Medical Research Archives

European Society of Medicine

OPEN ACCESS

Published: November 30, 2023

Citation: Candido, P., et al., 2023. Long-Term Effects of COVID-19 and Health-Related Quality of Life of Mild Cases an outpatient clinic. Medical Research Archives, [online] 11(11). https://doi.org/10.18103/mra.v11i11.4774

DOI: https://doi.org/10.18103/mra.v11i11.4774

ISSN: 2375-1924

RESEARCH ARTICLE

Long-Term Effects of COVID-19 and Health-Related Quality of Life of Mild Cases an outpatient clinic

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ABSTRACT

Background/aim: The clinical spectrum of COVID-19 infection ranges from asymptomatic infection to deadly and potentially lethal disease. Although some studies have been performed, data on the long-term effects and persistent symptoms after COVID-19 are limited. We aimed to evaluate the long-term effects in an adult population with SARS-CoV-2 infection treated in a patient clinic.

Materials and Methods: The study included a random sample of 231 adults (≥18 years) with a positive outpatient test result for SARS-CoV-2 who were not hospitalized. We adapted six quality of life questionnaires already validated. We performed an overall analysis of the frequency of responses and then statistically correlated the frequency of symptoms with gender, age, and presence of comorbidities. **Results:** The mean age was 40.25 years old, 62.8% were women, who had a higher frequency of various symptoms ($p < 0.05$). We found a higher frequency of symptoms associated with SARS-CoV-2 in patients under 40 years: Shortness of breath at rest ($p = 0.004$), Shortness of breath when walking at your own pace ($p = 0.007$), Shortness of breath when performing sexual activities ($p = 0.047$), Tired or low energy ($p = 0.002$), Difficulty in concentrating ($p = 0.047$), Heart change even without physical exertion ($p = 0.005$), Headache ($p = 0.007$) and Memory problems ($p = 0.031$).

Conclusion: Our study showed that individuals that required no hospitalization might have persistent quality of life symptoms after recovery from COVID-19 infection. Therefore, there is a need for long-term follow-up and rehabilitation strategies for patients should be developed.

Key words: COVID-19, quality of life, symptoms.

1. Introduction

Coronavirus disease 2019 (COVID-19) was started in December 2019 in Wuhan, China, and on March 12, 2020 it was declared a pandemic by the World Health Organization (WHO)[1]. There are currently more than 600 million confirmed cases in the world and more than six million deaths (data from September 5, 2022). The clinical spectrum of severe acute respiratory syndrome coronavirus (SARS-CoV-2) infection ranges from asymptomatic infection to life-threatening and lethal disease. To date much about the clinical course remains unclear, especially the possible long-term health/quality of life consequences. Post-acute COVID-19 is defined as the presence of symptoms that remain beyond 3 weeks since onset and chronic COVID-19 as extending beyond 12 weeks[2].

Regardless of the damage caused by an acute SARS-CoV-2 infection, with clinical severity ranging from virtually asymptomatic infection to a systemic illness requiring intensive care (occasionally leading to death), convincing evidence has emerged that the clinical burden of COVID-19 can extend far beyond the acute infectious period, with medium- and long-term consequences that can have a substantial impact on the quality of life of affected individuals, thus representing a significant challenge for global health[3]. In general, this condition has been defined as "COVID long" and is associated with substantial organic dysfunctions, being characterized as a syndrome in which there is a persistence of clinical symptoms beyond four weeks from the onset of acute symptoms. The typical clinical symptoms of "covid long" are tiredness, dyspnea, fatigue, cerebral confusion, autonomic dysfunction, headache, persistent loss of smell or taste, cough, depression, low-grade fever, palpitations, dizziness, muscle pain, and joint pain[4].

Although some studies have been conducted, there are still limited data on the long-term effects and persistent symptoms post-COVID-19. Side effects involving the pulmonary systems, neurologic, cardiovascular, renal, fertility, and others have been reported after recovery from COVID-19[5]. The post-acute syndrome is well recognized and reported in patients who required hospitalization and admission to the intensive care unit. In a previous study that evaluated the persistence of COVID-19 symptoms in a sample of 143 patients discharged from the hospital, only 12.6% of patients were completely free of any COVID-19-related symptoms after an average of 60 days from the initial symptom[6].

However, post-acute COVID-19 syndrome is also observed among patients that required no hospitalization. Thus, it is important to detail the long-term effects of COVID-19 infection after recovery to analyze, evaluate, and appropriately manage any persistent or emerging health consequences. Here, we aimed to evaluate the long-term effects in an adult population with SARS-CoV-2 infection treated in a patient clinic.

2. Material and Methods

This is an observational, quantitative described and analytical study conducted between February and May 2022. The study included a random sample of 231 adults (≥18 years) who had a positive outpatient test result for SARS-CoV-2 by reverse transcriptase–polymerase chain reaction. The mean follow-up time post-COVID-19 was 13 months.

Patients were identified in the electronic hospital database through a specific coding for COVID-19. Data collected included demographic characteristics, comorbidities, symptoms, radiological manifestations, and clinical management. Patients who required hospitalization were excluded from the study; only those patients with a positive diagnosis for the disease for at least six months and underwent follow-up without the need to stay in a hospital environment were included. This study was submitted and approved by the research ethics committee of the Hospital Moriah.

The informed consent form and an adaptation of six questionnaires already validated in the literature (supplementary material) on quality of life[7], frailty[8], dyspnea[9], depression[10], sleep disorders[11] and anxiety[12], were sent by email to the patients who could be included in our study (n = 1354). To complement the questionnaires, questions about some aspects that have been associated with SARS-CoV-2 infection were also asked: hair loss, memory loss, decreased smell could and taste, persistent cough, headache, skin rashes, and joint pain.

All questions were multiple choice with three response options as to whether the post covid symptom was absent, infrequent, or frequent. We initially performed a general frequency analysis of responses and then statistically correlated symptom frequency with gender, age, and presence of comorbidities. For this analysis the chi-square test was performed using SPSS® software 20.0 for windows and throughout the analysis was considered statistically significant when p was less than 0.05.

3. Results

We emailed the questionnaire to 1117 patients and only 231 patients agreed to participate in the study and answered the questionnaire. Six patients did not sign the consent form and were therefore excluded from the study.

The patients included were mostly young, the mean age was 40.25 (± 10.33) years, 50.6% were under 40 years old, mostly women (62.8%), without previous comorbidities (65.4%), and all included patients were not hospitalized. Here we show the significant results, and the complete data are in the supplementary materials.

The frequencies of the long-term symptoms are shown in Table 1. The most prevalent complain in our sample were “Problems performing your usual activities”, “Shortness of breath when walking at your own pace”, “Tired or low energy”, “Appetite change”, “Difficulty in concentrating”, “Emotional alteration”, “Headache”, “Loss or reduction of taste”, “Loss or diminished sense of smell”, “Sleep disorders”, “Memory problems” and “Increased hair loss”.

Table 1. Frequencies of long-term results.

	Absent	Infrequent	Frequent	Total
		% (n)		
Problems performing your usual activities	35.1 (81)	48.9 (113)	16.0 (37)	100 (231)
Shortness of breath at rest	57.4 (132)	36.5 (84)	6.1 (14)	100 (230)
Shortness of breath when walking at your own pace	39.7 (91)	44.5 (102)	15.7 (36)	100 (229)
Shortness of breath when performing sexual activities	63.2 (144)	31.1 (71)	5.7 (13)	100 (228)
Tired or low energy	19.9 (46)	43.7 (101)	36.4 (84)	100 (231)
Appetite change (lack or excess)	35.8 (82)	39.7 (91)	24.5 (56)	100 (229)
Difficulty in concentrating	35.4 (81)	37.6 (86)	27.1 (62)	100 (229)
Tremors	67.0 (154)	26.5 (61)	6.5 (15)	100 (230)
Persistent cough	48.7 (112)	33.9(78)	17.4 (40)	100 (230)
Emotional alteration (excessive nervousness or sensitivity)	35.5 (82)	40.3 (93)	24.2 (56)	100 (231)
You have felt your heart change even without physical exertion (e.g., tachycardia and dysrhythmia)	56.3 (130)	30.7 (71)	13.0 (30)	100 (231)
Headache	26.4 (61)	36.8 (85)	36.8 (85)	100 (231)
Tinnitus	67.1 (155)	23.4 (54)	9.5 (22)	100 (231)
Loss or reduction of taste	49.8 (115)	29.9 (69)	20.3 (47)	100 (231)
Loss or diminished sense of smell	48.5 (112)	25.1 (58)	26.4 (61)	100 (231)
Sleep Disorders	35.7 (82)	39.1 (90)	25.2 (58)	100 (230)
You have taken medicine to help you sleep	79.7 (184)	13.4 (31)	6.9 (16)	100 (231)

	Absent	Infrequent	Frequent	Total
		% (n)		
Paresthesia	64.3 (148)	27.0 (62)	8.7 (20)	100 (230)
Pain or muscle spasms	45.7 (105)	33.5 (77)	20.9 (48)	100 (230)
Memory problems	40.3 (93)	27.3 (63)	32.5 (75)	100 (231)
Urine with an altered odor or color	72.7 (168)	21.2 (49)	6.1 (14)	100 (231)
Edema or swelling	77.5 (179)	16.5 (38)	6.1 (14)	100 (231)
Thrombosis	95.2 (219)	3.5 (8)	1.3 (3)	100 (230)
Pruritus	73.6 (170)	21.2 (49)	5.2 (12)	100 (231)
Dizziness	51.1 (118)	39.0 (90)	10.0 (23)	100 (231)
Nausea	58.7 (135)	35.2 (81)	6.1 (14)	100 (230)
Increased hair loss	45.9 (106)	17.7 (41)	36.4 (84)	100 (231)
Difficulty in sexual intercourse	70.1 (162)	25.1 (58)	4.8 (11)	100 (231)

The data are presented as percentages (%) and absolute value (n).

We compared the frequencies of the symptoms long-term between gender. The significant results are shown in table 2. Women presented a statistically significant higher frequency of several symptoms, such as: Problems performing your usual activities ($p = 0.006$), Shortness of breath at rest ($p = 0.002$), Shortness of breath when walking at your own pace ($p = 0.000$), Tired or low energy ($p = 0.000$), Appetite change (lack or excess) ($p = 0.023$), Difficulty in concentrating ($p = 0.014$), Emotional alteration (excessive nervousness or sensitivity) ($p = 0.003$), heart change even without physical exertion ($p = 0.000$), Headache ($p = 0.000$), Loss or diminished sense of smell ($p = 0.045$), Pain or muscle spasms ($p = 0.004$), Memory problems ($p = 0.000$), Edema or swelling ($p = 0.001$), Dizziness ($p = 0.004$), Nausea ($p = 0.000$) and Increase hair loss ($p = 0.000$).

Table 2. Comparison of the frequencies of the results between gender.

	Female	Male	P value
	% (n)		
	Problems performing your usual activities		
Absent	27.6% (40)	47.7% (41)	
Infrequent	53.1% (77)	41.9% (36)	0.006
Frequent	19.3% (28)	10.5% (9)	
	Shortness of breath at rest		
Absent	49.0% (71)	71.8% (61)	
Infrequent	42.8% (62)	25.9% (22)	0.002
Frequent	8.3% (12)	2.4% (2)	
	Shortness of breath when walking at your own pace		
Absent	29,4% (42)	57,0% (49)	
Infrequent	48,3% (69)	38,4% (33)	0,000
Frequent	22,4% (32)	4,7% (4)	
	Tired or low energy		
Absent	15.2% (22)	27.9% (24)	
Infrequent	37.9% (55)	53.5% (46)	0.000
Frequent	46.9% (68)	18.6% (16)	
	Appetite change (lack or excess)		
Absent	29.9% (43)	45.9% (39)	
Infrequent	41.0% (59)	37.6% (32)	0.023
Frequent	29.2% (42)	16.5% (14)	
	Difficulty in concentrating		
Absent	29.4% (42)	45.3% (39)	
Infrequent	37.8% (54)	37.2% (32)	0.014
Frequent	32.9% (47)	17.4% (15)	
	Emotional alteration (excessive nervousness or sensitivity)		
Absent	28.3% (41)	47.7% (41)	
Infrequent	41.4% (60)	38.4% (33)	0.003
Frequent	40.3% (44)	14.0% (12)	
	Heart change even without physical exertion		
Absent	46.9% (68)	72.1% (62)	
Infrequent	34.5% (50)	24.4% (21)	0.000
Frequent	18.6% (27)	3.5% (3)	
	Headache		
Absent	17.9% (26)	40.7% (35)	
Infrequent	33,8% (49)	41.9% (36)	0.000
Frequent	48,3% (70)	17.4% (15)	

	Female	Male	P value
	% (n)		
	Loss or diminished sense of smell		
Absent	43.4% (63)	57.0% (49)	
Infrequent	24.8% (36)	25.6% (22)	0.045
Frequent	31.7% (46)	17.4% (15)	
	Pain or muscle spasms		
Absent	42.4% (61)	51.2% (44)	
Infrequent	29.9% (43)	39.5% (34)	0.004
Frequent	27.8% (40)	9.3% (8)	
	Memory problems		
Absent	29.7% (43)	58.1% (50)	
Infrequent	28.3% (41)	25.6% (22)	0.000
Frequent	42.1% (61)	16.3% (14)	
	Edema or swelling		
Absent	69.7% (101)	90.7% (78)	
Infrequent	21.4% (31)	8.1% (7)	0.001
Frequent	9.0% (13)	1.2% (1)	
	Dizziness		
Absent	42.8% (62)	65.1% (56)	
Infrequent	44.8% (65)	29.1% (25)	0.004
Frequent	12.4% (18)	5.8% (5)	
	Nausea		
Absent	48.6% (70)	75.6% (65)	
Infrequent	44.4% (64)	19.8% (17)	0.000
Frequent	6.9% (10)	4.7% (4)	
	Increased hair loss		
Absent	31.7% (46)	69.8% (60)	
Infrequent	16.6% (24)	19.8% (17)	0.000
Frequent	51.7 (75)	10.5% (9)	

The results are presented in percentage (%) and absolute value (n).

We divided our cohort into patients under 40 years old and those 40 years old and older. In this analysis, we surprisingly found a higher frequency of long-term symptoms in younger patients, significant data (table 3). The symptoms that had statistical significance between groups were Shortness of breath at rest ($p = 0.004$), Shortness of breath when walking at your own pace ($p = 0.007$), Shortness of breath when performing sexual activities ($p = 0.047$), Tired or low energy ($p = 0.002$), Difficulty in concentrating ($p = 0.047$), Heart change even without physical exertion ($p = 0.005$), Headache ($p = 0.007$) and

Memory problems (p = 0.031). We also performed an analysis according to comorbidities and the results are shown in supplementary table.

Table 3. Comparison of frequencies in patients under 40 years of age and 40 years and older.

	< 40 years-old	> 40 years-old	P value
Shortness of breath at rest			
Absent	48.7% (57)	66.4% (75)	
Infrequent	41.0% (48)	31.9% (36)	0.004
Frequent	10.3% (12)	1.8% (2)	
Shortness of breath when walking at your own pace			
Absent	36.8% (43)	42.9% (48)	
Infrequent	40.2% (47)	49.1% (55)	0.007
Frequent	23.1% (27)	8.0% (9)	
Shortness of breath when performing sexual activities			
Absent	55.3% (63)	71.1% (81)	
Infrequent	37.7% (43)	24.6% (28)	0.047
Frequent	7.0% (8)	4.4% (5)	
Tired or low energy			
Absent	11.1% (13)	28.9% (33)	
Infrequent	45.3% (53)	42.1% (48)	0.002
Frequent	43.6% (51)	28.9% (33)	
Difficulty in concentrating			
Absent	27.8% (32)	43.0% (49)	
Infrequent	43.5% (50)	31.6% (36)	0.047
Frequent	28.7% (33)	25.4% (29)	
Heart change even without physical exertion			
Absent	47.0% (55)	65.8% (75)	
Infrequent	34.2% (40)	27.2% (31)	0.005
Frequent	18.8% (22)	7.0% (8)	
Headache			
Absent	18.8% (22)	34.2% (39)	
Infrequent	35.9% (42)	37.7% (43)	0.007
Frequent	45.3% (53)	28.1 (32)	
Memory problems			
Absent	32.5% (38)	48.2% (55)	
Infrequent	33.3% (39)	21.1% (24)	0.031
Frequent	34.2% (40)	30.7% (35)	

The results are presented in percentage (%) and absolute value (n).

Next, we compared the "Absent/Infrequent" and "Frequent" frequencies of long-term symptoms between genders and between patients under 40 and 40 years of age or older (Table 4).

Table 1. Comparison of the frequencies "Absent/Infrequent" and "Frequent" between genders and between patients younger than 40 years and 40 years or more.

	Female	Male	P value
	% (n)		
Shortness of breath when walking at your own pace			
Absent/Unfrequent	77.6% (111)	95.3% (82)	0,000
Frequent	22.4% (32)	4.7% (4)	
Tired or low energy			
Absent/Unfrequent	53.1% (77)	81.4% (70)	0.000
Frequent	46.9% (68)	18.6% (16)	
Appetite change (lack or excess)			
Absent/Unfrequent	67.1% (96)	82.6% (71)	0.011
Frequent	32.9% (47)	17.4% (15)	
Difficulty in concentrating			
Absent/Unfrequent	29.4% (42)	45.3% (39)	0.014
Frequent	37.8% (54)	37.2% (32)	
Persistent cough			
Absent/Unfrequent	78.6% (114)	89.4% (76)	0.037
Frequent	28.4% (31)	10.6% (9)	
Emotional alteration (excessive nervousness or sensitivity)			
Absent/Unfrequent	69.7% (101)	86.0% (74)	0.005
Frequent	30.3% (44)	14.0% (12)	
Heart change even without physical exertion			
Absent/Unfrequent	81.4% (118)	96.5% (83)	0.001
Frequent	18.6% (27)	3.5% (3)	
Headache			
Absent/Unfrequent	51.7% (75)	82.6% (71)	0.000
Frequent	48,3% (70)	17.4% (15)	
Loss or diminished sense of smell			
Absent/Unfrequent	68.3% (99)	82.6% (71)	0.017
Frequent	31.7% (46)	17.4% (15)	
Paresthesia			
Absent/Unfrequent	88.2% (127)	96.5% (83)	0.031
Frequent	11.8% (17)	3.5% (3)	

	Female	Male	P value
	% (n)		
	Pain or muscle spasms		
Absent/Unfrequent	72.2% (104)	90.7% (78)	0.001
Frequent	27.8% (40)	9.3% (8)	
	Memory problems		
Absent/Unfrequent	57.9% (84)	83.7% (72)	0.000
Frequent	42.1% (61)	16.3% (14)	
	Edema or swelling		
Absent/Unfrequent	91.0% (132)	98.8% (85)	0.020
Frequent	9.0% (13)	1.2% (1)	
	Pruritus		
Absent/Unfrequent	92.4% (134)	98.8% (85)	0.035
Frequent	7.6% (11)	1.2% (1)	
	Increased hair loss		
Absent/Unfrequent	48.3% (70)	89.5% (77)	0.000
Frequent	51.7 (75)	10.5% (9)	
	< 40 years-old	> 40 anos years-old	
	Shortness of breath at rest		
Absent/Unfrequent	89.7% (105)	98.2% (111)	0.011
Frequent	10.3% (12)	1.8% (2)	
	Shortness of breath when walking at your own pace		
Absent/Unfrequent	76.9% (90)	92.0% (103)	0.002
Frequent	23.1% (27)	8.0% (9)	
	Tired or low energy		
Absent/Unfrequent	56.4% (66)	71.1% (81)	0.021
Frequent	43.6% (51)	28.9% (33)	
	Persistent cough		
Absent/Unfrequent	77.6% (90)	87.7% (100)	0.043
Frequent	22.4% (26)	12.3% (14)	
	Heart change even without physical exertion		
Absent/Unfrequent	81.2% (95)	93.0% (106)	0.010
Frequent	18.8% (22)	7.0% (8)	
	Headache		
Absent/Unfrequent	54.7% (64)	71.9% (82)	0.007
Frequent	45.3% (53)	28.1 (32)	

In this analysis, we observed that the results remained significant for most long-term symptoms in women and patients under 40.

4. Discussion

Although there are already published papers describing long-term symptoms in patients who were diagnosed with SARS-CoV2 infection, the majority evaluated patients with moderate or severe symptoms requiring hospitalization [6]. Our study focuses on the prevalence of long-term symptoms caused by the infection in patients that were not hospitalized and even in this population, the disease was followed by several symptoms that impacted their quality of life.

A meta-analysis study estimated that 80% of patients infected with SARS-CoV-2 developed one or more bad long-term symptoms. The five most common symptoms were fatigue (58%), headache (44%), attention disturbance (27%), hair loss (25%), and dyspnea (24%)[13]. Peñas et al. conducted a meta-analysis study and evaluated the prevalence of post-COVID-19 symptoms in non-hospitalized patients, in which the mean age was 44.3 years. They identified that among the most common symptoms were fatigue, headache, and shortness of breath, and some remained after 90 days of disease[14]. Augustin et al. noted that even after 7 months of post-COVID follow-up, the most present symptoms in their population were headache and hair loss[15].

In a sample of non-hospitalized individuals, Burke at al. report 50-75% patients describing symptoms, mainly fatigue during COVID-19, but there is little information about a longer follow-up[16]. Petersen et al. in a population-based study describe persistence of at least one symptom in more than half of patients, being fatigue present in almost on quarter of the individuals in a follow-up of 125 days after symptoms onset[17].

The majority of papers do not describe minutely the symptoms based in detailed questionaries. The use of such instruments reduces the subjectivity of answers allowing a better description and interpretation of the scores of the most varied symptoms[18].

One of these rare articles was published by Townsend et al., who reported fatigue in 52% of patients assessed by the Chalder scale (CFQ-11)[19]. Chatys-Bogacka et al. used a quality-of-life questionnaire in 300 non-hospitalized patients with a mean age of 36 years identifying memory loss as the most prevalent symptom, during the acute phase of COVID-19 and in the long term, being 79% females[20].

Similar to our findings, data from the literature have shown an increased prevalence of fatigue or other symptoms among women[19,21,22]. We identified that female gender reported more long-term symptoms, such as emotional change, headache, fatigue, and muscle spasms. Bai et al. found that women had a 3 times increased risk of being diagnosed with long term symptoms due to COVID-19[23]. Graham et al., investigated long-term symptoms in 100 non-hospitalized patients with a mean age of 43.2 years, in which 70% were female, and the most frequent symptoms were fatigue (85%), headache (68%), myalgias (66%), numbness/ stiffness (60%), and depression/anxiety (42%)[24]. Hormonal factors may explain these results since hormones may perpetuate the acute phase of the inflammatory state, even

after recovery[25,26]. In addition, higher IgG antibody production has been reported in women in the early phase of the disease[27]. It is also hypothesized that women are generally more attentive to their health and the associated distresses[23].

Most patients with COVID-19 have mild disease, although a significant proportion have severe symptoms requiring hospitalization, especially older individuals with comorbidities[6,28]. Surprisingly, our results showed that the frequency of post-COVID-19 symptoms was higher in patients under 40. The study by Soraas et al. revealed that COVID-19 patients aged 30 to 49 had a higher odds ratio for self-reported worsening health. In comparison, patients in other age groups had a lower probability of worsening health[29].

There are few studies that have investigated persistent neurocognitive deficits in patients with mild COVID-19[30,31]. We have shown that some neurological symptoms, such as memory loss and lack of concentration, are frequent.

Mechanisms underlying all these symptoms may be a prolonged pro-inflammatory response related to SARS-CoV-2 infection, an atypical immune system response leading to a cascade of events affecting the respiratory, immune, and central nervous systems[32]. Social and emotional factors associated with the pandemic, such as post-traumatic stress, hospitalization, treatments received, family situations, and psychological disorders, such as anxiety and depression, may contribute to these symptoms in the long-term. However, studies with longer follow-up should be conducted to elucidate the complexity and heterogeneity of post-COVID-19 symptoms[14].

The limitation of this study is a relatively small cohort, derived from a single center, that could result in a selection bias. It was based on self-reported symptoms and the clinical conditions before COVID-19 were often unknown. However, we believe that our data are important to raise awareness about the large number of individuals affected by the long-term symptoms associated with COVID-19, especially women and younger adults that could need longer health attention.

Our study has some limitations. Our cohort was conducted at a single center, which characterizes a potential selection bias. In addition, it was based on self-reported symptoms by patients, introducing an information bias. The patients' conditions before COVID-19 were often unknown, and it is possible that the outcomes we found were unrelated to the disease and may have been pre-existing. Long-term progression or regression of symptoms has not yet been evaluated. In addition, we are aware that our cohort of patients is small. However, we believe that the data from our study are important to raise awareness about the large number of individuals affected by the long-term symptoms associated with COVID-19, especially women and younger adults.

5. Conclusion

In conclusion, our study showed that individuals that required no hospitalization might have persistent symptoms after recovery from COVID-19 infection. The most reported symptoms were memory problems, hair loss, smell and taste changes, and tiredness. Therefore, there is a need for long-term follow-up and rehabilitation strategies for patients should be developed.

Conflicts of Interest Statement:

All authors should disclose any conflict of interest that may have influenced the conduct or the research presentation.

Acknowledgements Statement:

We thank the patients who kindly agreed to participate in the study and answered the questionnaires.

Funding Statement:

Not Applicable.

Availability of data and materials:

The datasets used and analyzed during the current study are available to the corresponding author upon reasonable request.

Ethical Approval and Consent to Participate:

The Research Ethics Committee of Moriah Hospital submitted and approved this study under protocol 5.378.841.

Author's contributions:

PC developed the design and wrote the manuscript. LOAM, POLP, EOV, CCM, MSM, and SC collected all the data. PR performed a questionnaire. KRML critical review, intellectual discussion, and review of the final manuscript. RP contributed to statistical analysis and the interpretation of the results. VS developed the design, intellectual discussion, and final manuscript review. STR developed the design, wrote the manuscript, and made the statistical analysis. All authors checked the data, discussed the results, and commented on the manuscript.

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