RESEARCH ARTICLE

Factors affecting symptom duration and recovery among home-treated COVID-19 patients in Baghdad-Iraq: a cross-sectional study

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Abstract

Objective: To determine the prevalence of Long COVID among home-treated coronavirus disease-2019 cases, and the factors that may influence the duration of symptoms.

Method: The cross-sectional study was conducted from February to July 2021 at 20 primary healthcare centres in 10 health districts of Baghdad, Iraq, after approval from the ethics review committee of the College of Medicine, Mustansiriyah University, Baghdad. Those included were adults of both genders who previously had coronavirus disease-2019 infection as diagnosed through on polymerase chain reaction test, and received supportive treatment during isolation at home. Data was collected through direct interview using a questionnaire which consisted of demographic characteristics, comorbidities, smoking history and symptoms of coronavirus disease-2019 along with their duration. Measurement of weight and height was also done for each subject. Data was analysed using SPSS 27.

Results: Of the 400 participants, 248(62%) were males and 152(38%) were females. The overall mean age was 40.8±12.8 years (range: 18-71 years). Of the total, 121(30.25%) subjects had persistent symptoms for >4 weeks. The mean duration of illness was 4.2±3.6 weeks (range: 1-16 weeks). The symptoms that lasted for >4 weeks were fatigue 94(23.5%), loss of smell or taste 59(14.75%), and cough 8(2%). Age, smoking status, comorbidities and the total number of initial symptoms showed a significant association with the duration of illness ($p<0.05$).

Conclusion: A substantial number of mild to moderate coronavirus disease-2019 cases suffered from persistent symptoms. The duration of illness could have been influenced by age, comorbidities, smoking status and total number of initial symptoms.

Key Words: COVID-19, Anosmia, Taste, Smoking, Cough, Polymerase, Fatigue,

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Introduction

Coronavirus disease-2019 (COVID-19) is a viral infection caused by an enveloped, single-stranded positive-sensing ribonucleic acid (RNA) coronavirus. The outbreak started in Wuhan city, China[1], and the novel virus, named the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV), causes COVID-19, as named by the World Health Organisation (WHO) in February 2020, which was declared a pandemic in March 2020[2].

The main symptoms of COVID-19 include fever, cough, shortness of breath, headache, fatigue, muscle or body aches, congestion or runny nose, loss of taste or smell or both, sore throat, nausea/vomiting and diarrhoea[3]. Following infectious diseases like COVID-19, in which a systemic inflammatory response occurs, a long-lasting compensatory inflammatory response occurs that leads to post-infectious immune-suppression[4]. Prolonged course of COVID-19 illness or persistence of the initial symptoms was a problem that became more widely noticed as time passed by. The term 'Long-COVID' describes the condition of individuals who have either recovered from the acute phase of COVID-19 but are still reporting persistent effects of the infection, or have had the usual clinical presentation but for far longer than would be expected, or having new symptoms other than the initial symptoms[5].

On December 18, 2020, a guideline for the management of long-term effects of COVID-19 was published by the National Institute for Health and Care Excellence (NICE), classified COVID-19 according to duration of symptoms into the following categories: Acute COVID-19 (signs and symptoms of COVID-19 for up to 4 weeks), Ongoing COVID-19 (signs and symptoms of COVID-19 for 4-12 weeks), and Post-COVID syndrome (signs and symptoms of COVID-19 continuing for >12 weeks). The term Long-COVID includes both ongoing COVID-19 and post-COVID syndrome cases. Thus, any case with symptoms continuing for >4 weeks is considered Long COVID[6].

The current study was planned to determine the prevalence of Long COVID among home-treated COVID-

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2019 cases, and the factors that may influence the duration of symptoms.

Subjects and Methods

The cross-sectional study was conducted from February to July 2021 at 20 primary healthcare centres (PHCs) in 10 health districts of Baghdad, Iraq, after approval from the ethics review committee of the College of Medicine, Mustansiriyah University, and the Board for Medical Specialisations, Iraq. Permission was obtained from Al-Karkh and Al-Rusafa health directorates of the Iraqi Ministry of Health.

The sample was raised using convenience sampling technique. Those included were adults of eithr gender who previously had symptoms of COVID-19 and a positive polymerase chain reaction (PCR) test at least 3 months earlier, and had received supportive treatment at home isolation without the need for any emergency intervention or hospitalisation. Those who required hospitalization or did not have a documented positive PCR test were excluded. After obtaining verbal consent from the subjects, data was collected by the researchers by direct interview using a questionnaire based on self-report data and consisting of demographic characteristics, comorbidities, smoking history and symptoms of COVID-19 with their duration. Weight and height of each subject were measured, and body mass index (BMI) values were calculated and categorised as per WHO definition[7].

Data was analysed using SPSS 27. Pearson chi-square test was used to evaluate the association of study variables with the duration of illness. Fisher Exact test was used appropriately. P≤0.05 was considered statistically significant.

Results

Of the 400 participants, 248(62%) were males and 152(38%) were females. The overall mean age was 40.8±12.8 years (range: 18-71 years), and most of the patients 196(49%) were aged 20-39 years, while those aged >70 years were only 5(1.25%). There were 253(63.2%) non-smokers, and 93(23.3%) had chronic diseases. The mean weight of the participants was 79.0±13.0kg (range: 50-115kg). The mean height was 170.6±9.1cm (range: 154-195cm). The mean BMI was 27.0±2.9 kg/cm^2 (range: 20.28-38.06kg/cm^2), with 247(61.7%) overweight and 61(15.2%) obese subjects. The most frequent COVID-19 symptom was fever 320(80%), while the least frequent was skin rash 6(1.5%). As for the total number of initial symptoms, 118(29.5%) participants had 5 symptoms, 88(22%) had 6 symptoms, 86(21.5%) had 4 symptoms, 6(1.5%) had 9 symptoms and

Table-1: Distribution of age and gender by the duration of illness.

	Duration of COVID-19						
	Acute COVID (<4 weeks)		Ongoing COVID (4-12)		Post-COVID syndrome (>12)		P value
	no	%	no	%	no	%	
Age (years)							
<20years	4	1.4	-	-	-	-	
20---29	98	35.1	-	-	-	-	
30---39	91	32.6	7	6.5	-	-	
40---49	53	19.0	30	27.8	1	7.7	0.0001*
50---59	25	9.0	46	42.6	6	46.2	
60---69	8	2.9	22	20.4	4	30.8	
=>70years	-	-	3	2.8	2	15.4	
Gender							
Male	173	62.0	70	64.8	5	38.5	0.181
Female	106	38.0	38	35.2	8	61.5	

*Significant using Pearson Chi-square test at 0.05 level.
COVID-19: Coronavirus disease-2019

Table-2: Association of smoking history and comorbidities wuth illness duration.

	Duration of COVID-19						
	Acute COVID (<4 weeks)		Ongoing COVID (4-12)		Post-COVID syndrome (>12)		P value
	no	%	no	%	no	%	
Smoking							
Smoker	56	20.1	52	48.1	5	38.5	0.0001*
Ex-smoker	22	7.9	10	9.3	2	15.4	
Non-smoker	201	72.0	46	42.6	6	46.2	
History of chronic diseases							
Yes	6	2.2	75	69.4	12	92.3	0.0001*
No	273	97.8	33	30.6	1	7.7	
Hypertension							
Yes	3	1.1	38	35.2	10	76.9	0.0001*
No	276	98.9	70	64.8	3	23.1	
Diabetes Mellitus							
Yes	3	1.1	34	31.5	4	30.8	0.0001*
No	276	98.9	74	68.5	9	69.2	
Coronary heart disease							
Yes	-	-	10	9.3	3	23.1	0.0001*
No	279	100.0	98	90.7	10	76.9	
Asthma							
Yes	-	-	9	8.3	1	7.7	0.0001*
No	279	100.0	99	91.7	12	92.3	
Renal diseases							
Yes	-	-	1	.9	-	-	
No	279	100.0	107	99.1	13	100.0	
Underweight (<18.5)--		-	-	-	-		
Body mass index (Kg/m^2)							
Normal (18.5-24.9)	90	32.3	2	1.9	-	-	0.0001*
Overweight (25-29.9)	83 1	65.6	59	54.6	5	38.5	
Obese (=>35)	6	2.2	47	43.5	8	61.5	

*Significant using Pearson Chi-square test at 0.05 level.
COVID-19: Coronavirus disease-2019.

Table-2: Association of smoking history and comorbidities wuth illness duration.

	Duration of COVID-19						
	Acute COVID (<4 weeks)		Ongoing COVID (4-12)		Post-COVID syndrome (>12)		P value
	no	%	no	%	no	%	
Total number of symptoms							
1	5	1.8	-	-	-	-	0.0001*
2	7	2.5	2	1.9	-	-	
3	34	12.2	-	-	-	-	
4	79	28.3	7	6.5	-	-	
5	81	29.0	33	30.6	4	30.8	
6	52	18.6	32	29.6	4	30.8	
7	13	4.7	27	25.0	3	23.1	
8	5	1.8	5	4.6	1	7.7	
9	3	1.1	2	1.9	1	7.7	

*Significant using Pearson Chi-square test at 0.05 level.
COVID-19: Coronavirus disease-2019.

5(1.3%) had 1 symptom. The mean duration of illness was 4.2±3.6 weeks (range: 1-16 weeks).There were 279(59.75%) participants who had symptoms for <4 weeks, 108(27%) had symptoms for 4-12 weeks, and 13(3.25%) had symptoms for >12 weeks. The symptoms that lasted for >4 weeks were fatigue 94(23.5%), loss of smell or taste 59(14.75%), and cough 8(2%). There was a significant association between age and duration of illness ($p<0.05$), while gender showed no significant association (Table 1). The presence of comorbidities and smoking status had a significant association with the duration of COVID-19 (Table 2). The total number of initial symptoms also had a significant association with illness duration (Table 3).

Discussion

COVID-19 has been one of the major pandemics in human history, and placed a pressure on health systems and economies globally. Reports of persistent symptoms and long-lasting COVID-19 illness even in mild and moderate cases have been rising, but little is known about the relevant prevalence and risk factors[8].

The current study revealed that 30.25% participants had persistent symptoms for >4 weeks after the onset of COVID-19 illness, which is in agreement with a study in the United States which revealed that 34% subjects had persistent symptoms when interviewed 21 days after the onset of symptoms[9]. A study in Egypt showed that 89.2% subjects had persistent symptoms after recovery[10]. Another study in Jordan revealed that 71.8% subjects had persistent symptoms after three months of illness onset[11]. The disparities may be explained by the difference in sample size, type of the study and the study population.

The current results revealed that fatigue, loss of smell or taste, and cough were the symptoms that lasted >4 weeks. Regarding fatigue, 23.5% participants reported its persistence for >4 weeks and continued up to 16 weeks. This is in alignment with a study in Turkey which showed that 29.3% subjects had persistent fatigue after 20 weeks[8]. A study in Jordan showed that fatigue did not resolve in 35.6% of the patients after three months[11]. A study in Egypt revealed that 72.8% of the study sample had persistent fatigue after recovery[10]. The disparity could be explained by the fact that fatigue depends on self-assessment and cannot be measured quantitatively.

The mechanism of post-COVID-19 fatigue is not completely understood. However, one probable explanation is that COVID-19 infection causes neuro-inflammation in the brain, which activates the innate immune system in the brain via humoral and retrograde neuronal impulses, and the activation of cytokines in neuro-inflammation can cause fatigue. The release of cytokines stops once the virus has been dealt with, but sometimes the cytokines fail to return to their normal level, causing ongoing symptoms[12].

Further, 14.75% of the participants in the current study reported the persistence of loss of smell or taste for >4 weeks which continued up to 16 weeks. A study in Italy showed that 10.4% patients had persistent anosmia or dysgeusia when interviewed six months after acute infection[13]. A study in Turkey showed that after 20 weeks of symptoms onset, 3.1% and 2.1% of participants had loss of smell and loss of taste, respectively[8]. In Jordan, only 35.8% participants had anosmia for >3 months[11]. Since the loss of smell and taste is a qualitative disorder, and inability to perform olfactory tests to confirm the complete return to normal state, this could be the possible explanation of the difference in results across the studies.

The olfactory epithelium is a part of the olfactory system and is responsible for detecting odours. The destruction of non-neuronal cells of the olfactory epithelium that express angiotensin-converting enzyme 2 (ACE2) receptors could be the possible cause of smell loss in COVID-19 patients[14]. The presence of olfactory dysfunction adversely affects the taste perception due to the close functional correlation between both chemosensory systems[15].

Regarding the cough, 2% of the participants had persistent cough for >4 weeks and up to 8 weeks in the current study. a study in Norway found that 10% of their study sample had cough for 4 months after the onset of illness[16] and in Jordan, 24.6% had persistent cough for >3 months[11]. The evaluation of cough resolution depends on

self-assessment, and this could explain the difference in the results.

There are many possible explanations of post-COVID-19 cough. One explanation could be the damage induced by the virus or the medications given during the illness, such as fibrosis of the lung parenchyma or damage to the airways. In 10-20% of COVID-19 patients, fibrotic changes in the lungs occurred in a study, and these fibrotic alterations could increase cough reflex sensitivity in response to mechanical chest wall stimulation[17].

The current results were similar to those in Turkey and France that found a significant association between age and the duration of COVID-19[8,13]. In contrast, a study in the United States did not find this association[9]. This difference could be related to the sample size or the difference in quality of healthcare service.

The association between age and Long COVID could be explained by the age-related decline and dysregulation of the immune system. In many infections, immune response from vaccination or previous exposure to the same pathogen can provide partial immune protection, called adaptive immunity. Since SARS-CoV-2 is a novel virus, there was no previous exposure or herd immunity, and the whole population was susceptible. So, in the absence of adaptive immunity, old-aged people depended on their innate immunity which had already undergone remodelling and decline due to aging, and this reflected on the duration and outcome of COVID-19 illness[18].

As for gender, the current results showed no significant association with the duration of symptoms. The finding was in agreement with studies done in Turkey and the US[8,9]. Another study in the US suggested that male gender affected severity, mortality and outcome of COVID-19 illness, and explained that the social and behavioural factors related to male gender, like smoking and less likely to seek medical health for illness, were the contributing fators. Another explanation was the difference in ACE2 receptors expression caused by sex hormones and the gender-based difference in immunological response[19]. A study in Jordan revealed that the female gender carried more risk of prolonged illness, and explained that by the Arab culture where females make more effort in terms of taking care of family members during illnesses[11].

Regarding the presence of chronic diseases, the current results were similar to studies in Turkey and Egypt.[8,10]

The activation of renin-angiotensin-aldosterone system (RAAS) by hypertension could be the possible explanation of the relation between the presence of hypertension and the duration and outcome of COVID-19 illness[20]. As for the role of diabetes mellitus, this could be due to the unfavourable hormone environment in diabetic patients which leads to a state of chronic low-grade inflammation that results in dysregulation of the immune response and microvascular dysfunction[20].

As for smoking, the current results revealed a significant association with the duration of COVID-19 symptoms. This finding is in agreement with a systematic review about smoking and COVID-19 discussed in 5 studies done in China, which concluded that smoking negatively affects the progression and adverse outcomes of COVID-19[21]. Since ACE2 receptors are the main receptors for SARS-CoV-2 to gain entry to host cells, the upregulation and increased gene expression of ACE2 receptors in current smokers than in ex-smokers and non-smokers could be the possible explanation for the association between smoking and duration of COVID-19 symptoms[22].

The BMI status in the current study showed a significant association with the duration of COVID-19 symptoms, which is similar to studies done in Egypt and Turkey[10,8]. The possible explanation of this association is the negative effect of obesity on the immune system. The adipose tissue acts as a reservoir for macrophages and T-lymphocytes, and excess body fat leads to poor functioning of the T-lymphocytes and macrophages. The adipose tissue also secretes adipokines, and obese persons usually have chronic alteration in circulatory inflammatory mediators derived from adipokines[23].

Regarding the total number of initial COVID-19 symptoms, the current results showed a significant association with the duration of illness. A study done in the United Kingdom showed that the number of symptoms in the first week of illness was predictive of the duration and persistence of symptoms[24]. The possible explanation of this association is that more initial symptoms mean more viraemia. The viral load and viraemia have clear relationship with the course of illness, lymphocyte count, levels of inflammatory markers and increased risk of prolonged illness[25].

Limitation: The current study has its limitations as self-report data may have suffered from recall bias. Besides, the sample size was not calculated and the sample was small compared to the total number of confirmed COVID-19 cases in Baghdad. The study did not measure the persistent symptoms, like fatigue, quantitatively, and, finally, there was no specific diagnostic tool to evaluate resolution of symptoms and return to normal state.

Conclusion

A substantial number of mild to moderate COVID-19 cases suffered from persistence of symptoms. The symptoms that persisted for >4 weeks were fatigue, cough and loss of smell or taste. The duration of COVID-19 illness and clinical recovery could be influenced by age, presence of comorbidities, smoking history and the total number of initial symptoms.

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