reported previously for the population of Saudi Arabia.

This study identified that late symptoms (beyond 4 weeks of diagnosis) occurred in 22.5% of participants. Similar results were reported in a population representative study done in the UK, where 21% of the included cases had late symptoms lasting beyond 5 weeks of infection [20]. In contrast, Sudre et al. reported a lower percentage of 13% with symptoms lasting 28 days after symptom onset in another cohort in the UK [21]. In the Netherlands and Belgium, Goertz et al. reported that over 99% of infected cases did not fully recover within 12 weeks after symptom onset. The huge number of persistent late symptoms could be explained by the fact that the sample was from a Facebook group of patients with persistent complaints [22]. Nehme et al., reported 33% of cases with symptoms 30–45 days after diagnosis in hospital outpatient settings in Switzerland [23]. A large-scale observational study involving 38 participants in Michigan, USA also showed similar results where 32.6% of their participants experienced chronic symptoms [24].

The most common late symptoms in our population were loss of smell, loss of taste, fatigue, shortness of breath, and cough. Fatigue and shortness of breath were also commonly reported in different studies [14,22–24].

Only 5.5% of participants continued to have symptoms more than 12 weeks after diagnosis in this study, compared with 10% and 2% in different studies in the UK [20,21]. The following symptoms were reported: loss of smell, loss of taste, fatigue, shortness of breath, and fever (32.6%, 15.8%, 7.4%, 5.3% and 5.3% of post-COVID-19 symptomatic patients respectively). Loss of smell continued to be the top persistent complaint in our population. This should direct the focus of public education toward the course of olfactory inflammation and set recovery expectations [15].

Hospital admission, female sex and the presence of early symptoms were found to be top predictors for the occurrence of late symptoms in our population. Similarly, a Chinese post-acute COVID-19 investigation identified sex-based differences, with females more likely to experience fatigue and anxiety/depression at 6 months of follow-up [25].

A concerning percentage of those who had the late symptoms beyond 4 weeks (31%), reported that the symptoms affected their social and work-related activities. The majority of patients who had late symptoms (beyond 4 weeks) reported no alleviating (72.7%) or aggravating factors (94.8%).

Our study had limitations due to the nature of a retrospective, cross-sectional design where only a sample of participants was

The distribution of ongoing symptomatic COVID-19 and post-COVID-19 syndrome patients.

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	COVID-19 symptoms						
	Ongoing sympt	Ongoing symptomatic COVID-19 n = 225			Post-COVID-19 syndrome n = 92		
	Counts	% Total	% of Symptomatic	Counts	% Total	% of Symptomatic	
Loss of smell	118	11.8	52.4	35	3.5	38	
Loss of taste	70	7	31.1	15	1.5	16.3	
Fatigue	26	2.6	11.5	7	0.7	7.6	
Shortness of breath	23	2.3	10.2	5	0.5	5.4	
Cough	20	2	8.9	2	0.2	2.2	
Joint pain	19	1.9	8-4	4	0.4	4.3	
Headache	11	1.1	4.9	3	0.3	3.3	
Chest pain	11	1.1	4.9	3	0.3	3.3	
Hair loss	9	0.9	4	1	0.1	1.1	
Fever	5	0.5	2.2	5	0.5	5.4	
Myalgia	5	0.5	2.2	1	0.1	1.1	
Diarrhea	5	0.5	2.2	1	0.1	1.1	
Sore throat	5	0.5	2.2	2	0.2	2.2	
Low mood	4	0.4	1.8	2	0.2	2.2	
Loss of appetite	3	0.3	1.3	1	0.1	1.1	
Sputum	3	0.3	1.3	1	0.1	1.1	
Nausea	2	0.2	0.9	1	0.1	1.1	
Numbness	2	0.2	0.9	1	0.1	1.1	
Anxiety	1	0.1	0.4	1	0.1	1.1	
Chronic sinusitis	1	0.1	0.4	1	0.1	1.1	
Nasal congestion	1	0.1	0.4	1	0.1	1.1	
Dry eye	1	0.1	0.4	1	0.1	1.1	
Tinnitus	1	0.1	0.4	1	0.1	1.1	
Change of taste	2	0.2	0.9				
Red-eye	2	0.2	0.9				
Dizziness	2	0.2	0.9				
Insomnia	2	0.2	0.9				
Amnesia	2	0.2	0.9				
Abdominal pain	1	0.1	0.4				
Sneezing	1	0.1	0.4				

Table 4

The characteristics of ongoing symptomatic COVID-19, relieving and aggravating factors, and the clinical outcome (total patients: 225).

Factor	Counts	% of Symptoms
Post-COVID-19 syndrome symptoms (95 symptoms)	55	24.4%
Ongoing symptomatic COVID-19 (354 symptoms)	92	40.9%
Duration of persistent symptoms (days):		
Mean+SD	28.3 + 34.7	
Median (IQR)	16.3 (10.1, 32.1)	
Range	4.7-139.8	
Relieving factors:		
Analgesic or antipyretic	23	7.5
Vitamins	19	6.2
Herbal preparations	8	2.6
Zinc	7	2.3
Cough syrup/expectorant	7	2.3
Strong odors	5	1.6
Change in physical activity	4	1.2
Antibiotic	3	1.0
Nasal drops	2	0.6
Oxygen	2	0.6
Hypnotic	1	0.3
Antidepressants	1	0.3
Muscle relaxant	1	0.3
Religious practices	1	0.3
No reported alleviating factor	224	72.7
Aggravating factors:		
Change in physical activity	8	2.6
Smoking	3	1.0
Cough	2	0.6
Strong odors	2	0.6
Common cold	1	0.3
No reported aggravating factor	292	94.8
Similar symptom in family	43	19.1
Symptoms affected social and work-related activities	70	31%
Hospital admission for COVID-19	64	6.4%
ICU admission for COVID-19	9	0.9%
Death after acute SARS-CoV-2 infection	4	0.4%
Length of hospital stay, days:		
Mean+SD	8.0 + 7.9	
Range	1–30	

Factors associated with the occurrence of COVID-19 symptoms beyond 4 weeks of diagnosis.

	Univariate analysis		Multivariate analysis	
	Mean Dif/Unadjusted OR (95%CI)	P-value	Adjusted OR	P-value
Age-years	0.91 (0.86-2.67)	0.442	0.99 (0.9–1.0)	0.008
Male sex	Reference	0.034a	1.3 (0.98,-1.98)	0.157
Female sex	1.4 (1.03–1.87)			
Occupation				
Not working	Reference			
Employed	0.79 (0.57-1.1)	0.17	0.92 (0.6-1.4)	0.688
Healthcare employed	0.81 (0.39-1.6)	0.55	0.93 (0.4–1.8)	0.648
Retired	0.79 (0.42-1.5)	0.48	1.1 (0.5-2.4)	0.799
Student	2.1 (0.9-5.0)	0.080	1.8 (0.7-4.5)	0.191
Smoking				
Current	Reference			
Never	1.3 (0.85-1.9)	0.76		
Past	1.4 (0.76-2.6)	0.255		
Comorbidity	1.3 (0.94–1.8)	0.108		
No comorbidity	Reference			
1	1.4 (0.95-2.1)	0.088	1.3 (0.8-1.8)	0.215
>2	1.1 (0.7-1.9)	0.61	0.7 (0.2-2.4)	0.645
Presence of acute symptoms of COVID-19	6.8 (2.5-18.8)	< 0.0001 a	6.5 (2.3-18.04)	0.0001a
No symptoms	Reference			
<6	12.8 (1.7-93.5)	0.012a		
>6	27.6 (3.7-203.8)	0.001 a		
Family history of the same symptoms	0.69 (0.28-1.69)	0.412		
Hospital admission	2.33 (1.4-4.0)	0.001 a	2.4 (1.3-4.2)	0.002a
Length of stay	0.77 (-5.2-3.6)	0.730		

^a Statistically significant (P < 0.05).

assessed at a certain time. However, the results of this study are valid due to the careful representative sampling methodology.

Conclusions

Saudi patients with the post-acute COVID-19 condition experience a wide range of symptoms, which is consistent with what has been documented in other countries. Loss of smell, loss of taste, shortness of breath, and fatigue are among the persistent symptoms. These symptoms substantially influence social and work-related activities. The impact of this condition should be one of the focus areas for future COVID-19- related research. Regular follow-up of COVID-19 survivors is highly recommended to minimize the burden of the post-acute COVID-19 condition and improve the quality of life of patients.

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Ethical approval

This study was approved by Princess Nourah bint Abdulrahman University IRB log no. 21–0172 on 11 March 2021. All participants were clearly informed about their enrollment in the study and oral consents were obtained. Privacy and confidentiality of patient data were assured throughout the study and only accessed by study primary investigator without identifiers.

Author contributions

FAA, conceptualization, project administration, methodology, Funding, participation in writing the original and final draft. FA, conceptualization, project administration, methodology, Data collection, Data analysis, Writing, Review & Editing. MA, participation in writing the original and final draft. MSA participation in writing the original and final draft, Article submission. YA, YA & AK participated in methodology, Formal analysis, data collection, Writing – Review & Editing. AA & AA did the data Collection, analysis, writing original draft, editing, resources & investigation. All authors reviewed and approved the submission and take responsibility for the integrity and accuracy of the results.

Data sharing statement

Data are available upon reasonable request.

Declaration of interests

None declared.

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