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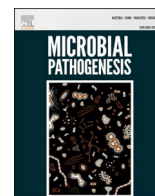
Characterization of long COVID-19 manifestations and its associated factors: A prospective cohort study from Iran

Mona Sadat Larijani [a],[1], Fatemeh Ashrafian [a],[1], Fahimeh Bagheri Amiri [b],[**],
Mohammad Banifazl [c], Anahita Bavand [a], Afsaneh Karami [d], Fatemeh Asgari Shokooh [a],
Amitis Ramezani [a],[*]

[a] Clinical Research Dept., Pasteur Institute of Iran, Tehran, Iran
[b] Department of Epidemiology and Biostatistics, Research Centre for Emerging and Reemerging Infectious Diseases, Pasteur Institute of Iran, Tehran, Iran
[c] Iranian Society for Support of Patients with Infectious Disease, Tehran, Iran
[d] Department of Infectious Disease, Zanjan University of Medical Sciences, Zanjan, Iran

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ABSTRACT

The prevalence and variety complaints of COVID-19 cases in a long term have been investigated in recent studies. The symptoms over the time are various and unpredictable which may persist several weeks after full recovery. The importance of long-COVID-19 manifestations includes its effect on the recovered cases which requires a rational management based on an accurate guideline to handle post-acute COVID-19 state. The aim of this study was to evaluate the incidence of post-acute COVID-19 syndrome and to identify the associated risk factors as well as to compare new and persistent symptoms at different post-acute phases.

Totally 254 individuals from Pasteur Institute of Iran (or/and their relatives) were investigated who had a previously confirmed COVID-19 PCR test. The long-term manifestations of the virus were categorized through a time window as acute, ongoing, post-COVID and persistent phases and the individuals were assessed by the face-to-face or the phone call interview according to their complaints. The data were then statistically analyzed to determine the frequency of the symptoms and also the associated factors in which a p value < 0.05 was considered significant.

Except a small asymptotic group of five, 249 cases progressed the symptoms to acute phase among which 64.1% reported at least one symptom in post-acute phase. Neurological sequelae were found as the most frequent symptom (91.6%). Furthermore, there was a significant association between the underlying diseases, age and acute phase symptoms to the post-acute phase syndrome susceptibility (p < 0.05).

In conclusion, the increasing number of the reports and studies on long COVID-19 which can hugely affect the life quality should be more investigated and explored in terms of the pathophysiology to achieve appropriate treatments in time. The clusters of symptoms, specially a combination of neurological signs, presenting over months after the recovery impose a huge difficulty to the recovered population.

1. Introduction

The early stages of SARS-CoV-2 era, mainly distressed people by its mortality and acute symptoms. COVID-19 which is caused by the virus, primarily is considered as a respiratory disease from which most infected individuals experience mild or moderate symptoms and about 10–15% of cases progress the severe form of the disease [1,2]. The recovery time of COVID-19 is usually achieved after 2–6 weeks [3–6]. Nevertheless, as the studies expanded, the long-term consequences of COVID-19 came to public attention. Post-infectious symptoms had been

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previously recognized for other infections such as glandular fever, Q-fever and Legionnaires' disease as well as psychological complaints reduced quality of life after a SARS-infection [7–10].

Post-acute COVID-19 is defined as a condition in which the illness manifestations are extended beyond three weeks since the onset of symptoms including fatigue, anosmia, headache and cough. Moreover, long-COVID is described as symptoms extending beyond 12 weeks from symptoms initiation although distinguish between post-acute and long-COVID does not seem essential, it is relevant to a better understand of phases and the consequences of the disease on the short and long term [11]. Therefore, an increasing number of studies has been focused on post COVID manifestations and also the related risk factors [3,12,13]. Despite the importance of this matter, there is no exact definition of the long-term post COVID which may start shortly after discharge or even several months post full recovery. Moreover, the wide range of the long form presentation from different studies is also considerable. It is to say that, long COVID-19 may affect the individuals in terms of different manifestation and time window [14–16].

Post-acute COVID-19 highlights the importance of patients' management as the symptoms can impose a major impact on daily functioning as well for the development of knowledge about the natural course of a COVID-19 infection [17]. Therefore, we designed a study to describe the symptoms immediately after the initial phase, for instance symptoms persisting more than 3 weeks; and the symptoms in the chronic phase (such as those take longer than 3 months; long-COVID) to make a landscape of the persistence and frequency of the experienced manifestations among Iranian patients with COVID-19. Moreover, the incidence of new and persistent symptoms was evaluated at different post-acute phases.

2. Methods

2.1. Population design

From March to October 2021, all PCR positive health care workers (and/or their relatives) of Pasteur Institute of Iran were invited to participate in the study. The including criteria was having confirmed positive COVID-19 PCR test and age ≥18. This study was approved by the ethical board of the Pasteur Institute of Iran (Reference number: IR. PII.REC.1399.064). All enrolled participants signed the informed consent.

According to the studied cases who presented different symptoms through various period of time, we preferably divided COVID-19 manifestations by the time:

1) Acute phase; in which COVID-19 related symptoms last in first 3 weeks from the symptoms onset.
2) Ongoing phase; in which COVID-19 related symptoms present 4–12 weeks after the onset.
3) Post COVID-19 phase; in which the related symptoms manifest up to 24 weeks after the onset.
4) Persistent COVID-19; in which the associated symptoms last beyond 24 weeks after the onset.

Moreover, a syndrome characterized by persistent symptoms or delayed or long-term complications beyond 4 weeks from the symptoms onset has been considered as post-acute phase of COVID-19, which includes ongoing, post-COVID-19, and persistent phase of COVID-19.

Therefore, the same case might be present in more than one timing category.

2.2. Data collection

A data collection list, including demographic characteristics, underlying disease, date of PCR positive test and severity of disease, symptoms and their durations were used. The list was completed

Table 1
Demographic characteristic, basic information and frequency of underlying diseases of the participants.

Variable	Subgroup	N (%)	Men	Women
Age	median age	41.0	42.0	39.5
	(IQR)	(35.0–49.0)	(37.0–49.0)	(32.0–48.8)
BMI	median	24.7	25.5	24.0
	(IQR)	(23.1–27.7)	(23.5–29.1)	(22.9–26.8)
Severity of disease	Mild	211 (85.8%)	113 (86.3)	98 (85.2)
	Moderate	26 (10.6%)	12 (9.2)	14 (12.2)
	Sever	9 (3.7%)	6 (4.6)	3 (2.6)
Hospitalization	No	238 (93.7%)	131 (95.6)	107 (92.2)
	Yes	16 (6.3%)	6 (4.4)	9 (7.8)
ICU	No	12 (75.0%)	136 (99.7)	114 (97.4)
	Yes	4 (25.0%)	1 (0.7)	3 (2.6)
Vaccination	No	24 (9.8%)	11 (8.5)	14 (11.3)
	Yes	221 (90.2%)	119 (91.5)	102 (88.7)
Type of vaccine	Sputnik	10 (4.5%)	4 (3.1)	6 (5.2)
	AstraZeneca	55 (25.0%)	28 (21.5)	27 (23.5)
	Bharat (COVXIN)	101 (45.9)	61 (46.9)	40 (34.6)
	Soberana	15 (6.8)	7 (5.4)	8 (7.0)
	Sinopharm	39 (17.7)	19 (14.6)	20 (17.4)
CVD (Cardiovascular disease)	No	238 (93.7%)	128 (93.4)	110 (94.0)
	Yes	16 (6.3%)	9 (6.6)	7 (6.0)
Lung diseases	No	247 (97.2%)	131 (95.6)	116 (99.1)
	Yes	7 (2.8%)	6 (4.4)	1 (0.9)
Diabetes	No	244 (96.1%)	129 (94.2)	115 (98.3)
	Yes	10 (3.9%)	8 (5.8)	2 (1.87)
Kidney diseases	No	250 (98.4%)	133 (97.1)	137 (100.0)
	Yes	4 (1.6%)	4 (2.9)	0 (0.0)
Chronic bronchitis	No	252 (99.2%)	136 (99.3)	116 (99.1)
	Yes	2 (0.8%)	1 (0.7)	1 (0.9)
Thyroid diseases	No	251 (98.8%)	137 (100.0)	114 (97.4)
	Yes	3 (1.2%)	0 (0.0)	3 (2.6)
Asthma	No	249 (98.0)	134 (97.8)	115 (98.3)
	Yes	5 (2.0%)	3 (2.2)	2 (1.7)
Hypertension	No	249 (98.0%)	134 (97.8)	115 (98.3)
	Yes	5 (2.0%)	3 (2.2)	2 (1.7)
Hashimoto diseases	No	253 (99.6%)	137 (100.0)	116 (99.7)
	Yes	1 (0.4%)	0 (0.0)	1 (0.9)
Minor thalassemia	No	253 (99.6%)	136 (99.3)	117 (100.0)
	Yes	1 (0.4%)	1 (0.7)	0 (0.0)
Cancer	No	253 (99.6%)	137 (100.0)	116 (99.1)
	Yes	1 (0.4%)	0 (0.0)	1 (0.9)
Gout disease	No	253 (99.6%)	136 (99.7)	117 (100.0)
	Yes	1 (0.4%)	1 (0.7)	0 (0.0)
MI (Myocardial infarction)	No	252 (99.2%)	135 (98.5)	117 (100.0)
	Yes	2 (0.8%)	2 (1.5)	0 (0.0)
MS (Multiple sclerosis)	No	253 (99.6%)	136 (99.7)	117 (100.0)
	Yes	1 (0.4%)	1 (0.7)	0 (0.0)
RA (Rheumatoid arthritis)	No	253 (99.6%)	136 (99.7)	117 (100.0)
	Yes	1 (0.4%)	1 (0.7)	0 (0.0)
PsO (Psoriasis)	No	253 (99.6%)	136 (99.7)	117 (100.0)
	Yes	1 (0.4%)	1 (0.7)	0 (0.0)

through a face-to-face or phone interview by an informed expert. What is more, the symptoms which persisted at least 4 weeks from the COVID-19 initiation, were considered as persistent symptoms. Finally, the symptoms which did not exist in the acute phase and appeared in the post-acute phases were classified as the new symptoms.

2.3. Statistical analysis

Continuous variables are presented as the median and interquartile range (IQR), and categorical variables are presented as frequency and percentage. Chi-square test or Fisher's exact were applied to test the categorical variables. Univariate and multivariate logistic regressions were used to analyze risk factors associated with developing symptoms in post-acute phase and the corresponding odds ratios (ORs) and 95% confidence intervals (CIs) were determined. Variables from univariate analyses with p < 0.20 were recruited for the multivariate logistic regression model. Multivariate logistic regressions were performed in a
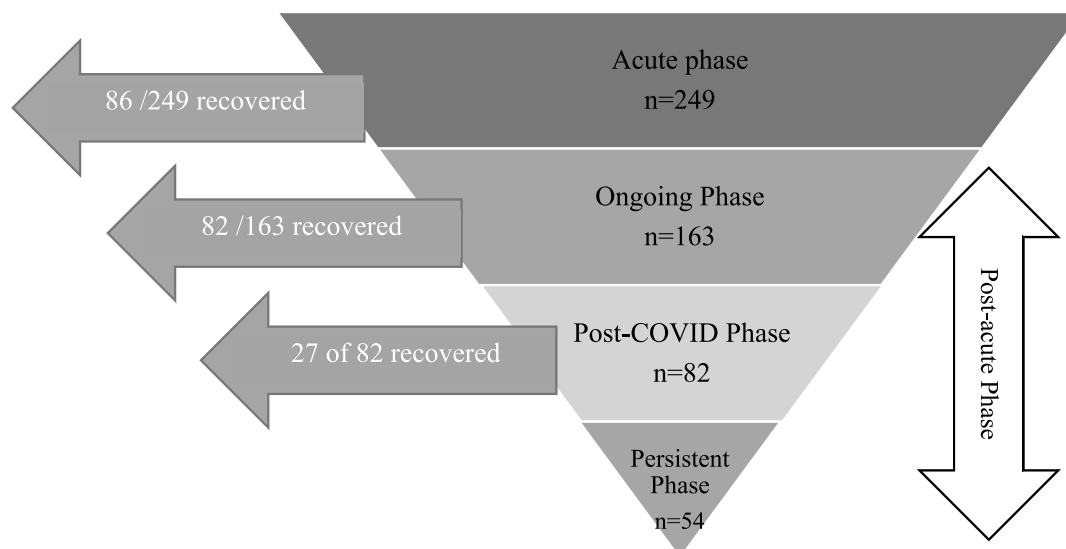
Fig. 1. Number of participants with at least one symptoms in each phase of the study.

Table 2
The frequency and percentage of symptoms in the categorized phases (acute, ongoing, Post-COVID, and Post-Acute).

Category	Acute N = 249	Post-acute N = 163	Sign	Total event n	Acute N = 249	Ongoing N = 163	Post-COVID N = 82	Persist N = 54	Post-Acute N = 163
Respiratory system N = 179 (71.9%)	179 (71.9)	53 (32.3)	Dry cough	120	120 (48.2)	29 (17.8)	5 (6.1)	4 (7.4)	29 (17.8)
			Sputum	64	64 (25.7)	17 (10.4)	3 (3.7)	1 (1.9)	17 (10.4)
			Dyspnea	88	88 (35.3)	28 (17.2)	10 (12.2)	6 (11.1)	28 (17.2)
			Pulmonary fibrosis	3	3 (1.2)	3 (1.8)	1 (1.2)	0 (0.0)	3 (1.8)
			Chest pain	56	56 (22.5)	14 (8.6)	5 (6.1)	4 (7.4)	14 (8.6)
			Runny nose	70	70 (28.1)	3 (1.8)	2 (2.4)	2 (3.7)	3 (1.8)
Gastrointestinal sequelae N = 93 (37.3%)	92 (36.9)	12 (7.3)	Difficulty swallowing	16	16 (6.4)	1 (0.6)	1 (1.2)	1 (1.9)	1 (0.6)
			Nausea/vomiting	41	40 (16.1)	5 (3.1)	1 (1.2)	1 (1.9)	5 (3.1)
			Abdominal pain	65	65 (26.1)	7 (4.3)	0 (0.0)	0 (0.0)	7 (4.3)
Neurological sequelae N = 228 (91.6%)	227 (91.2)	121 (73.8)	Attention disorder	35	32 (12.9)	23 (14.1)	13 (15.9)	9 (16.7)	23 (14.1)
			Headache	155	155 (62.2)	21 (13.9)	8 (9.8)	3 (5.6)	21 (13.9)
			Anosmia	138	136 (54.6)	56 (34.4)	10 (12.2)	7 (13.0)	56 (34.4)
			Paresthesia	30	30 (12.0)	12 (7.4)	5 (6.1)	5 (9.3)	12 (7.4)
			Depression	30	32 (12.9)	19 (11.7)	4 (4.9)	2 (3.7)	19 (11.7)
			Sleep disorder	73	71 (28.5)	28 (17.2)	15 (18.3)	9 (16.7)	28 (17.2)
			Dizziness	77	76 (30.5)	23 (14.1)	5 (6.1)	3 (5.6)	23 (14.1)
			Ageusia	107	103 (41.4)	41 (25.2)	6 (7.3)	3 (5.6)	41 (25.2)
			Hear loss	12	11 (4.4)	7 (4.3)	3 (3.7)	3 (5.6)	7 (4.3)
			Mood disorders	49	44 (17.7)	27 (16.6)	14 (17.1)	8 (14.8)	27 (16.6)
			Anxiety	68	66 (26.5)	38 (23.3)	14 (17.1)	11 (20.4)	38 (23.3)
			Memory loss	37	30 (12.0)	26 (16.0)	18 (22.0)	10 (18.5)	26 (16.0)
Dermatologic sequelae N = 76 (29.9%)	54 (21.7)	57 (34.8)	Hair losing	59	37 (17.8)	49 (30.1)	32 (39.0)	19 (35.2)	49 (30.1)
			Itching	27	24 (9.6)	9 (5.5)	3 (3.7)	2 (3.7)	9 (5.5)
CVD N = 52 (20.9%)	51 (20.5)	19 (11.6)	Hypertension	7	7 (2.8)	3 (1.8)	1 (1.2)	0 (0.0)	3 (1.8)
			Tachycardia	39	37 (14.9)	13 (8.0)	7 (8.5)	6 (11.1)	13 (8.0)
			Myocarditis	1	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
			Arrhythmia	23	21 (8.4)	10 (6.1)	6 (7.3)	4 (7.4)	10 (6.1)
Others			Red eye	32	32 (12.9)	6 (3.7)	1 (1.2)	0 (0.0)	6 (3.7)
			Weight loss	76	73 (29.3)	40 (24.5)	4 (4.9)	1 (1.9)	40 (24.5)
			Diabetes mellitus	3	3 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)	1 (0.6)
			Arthritis	13	11 (4.4)	5 (3.1)	5 (6.1)	4 (7.4)	5 (3.1)
			Dry throat	94	92 (36.9)	18 (11.0)	3 (3.7)	4 (7.4)	18 (11.0)
			Earache	30	29 (11.6)	7 (4.3)	5 (6.1)	4 (7.4)	7 (4.3)
			Hypotension	16	16 (6.4)	7 (4.3)	1 (1.2)	1 (1.9)	7 (4.3)
			Fever	168	168 (67.5)	6 (3.7)	1 (1.2)	1 (1.9)	6 (3.7)
			Body pain	178	178 (71.5)	11 (6.7)	2 (2.4)	2 (3.7)	11 (6.7)
			Sweating	91	91 (36.5)	7 (4.3)	1 (1.2)	1 (1.9)	7 (4.3)
			Fatigue	198	198 (79.5)	51 (31.3)	10 (12.2)	6 (11.1)	51 (31.3)
			Anorexia	123	123 (49.4)	15 (9.2)	4 (4.9)	2 (3.7)	15 (9.2)

backward stepwise approach with results from the final model reported in this study. The two-sided statistical significance level, p-value, was set at 0.05 for all analyses in this study. All statistical analyses were performed using SPSS statistics software (version 26.0).
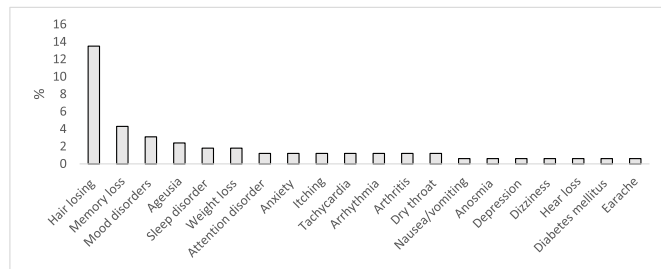
Fig. 2. Frequency of new incident symptoms in post-acute phase.

3. Results

3.1. Participants

Totally 254 participants (46.1% female and 53.9% male) with median age of 41.0 (35.0–49.0) were included in this study. The demographic data are shown in Table 1. Cardiovascular disease (6.3%) has been found as the most frequent underlying disease among the cases.

3.2. Acute and post-acute symptoms

According to the analytic data, five participants (2.0%) were asymptomatic, 249 (98.0%) presented symptoms in the acute phase, 163 (64.2%) had symptoms at ongoing phase, 82 (32.3%) during the post-COVID phase and finally 54 (21.3%) cases suffered from the symptoms in the persistent post COVID-19 phase. Totally 163 (64.2%) experienced at least one symptom in post-acute phase (ongoing or post-COVID or persistent state). The symptoms of 86 (34.5%), 82 (50.3%) and 27 (33.3%) of participants didn't continue in the ongoing, post-COVID and persistent phase, respectively (Fig. 1).

Neurological consequences have been found as the most frequent manifestation accounting for 91.6% of the cases from whom 53.1% had at least one symptom in the post-acute phase. The most prevalent symptom in the acute and persistent phase was fatigue (Table 2).

Furthermore, the new incidence symptoms in post-acute phase, which did not exist in the acute phase, were investigated. Among 163 studied cases who had at least one symptom in the post-acute step, some new incidence symptoms were found. The most frequent symptom was

hair loss which was reported by 22 (13.5) individuals (Fig. 2).

3.3. Predictors of post-acute syndrome

Univariate analysis indicated that age, history of underlying disease, severity of the disease, and symptoms in acute phase are associated with the development of symptoms in the post-acute state (p < 0.05). Multivariate analysis showed that people with underlying disease (OR: 2.48, 95% CI: 1.01–6.13), severe or moderate disease (OR:10.28, 95% CI:2.23–47.32) having some sings in acute phase like neurological sign in acute phase (OR:4.36, 95% CI:1.50–12.65), history of skin sequelae in acute phase (OR: 3.91, 95% CI:1.51–10.10), weight loss (OR: 3.22, 95% CI: 1.46–7.09) were more susceptible to develop symptoms into the post-acute phase (Table 3).

4. Discussion

Since the initiation of the COVID-19 pandemic, various symptoms have been characterized in the acute phase. However, according to the recent reports, symptoms may present or persist after several weeks which is described as long COVID syndrome [18]. Long COVID can appear following severe, mild or asymptomatic SARS-CoV-2 infection as a multisystem illness. There are not any fully accepted definitions of long COVID; nonetheless, it might be broadly described as a delayed recovery from SARS-CoV-2 infection. What is more, it is characterized by durable effects of the infection, unexplained persistent signs or even new onset of chronic diseases [19].

A common complication of SARS-CoV-2 has been immune-related disease with around 3000 reported cases around the world. Apart from the predominant respiratory system inflammation as a typical COVID-19 manifestation, some patients may develop some unusual kinds of inflammation such as extra-pulmonary tissues with different clinical phenotypes which are possibly associated with sex, age and/or race [20]. This also included children which was termed as multisystem inflammatory syndrome in children (MIS-C) [21,22] which presented through gastrointestinal, respiratory, mucocutaneous symptoms. Therefore, SARS-CoV-2 is currently known to be associated with a wide range of pediatric complications [23–26].

Hereby, we characterized long COVID-19 in 254 cases who suffered from at least one symptom three weeks or longer (more than 6 months)

Table 3
Univariate and multivariate analysis for assessing risk factors for advance symptoms in post-acute phase.

Variables	Post- acute		Univariate analysis		Multivariate analysis	
	No (%)	Yes (%)	OR (95% CI)	P value	OR (95% CI)	P value
Gender (Female)	32 (37.2)	83 (50.9)	1.75 (1.03–2.99)	0.04	1.83 (0.99–3.41)	**0.06**
Age>41	77 (89.5)	157 (96.3)	3.06 (1.05–8.90)	0.03		
BMI>24.7[a]	27 (42.9)	74 (53.2)	1.52 (0.83–277)	0.17		
Moderate/severe COVID-19	2 (2.4)	33 (20.9)	10.69 (2.50–45.78)	<0.001	10.28 (2.23–47.32)	**0.003**
Underlying disease	8 (9.3)	36 (22.1)	2.76 (1.22–6.25)	0.01	2.48 (1.01–6.13)	**0.049**
Symptoms in acute phase						
Neurological signs	71 (82.6)	156 (95.7)	4.71 (1.84–12.05)	0.001	4.36 (1.50–12.65)	**0.01**
Cardiovascular	7 (8.1)	43 (26.4)	4.04 (1.73–9.44)	0.001		
Skin	6 (7.0)	48 (29.4)	5.57 (2.27–13.63)	<0.001	3.91 (1.51–10.10)	**0.01**
Respiratory	59 (68.6)	120 (73.6)	1.28 (0.72–2.27)	0.40		
Gastrointestinal	23 (26.7)	69 (42.3)	2.01 (1.14–3.55)	0.02		
Red eye	8 (9.3)	24 (14.7)	1.68 (0.72–3.93)	0.22		
Weight loss	12 (14.0)	61 (37.4)	4.36 (2.15–8.84)	<0.001	3.22 (1.46–7.09)	**0.004**
Dry throat	26 (30.2)	66 (40.5)	1.57 (0.90–2.74)	0.11		
Earache	6 (7.0)	23 (14.1)	2.19 (0.86–5.61)	0.10		
Hypotension	3 (3.5)	13 (8.0)	2.40 (0.66–8.66)	0.17		
Fever	53 (61.6)	115 (70.6)	1.49 (0.86–2.59)	0.15		
Arthritis	1 (1.2)	10 (6.1)	5.56 (0.70–44.14)	0.10		
Body pain	54 (62.8)	124 (76.1)	1.88 (1.07–3.32)	0.03		
Sweating	24 (27.9)	67 (41.1)	1.80 (1.03–3.18)	0.04		
Fatigue	66 (76.7)	132 (81.0)	1.29 (0.68–2.44)	0.43		
Anorexia	39 (45.3)	84 (51.5)	1.28 (0.76–2.16)	0.35		

[a] BMI was not included in multivariate analysis because of the missing data.

post the infection initiation.

Of the first phase, (acute-COVID; up to three weeks) 249 cases presented different symptoms from which neurological associated symptoms were the most common. The second timing category, (ongoing phase; days 22–90) was observed in 163 individuals in which anosmia was the most frequent event (51 cases). Post-COVID phase (day 91–180) was seen in 82 subjects who mostly suffered from hair losing. Persistent phase (beyond 24 weeks) included 54 cases who shared a common symptom with the previous phase as hair loss.

In an international cohort study, the majority of cases (>91%) recovered after 35 weeks. We also followed the cases for over six months, however, 54 out of 254 individuals recovered after the extended recovery time of 6 months. The most frequent symptom after month 6 was fatigue whereas hair loss in our study. Similar to our findings, symptoms prevalence were different over time [27].

In a massive study by Taquet et al., 236 379 COVID-19 patients were followed over 6 months to evaluate a neurological or psychiatric incidence. They found that 33·62% of the cases experienced a kind of neurological disorders from whom 12·84% had never been diagnosed in terms of this incidence [28]. Neurological sequelae were the most frequent disorders in our cases accounting for 91.6% from whom 53.1% faced at least one symptom in the post-acute phase.

Sonnweber et al. investigated a prospective study on 145 COVID-19 patients 60 and 100 days after confirmed diagnosis [29]. The results showed that 41% of the subjects presented persistent symptoms 100 days post COVID-19 onset, with dyspnea as the most frequent symptom accounting for 36%. Respiratory related incidences were estimated in 179 (71.9%) individuals of our subjects from whom 88 cases faced dyspnea in the acute phase (up to 3 weeks) but only 6 (10.7%) in the persistent phase (over 6 months).

In another study, 152 recovered patients were followed 30–40 days after discharge. Totally 113 (74%) cases reported shortness of breath. Moreover, they reported their mental and physical condition as worse in their post-COVID phase compared to their prior state [30]. The respiratory system involvement in the acute phase of our studied subjects mainly evolved around dry cough (48.2%) following by dyspnea and sputum (Table 2). However, dyspnea was the dominant chronic respiratory symptom in the persistent state.

Blackett et al. studied gastrointestinal (GI) symptoms among 147 recovered COVID-19 cases with no GI history. They discovered that diarrhea, nausea/vomiting and abdominal pain were the most common GI symptoms the admission time. Nevertheless, after a median following up of 106 days, abdominal pain (7.5%) was the most frequent symptom followed by constipation, diarrhea and vomiting [31]. Hereby, Gastrointestinal sequelae stood for 93/249 (37.3%) cases in which abdominal pain was dominant following by nausea and difficulty in swallowing in both acute and the persistent states.

Hair loss was the dominant dermatologic consequence in our findings which was observed in 17.8% of the cases during the acute phase. It interestingly increased to 33.9% in the persistent state. Telogen effluvium (TE) is a type of diffuse hair loss which occurs after COVID-19 recovery. In a study composed of 465 cases diagnosed by hair loss, a mean duration of 74 days from COVID-19 symptom initiation to acute TE was estimated [32].

In addition to all above, underlying diseases such as cardio vascular disease, lung diseases, diabetes and kidney disease were spotted as the powerful predictors of long COVID-19 in our findings (p < 0.01). Moreover, experiencing more symptoms in the acute phase and age were associated with the development of symptoms in post-acute phase (p < 0.05). Similar to our observation, Peghin et al. found that several symptoms experience during the first week of infection was associated with long COVID which could be considered as a significant risk factor for SARS-CoV-2 long manifestation [33]. Furthermore, having more symptoms in the illness initiation usually cause a severe form of COVID-19 which triggers a severe immune response and cytokine activation. Therefore, it is rational to face more organ damage which must be intensively cared and treated which may result in long-lasting sequelae [34].

Various approaches have been explored and reviewed by Adeloye et al. in order to come up with a neat solution to manage long COVID-19 manifestations and highlight research priorities for these conditions worldwide. The key findings indicated that the patients suffering from pre-existing respiratory disease are more prone to present serious outcomes from acute COVID-19. Therefore, the airways related illnesses are the priority to be investigated in researching studies. The other important key is determination of the possible COVID-19 related disorders including anxiety, fatigue, cardiovascular diseases, depression and also difference between theses complications among those with or without respiratory underlying disease which could be powerful predictors of hospitalization. Thus, determination of research priorities to develop better knowledge of the long-term COVID-19 outcomes concerning airways disease seems to be essential to bring proper answers during this era with limited resources [35,36].

Post COVID-19 manifestation as the syndrome signs and symptoms which develop during or after the SARS-CoV-2 infection may last for more than six months and not attributable to alternative diagnosis. Patients who had more severe symptoms with a history of underlying diseases developed more manifestations. The clusters of signs that last longest included a combination of neurological symptoms. Considering persistent symptoms of post-COVID-19 syndrome, careful attention must be considered for patients with underlying disorders.

In addition to all findings in this study, there have been some limitations including missing data and the patients who were not monitoring and also some criteria like hormone changes in females which were not tracked.

5. Conclusion

The COVID-19 outbreak has imposed its long-term manifestation to the recovered worldwide. Hence, knowledge about the trend of this manner is in need and future studies must be done to contribute a practical guideline for this issue as well as a clear vision of its probable pathophysiology.

Designing cohort studied to follow patients over months after the infection onset can spot the underlying trend according to different consequences and their risk evaluation.

CRediT authorship contribution statement

Mona Sadat Larijani: Writing – original draft, Data curation. **Fatemeh Ashrafian:** Writing – original draft, Data curation. **Fahimeh Bagheri Amiri:** Formal analysis. **Mohammad Banifazl:** Data curation. **Anahita Bavand:** Data curation. **Afsaneh Karami:** Data curation. **Fatemeh Asgari Shokooh:** Data curation. **Amitis Ramezani:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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