Original Article

Persistent/Late-Onset Complications of COVID-19 in General Population: A Cross-Sectional Study in Tehran, Iran

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Abstract

Background: After recovery from acute phase of the COVID-19, some patients suffer from persistent/late-onset complications. The main objective of this study was to investigate the prevalence of such complications in a large scale of COVID-19 patients in Tehran, Iran.

Methods: In this cross-sectional study, those patients who called Tehran emergency medical services center and were visited by the emergency medical technicians from 20 March 2020 until 21 September 2020 and diagnosed as a confirmed COVID-19 case were enrolled. The minimum required sample size was estimated 385 cases, and they were selected randomly. The patients were interviewed by phone at least 4 weeks since initiation of their symptoms. Using a pre-prepared checklist, made by an expert panel who were involved in management of COVID-19 patients, data were collected on the types and duration of the complications, clinical information, and factors which could interfere with developing the complications. All analyses were performed using STATA 16 software. The association of the prevalence of each complication with independent factor was assessed using Chi-square test (or Fisher's exact test) for categorical variable, and the mean difference of numerical variables in the two groups (with and without complication) was assessed using independent t-test. Statistical significance was accepted at P value<0.05.

Results: Four-hundred forty-seven patients participated in the study. Among our total population, 345 (77.2%) patients experienced at least one of the persistent/late-onset complications. Cardiopulmonary and then skin-related symptom categories were reported in 179 (40.0%) and 173 (38.7%) patients, respectively, and were the most prevalent persistent/late-onset complications. The associations of long term persistent/late-onset complications with older ages (P=0.04), female (P<0.001), psychological stress (P=0.01), and inadequate rest after illness (P<0.001) were significant.

Conclusion: The findings of this study indicate that a significant number of patients will experience persistent/late-onset complications, both physically and mentally, after recovering from acute phase of COVID-19. Thus, physicians should have adequate resources and support to care for the patients to help them cope with the condition.

Keywords: Medically unexplained symptoms, COVID-19, Post-acute COVID-19 syndrome

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Introduction

Corona virus disease 2019 (COVID-19) which has been established as a pandemic since March 2020 is the most widespread coronavirus in the century.[1] While everyone is emphasizing on lowering the mortality rates and mitigating hospital intensive care loads in acute phase of the disease, there are also concerns about long term consequences of COVID-19 that has its own importance, and challenges health care services for a much longer period to manage these consequences.[2, 3]

After recovery from acute phase of the COVID-19, some patients, although not having severe forms of the disease, suffer from persistent/late-onset complications. Such complications lead to frequent visits to medical centers, and the health system may not respond well due to lack of preparation and information. The ignorance of the people and the medical staff about the prevalence of such complications after the acute phase of the disease has passed may lead to the emergence of false emotions in the patients, their family, and the community.[4]

Several studies with different methodologies were conducted in various parts of the world in this regard. Dyspnea, extreme fatigue, weakness, headache, sleep difficulties, loss of taste and smell, skin rash, diarrhea, and vomiting are among the most common persistent/late-onset complications.[5-7] Long-term cardiac and neurological consequences were also reported in literature,[8, 9] but respiratory complications were reported as the most common long-term complication of COVID-19. However, the type and frequency of the complications were reported with considerable difference.[5]

Iran is among the countries mostly affected by the disease. Despite several studies conducted in various countries on persistent/late-onset complications of COVID-19, there are few single referral institution studies on this topic in Iran.[10-12] It seems that there is a need for more information after recovery from acute phase of COVID-19 in a large scale in this country. Therefore, in this study, we aimed to investigate the prevalence of persistent/late-onset complications of COVID-19 patients in Tehran, the capital city of Iran.

Methods

In this cross-sectional study, databank of Tehran EMS center was used, and the patients were selected from all parts of the city and different areas. Those patients who called Tehran emergency medical services (EMS) center and based on the classification provided by world health organization (WHO) were considered as a suspected/probable/confirmed case of COVID-19,[13] and were visited by the emergency medical technicians (EMTs) from 20 March 2020 until 21 September 2020 and later diagnosed as a definite COVID-19 case (based on the findings of their lung computed tomography (CT) scan and/or a positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) test) were enrolled. Those whose final diagnosis was a disease other than confirmed COVID-19, beside a negative RT-PCR test, those who were still hospitalized 4 weeks after admission, and those who died by any cause were excluded.

The required sample size was determined based-on the aim of the study (prevalence of complications of COVID-19 patients). In previous studies, the magnitude of this prevalence has been reported to vary and unknown.[5, 7, 14] Therefore, in this study, assuming a prevalence of 50% for the complications, the Type-I error of 5%, and also based on the 95% confidence interval, the minimum required sample size of 385 people was calculated [$n=(Z^2\times P\times(1-P))/e^2$]. This was the least required sample size, and finally 447 patients (16% more) participated in this study. Relative to each month's number of COVID-19 patients, sample size was determined for each month till it covered our total desired sample size. Patients were selected using computer-generated random number.

A panel of experts (consisting of an internist, a pulmonologist, an intensivist, two emergency

medicine specialists, and a cardiologist) who were involved in management of COVID-19 patients was formed, and a checklist was prepared via literature review and also their experience. For further explanation, it should be noted that the research team invited some physicians who were directly involved in the treatment of patients with COVID-19 and presented the results of studies on the types of persistent/late-onset complications of COVID-19 that had been published until then; primary checklist was prepared, and the basic items of the checklist were categorized. Using the checklist, we performed a pilot study on the EMTs COVIED-19 cases who work for Tehran EMS center. They were interviewed in person by the center's research affairs expert and internal specialist, and if necessary, further examinations were performed. Subsequently, ultimate changes were made to the items of the checklist.

Persistent/late-onset complications of COVID-19 such as the persisting symptoms more than 4 weeks (based on the findings of a pilot study that were performed by the researchers that were also involved in this study) were categorized into 6 groups: gastrointestinal, cardiopulmonary, skin-related, psychological, neurological, and any other symptoms which could not been categorized into any of the above-mentioned categories. Diarrhea, constipation, dyspepsia, nausea, and heartburn are categorized as gastrointestinal complications. Exertional dyspnea, cough, orthopnea, worsening asthma attacks, chest pain and palpitation are categorized as cardiopulmonary complications. Pruritus, skin rashes, and hair loss are categorized as skin related complications. Sleep disturbances, depression, and anxiety are categorized as psychological complications. Headache, blurred vision, anosmia, dysgeusia, and hearing disturbances are categorized as neurological complications. Fatigue, sore throat, weight loss, and myalgia are categorized as unclassified complications. Types and duration of complications; clinical information including demographic characteristics, length of hospital stay, intensive care unit versus ward admission; and factors which could interfere with development of persistent/late-onset complications (body mass index (BMI), marital status, education level, economic status, employment status, ethnicity, smoking or hookah, area of residence, hospitalization, adequate rest, history of chronic disease, taking a drug supplement, stress of COVID-19 before/after infection, psychological distress, exercise before/after COVID-19 infection) were gathered during the interview from patients or family members who were aware. To assess psychological distress, the Kessler Psychological Distress Scale (K6) was used. It is a simple measure of psychological distress which involves 6 questions about a person's emotional state.[15, 16] The reliability and validity of the Farsi version of the K6 were previously examined, showing satisfactory results (Cronbach's alpha=0.885).[17]

The included population were interviewed by phone at least 4 weeks since initiation of their symptoms upon a pre-developed checklist. After making the call, one of the researchers (who had also experience as an EMS dispatcher), while introducing herself and mentioning the main purpose of the interview, completed the checklist if the interviewee agreed to collaborate, and the presence or absence of any complication was determined.

This study was conducted by obtaining informed verbal consent from the participants and commitment to keep the information of individuals confidential and their privacy and not mentioning their names and details in the reports related to this study. This study obtained the ethics committee approval from Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1399.1021).

First, we describe study variables with frequency (%) or mean±SD statistic, as appropriate. The prevalence of each persistent/late-onset complication was estimated. The association of this prevalence with independent factors was assessed using Chi-square test (or Fisher's exact test) for categorical variables. Statistical significance was accepted at $P<0.05$.

Table 1: The distribution of study variables and their association with the prevalence of persistent/late-onset complications of COVID-19

Variable	N (%)	Persistent/late-onset complication category						
		At least one (n=345)	Gastrointestinal (n=112)	Cardiopulmonary (n=179)	Skin related (n=173)	Psychological (n=138)	Neurological (n=100)	Others (n=163)
Age group (year), (n=447)								
Lower than 35	79 (17.67)	54 (15.65)	11 (9.82)	26 (14.53)	23 (13.29)	18 (13.04)	16 (16.00)	26 (15.95)
35–49	167 (37.36)	124 (35.94)	29 (25.89)	61 (34.08)	68 (39.31)	38 (27.54)	38 (38.00)	54 (33.13)
50–64	115 (25.73)	95 (27.54)	36 (32.14)	47 (26.26)	52 (30.06)	48 (34.78)	29 (29.00)	42 (25.77)
65 and more	86 (19.24)	72 (20.87)	36 (32.14)	45 (25.14)	30 (17.34)	34 (24.64)	17 (17.00)	41 (25.15)
P value*		0.04	<0.001	0.05	0.12	0.001	0.78	0.10
Sex, (n=447)								
Female	189 (42.28)	161 (46.67)	54 (48.21)	89 (49.72)	104 (60.12)	76 (55.07)	59 (59.00)	88 (53.99)
Male	258 (57.72)	184 (53.33)	58 (51.79)	90 (50.28)	69 (39.88)	62 (44.93)	41 (41.00)	75 (46.01)
P value*		0.001	0.14	0.01	<0.001	<0.001	<0.001	<0.001
Marital status, (n=445)								
Single	52 (11.69)	33 (9.62)	3 (2.68)	12 (6.74)	16 (9.25)	6 (4.35)	7 (7.14)	13 (8.02)
Married	328 (73.71)	256 (74.64)	85 (75.89)	137 (76.97)	124 (71.68)	100 (72.46)	74 (75.51)	115 (70.99)
Divorced or separated	65 (14.61)	54 (15.74)	24 (21.43)	29 (16.29)	33 (19.08)	32 (23.19)	17 (17.35)	34 (20.99)
P value*		0.03	<0.001	0.03	0.03	<0.001	0.23	0.01
Education, (n=393)								
Illiterate/ primary	124 (31.55)	97 (32.44)	39 (43.33)	49 (32.24)	48 (31.79)	46 (40.00)	25 (28.74)	50 (35.71)
Under diploma/ diploma	173 (44.02)	133 (44.48)	36 (40.00)	64 (42.11)	66 (43.71)	48 (41.74)	41 (47.13)	55 (39.29)
Academic	96 (24.43)	69 (23.08)	15 (16.67)	39 (25.66)	37 (24.50)	21 (18.26)	21 (24.14)	35 (25.00)
P value*		0.52	0.02	0.82	0.99	0.04	0.77	0.31
Economic status, (n=441)								
High	59 (13.38)	51 (14.96)	19 (17.12)	30 (16.95)	28 (16.47)	28 (20.29)	22 (22.45)	26 (16.25)
Moderate	194 (43.99)	146 (42.82)	55 (49.55)	72 (40.68)	69 (40.59)	57 (41.30)	33 (33.67)	68 (42.50)
Low	146 (33.11)	109 (31.96)	30 (27.03)	59 (33.33)	53 (31.18)	38 (27.54)	30 (30.61)	48 (30.00)
Very low	42 (9.52)	35 (10.26)	7 (6.31)	16 (9.04)	20 (11.76)	15 (10.87)	13 (13.27)	18 (11.25)
P value*		0.19	0.12	0.30	0.22	0.02	0.01	0.36
Employment status, (n=445)								
Employed or student	224 (50.34)	161 (46.80)	45 (40.18)	82 (45.81)	68 (39.31)	46 (33.33)	42 (42.42)	69 (42.59)
Unemployed [a]	221 (49.66)	183 (53.20)	67 (59.82)	97 (54.19)	105 (60.69)	92 (66.67)	57 (57.58)	93 (57.41)
P value*		0.01	0.02	0.12	<0.001	<0.001	0.07	0.01
Ethnicity, (n=445)								
Fars	211 (47.31)	156 (45.35)	42 (37.50)	74 (41.34)	83 (47.98)	57 (41.30)	43 (43.43)	71 (43.83)

Non-Fars	235 (52.69)	188 (54.65)	70 (62.50)	105 (58.66)	90 (52.02)	81 (58.70)	56 (56.57)	91 (56.17)
P value*		0.13	0.02	0.04	0.82	0.09	0.38	0.27
Smoking or hookah, (n=446)								
No	362 (81.17)	276 (80.23)	88 (78.57)	142 (79.33)	145 (83.82)	116 (84.06)	78 (78.79)	129 (79.63)
Yes	84 (18.83)	68 (19.77)	24 (21.43)	37 (20.67)	28 (16.18)	22 (15.94)	21 (21.21)	33 (20.37)
P value*		0.36	0.42	0.42	0.26	0.30	0.49	0.53
Area of residence, (n=417)								
North	39 (9.35)	29 (8.98)	4 (3.85)	13 (7.93)	17 (10.69)	13 (10.24)	6 (6.67)	11 (7.33)
South	169 (40.53)	136 (42.11)	39 (37.50)	74 (45.12)	60 (37.74)	53 (41.73)	41 (45.56)	57 (38.00)
West	82 (19.66)	60 (18.58)	20 (19.23)	28 (17.07)	31 (19.50)	22 (17.32)	18 (20.00)	26 (17.33)
East	93 (22.30)	72 (22.29)	29 (27.88)	37 (22.56)	37 (23.27)	28 (22.05)	19 (21.11)	45 (30.00)
Center	34 (8.15)	26 (8.05)	12 (11.54)	12 (7.32)	14 (8.81)	11 (8.66)	6 (6.67)	11 (7.33)
P value*		0.74	0.07	0.53	0.87	0.94	0.74	0.08
Hospitalization, (n=447)								
No	286 (63.98)	209 (60.58)	61 (54.46)	95 (53.07)	107 (61.85)	69 (50.00)	54 (54.00)	88 (53.99)
Yes	161 (36.02)	136 (39.42)	51 (45.54)	84 (46.93)	66 (38.15)	69 (50.00)	46 (46.00)	75 (46.01)
P value*		0.01	0.02	<0.001	0.46	<0.001	0.02	0.001
Adequate rest [b], (n=437)								
Yes	233 (52.13)	158 (45.80)	41 (36.61)	69 (38.55)	71 (41.04)	42 (30.43)	38 (38.00)	53 (32.52)
No/ somewhat	214 (47.87)	187 (54.20)	71 (63.39)	110 (61.45)	102 (58.96)	96 (69.57)	62 (62.00)	110 (67.48)
P value*		<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001
History of chronic disease, (n=447)								
No	262 (58.61)	188 (54.49)	41 (36.61)	87 (48.60)	97 (56.07)	59 (42.75)	54 (54.00)	79 (48.47)
Yes	185 (41.39)	157 (45.51)	71 (63.39)	92 (51.40)	76 (43.93)	79 (57.25)	46 (46.00)	84 (51.53)
P value*		0.001	<0.001	<0.001	0.39	<0.001	0.29	0.001
Taking a drug supplement, (n=447)								
No	225 (50.34)	172 (49.86)	68 (60.71)	97 (54.19)	61 (35.26)	67 (48.55)	46 (46.00)	79 (48.47)
Yes	222 (49.66)	173 (50.14)	44 (39.29)	82 (45.81)	112 (64.74)	71 (51.45)	54 (54.00)	84 (51.53)
P value*		0.71	0.01	0.18	<0.001	0.61	0.33	0.55
BMI, (n=441)								
Normal	160 (36.28)	123 (35.96)	35 (31.53)	60 (33.90)	59 (34.10)	52 (37.96)	27 (27.55)	58 (35.80)
Overweight	205 (46.49)	163 (47.66)	60 (54.05)	91 (51.41)	76 (43.93)	58 (42.34)	48 (48.98)	71 (43.83)
Obese	76 (17.23)	56 (16.37)	16 (14.41)	26 (14.69)	38 (21.97)	27 (19.71)	23 (23.47)	33 (20.37)
P value*		0.56	0.18	0.21	0.11	0.45	0.06	0.39

Stress of COVID-19 before infection, (n=446)								
Never	283 (63.45)	205 (59.59)	59 (52.68)	93 (51.96)	99 (57.23)	69 (50.00)	58 (58.59)	88 (54.32)
Low to moderate	79 (17.71)	68 (19.77)	28 (25.00)	44 (24.58)	33 (19.08)	29 (21.01)	19 (19.19)	39 (24.07)
High	84 (18.83)	71 (20.64)	25 (22.32)	42 (23.46)	41 (23.70)	40 (28.99)	22 (22.22)	35 (21.60)
P value*		0.01	0.02	<0.001	0.06	<0.001	0.50	0.01
Stress of COVID-19 after infection, (n=446)								
Never	244 (54.71)	175 (50.87)	53 (47.32)	76 (42.46)	86 (49.71)	54 (39.13)	45 (45.45)	78 (48.15)
Low to moderate	104 (23.32)	85 (24.71)	33 (29.46)	54 (30.17)	40 (23.12)	34 (24.64)	24 (24.24)	40 (24.69)
High	98 (21.97)	84 (24.42)	26 (23.21)	49 (27.37)	47 (27.17)	50 (36.23)	30 (30.30)	44 (27.16)
P value*		0.01	0.13	<0.001	0.09	<0.001	0.05	0.07
Psychological distress, (n=440)								
Negative	365 (82.95)	270 (79.41)	84 (75.68)	134 (76.57)	132 (77.65)	87 (63.97)	64 (64.00)	118 (73.75)
Positive	75 (17.05)	70 (20.59)	27 (24.32)	41 (23.43)	38 (22.35)	49 (36.03)	36 (36.00)	42 (26.25)
P value*		<0.001	0.02	0.004	0.02	<0.001	<0.001	<0.001
Exercise [c] before COVID-19 infection, (n=442)								
No	208 (47.06)	165 (48.53)	62 (55.86)	87 (49.71)	72 (42.35)	67 (48.91)	48 (48.48)	84 (52.50)
Yes	234 (52.94)	175 (51.47)	49 (44.14)	88 (50.29)	98 (57.65)	70 (51.09)	51 (51.52)	76 (47.50)
P value*		0.26	0.03	0.37	0.12	0.60	0.75	0.08
Exercise [c] after COVID-19 infection, (n=440)								
No	316 (71.82)	255 (75.44)	89 (80.91)	136 (78.16)	123 (73.21)	107 (78.68)	78 (80.41)	127 (80.38)
Yes	124 (28.18)	83 (24.56)	21 (19.09)	38 (21.84)	45 (26.79)	29 (21.32)	19 (19.59)	31 (19.62)
P value*		0.002	0.01	0.02	0.61	0.03	0.03	0.003

a. Unemployed or housewife or retired; b. Return to work or daily chores after complete recovery from COVID-19; c: Moderate to vigorous exercise or physical activity at least once a week for at least 10 minutes (moderate to vigorous activity is meant to make a person breathe faster). BMI: Body mass index; * Chi-square test

In the second approach, we used a logistic regression model considering a binary outcome (presence or absence of persistent/late-onset complication). For this purpose, we first assessed each independent variable in a univariable model. Then, variables with a P<0.2 were included in a multivariable logistic regression model. All statistical analyses were done using STATA software (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC).

Results

Totally, 7226 individuals were visited by EMTs due to related symptoms of COVID-19 during the study period; of them, 876 cases selected randomly. One hundred and three patients died (96 cases due to COVID-19, and 7 cases due to other causes). From those who survived, 129 cases were diagnosed with a disease other than COVID-19. One hundred and ninety-seven individuals did not accept to collaborate. Finally, 447 patients participated in this study, of whom 258 (57.7%) were male. Mean age of the studied population was 49.6±16.0 with the range of 8- 84 years old. Body mass index (BMI) range of the study population was 16.0 to 44.1 with a mean of 26.7±3.9; The distribution of age and BMI was normal. Basic information of the participants is presented in Table 1.

Among our total population, 345 (77.2%) patients experienced at least one of the persistent/late-onset complications. Cardiopulmonary and then skin related symptom categories were reported in 179 (40.0%) and 173 (38.7%) patients, respectively, and they were the most prevalent persistent/late-onset complications. Among all of the studied complications, hair loss (reported by 145 (32.4%) cases) and fatigue (reported by 139 (31.1%) cases) were the most prevalent ones (Figure 1).

Of the participants with persistent/late-onset complications (n=345), only 105 (30.4%) patients experienced only one persistent/late-onset complication. 114 (33.0%), 92 (26.7%), 62 (18.0%), and 43 (12.5%) had experienced two, three, four and more than four persistent/late-onset complications at the same time, respectively (Figure 2).

Logistic regression analysis of the factors associated with at least one persistent/late-onset complication in COVID-19 patients is presented in Table 2. Univariate logistic regression analysis showed that higher ages (P=0.02 for 65 age year and more, also 50-64 years old vs. lower than 35), female (P=0.001), married and divorced or separated marital status (P=0.02), unemployed (P=0.01), hospitalization (P=0.01), non-adequate rest (P<0.001), positive history of chronic diseases (P=0.001), high stress of COVID-19 before and after infection (P=0.03 and P=0.01, respectively), low to moderate stress of COVID-19 before and after infection (P=0.02 and P=0.05, respectively), psychological distress (P<0.001), and lack of exercise after COVID-19 infection (P=0.002) were associated with at least one persistent/late-onset complication of COVID-19.

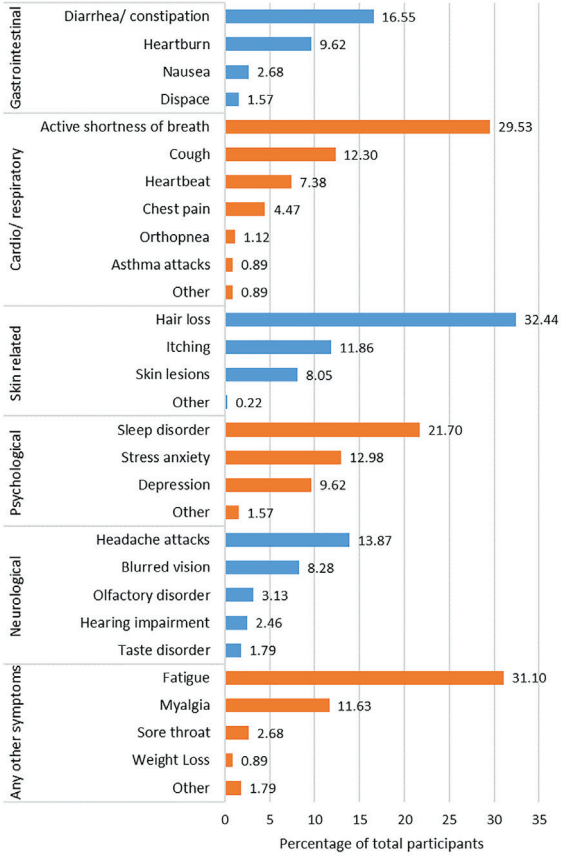

Figure 1: The prevalence of persistent/late-onset complications of COVID-19 by six categories in total participants (n=447).

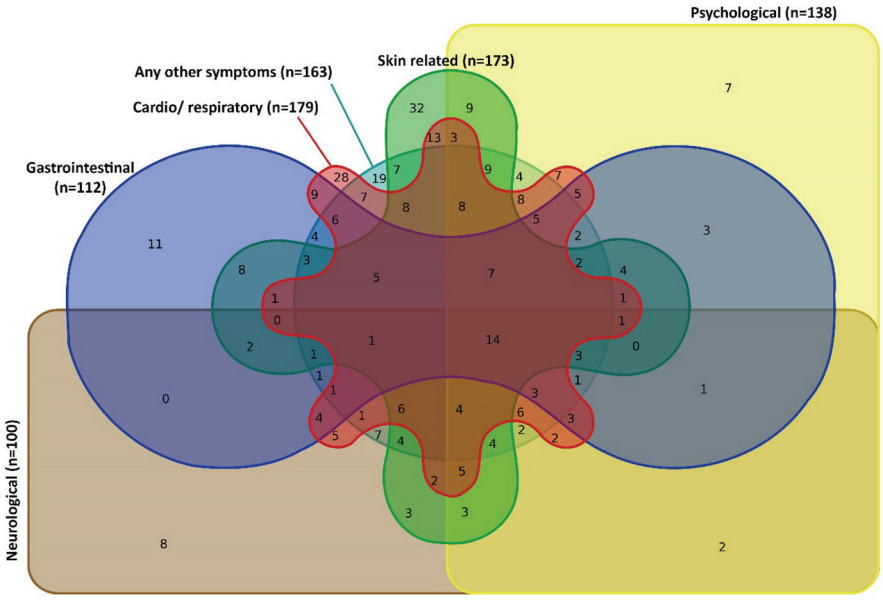

Figure 2: Distribution of persistent/ late-onset complications in COVID-19 patients with at least one of the complications (n=345).

In the multivariable regression analysis, female (P=0.02), non-adequate rest (P=0.004), and psychological distress (P=0.01) were significantly associated with at least one persistent/late-onset complication of COVID-19. Thus, odds of at least one persistent/late-onset complication of COVID-19 were 2.15 times more in female than male and also 2.34 times more in patients without adequate rest compared with those with adequate rest. The psychological distress was more associated with persistent/late-onset complications and odds of these complications in patients with psychological distress was 3.51 times more than those without psychological distress.

Discussion

In this study, we investigated persistent/late-onset complications of COVID-19 patients in Tehran and found that the majority of the patients that participated in this study experienced at least one persistent/late-onset complication and cardiopulmonary was the most frequent complication category reported by the study population. Female sex, inadequate rest, and psychological distress were more associated with persistent/late-onset complications.

Among our studied population, almost 70% of the patients suffered from persistent/late-onset COVID-19. The reported rates of late onset/persistent symptoms after COVID-19 are very different.[6, 7, 14] Some investigators assessed such findings in non-critical care cases, while some other just evaluated critical ones; duration of the follow up were also different in various studies; the ways the investigators assessed their study population were also different; the discrepancy between the results in the published articles prompted us to implement this study. Recently, a systematic review was published in which such discrepancy is well evident.[5]

In this study, cardiopulmonary and skin-related complications were the most prevalent persistent/late-onset complication categories, respectively; however, hair loss from skin related category and fatigue under the category of unclassified complications were among the most prevalent persistent/late-onset complications, respectively. Our findings, in line with other studies' findings across the world, tell us that fatigue and cardiopulmonary symptoms are the most prevalent persistent/late-onset complication following COVID-19.[14, 18-20] It should be mentioned that there is a systematic review of persistent COVID-19 symptoms which

Table 2: Logistic regression analysis of the factors associated with at least one persistent/late-onset complication in COVID-19 patients

Variable	N (%)	Univariable			Multivariable		
		Crude OR	95% CI	P value**	Adjusted OR	95% CI	P value***
Age group (year)							
Lower than 35*	79 (17.67)	1.0			1.0		
35–49	167 (37.36)	1.34	0.74 to 2.40	0.34	1.12	0.54 to 2.33	0.77
50–64	115 (25.73)	2.19	1.12 to 4.32	0.02	1.51	0.59 to 3.88	0.39
65 and more	86 (19.24)	2.38	1.13 to 5.01	0.02	1.69	0.52 to 5.47	0.38
Sex, female	189 (42.28)	2.31	1.43 to 3.75	0.001	2.15	1.14 to 4.07	0.02
Marital status							
Single*	52 (11.69)	1.0			1.0		
Married	328 (73.71)	2.05	1.10 to 3.81	0.02	1.03	0.45 to 2.34	0.95
Divorced or separated	65 (14.61)	2.83	1.20 to 6.68	0.02	0.57	0.17 to 1.89	0.36
Education							
Illiterate/ primary*	124 (31.55)	1.0					
Under diploma/ diploma	173 (44.02)	0.93	0.53 to 1.61	0.78			
Academic	96 (24.43)	0.71	0.38 to 1.32	0.28			
Economic status							
High*	59 (13.38)	1.0					
Moderate	194 (43.99)	1.28	0.42 to 3.84	0.67			
Low	146 (33.11)	0.61	0.25 to 1.46	0.27			
Very low	42 (9.52)	0.59	0.24 to 1.44	0.25			
Employment status							
Employed or student*	224 (50.34)	1.0			1.0		
Unemployed [a]	221 (49.66)	1.88	1.20 to 2.97	0.01	0.69	0.34 to 1.42	0.31
Ethnicity							
Fars*	211 (47.31)	1.0			1.0		
Non-Fars	235 (52.69)	1.41	0.91 to 2.20	0.13	1.19	0.72 to 1.95	0.49
Smoking or hookah, yes	84 (18.83)	1.32	0.73 to 2.40	0.36			
Area of residence							
Center*	39 (9.35)	1.0					
North	169 (40.53)	0.89	0.31 to 2.60	0.84			
South	82 (19.66)	1.27	0.53 to 3.05	0.60			
West	93 (22.30)	0.84	0.33 to 2.13	0.71			
East	34 (8.15)	1.06	0.42 to 2.67	0.91			
Hospitalization, yes	161 (36.02)	2.00	1.22 to 3.31	0.01	1.16	0.62 to 2.18	0.64
Adequate rest [b]							
Yes*	233 (52.13)	1.0			1.0		
No/ somewhat	214 (47.87)	3.29	2.02 to 5.36	<0.001	2.34	1.31 to 4.12	0.004
History of chronic disease, yes	185 (41.39)	2.21	1.36 to 3.58	0.001	1.37	0.70 to 2.69	0.35
Taking a drug supplement, yes	222 (49.66)	1.09	0.70 to 1.69	0.71			
BMI							
Normal*	160 (36.28)	1.0					
Overweight	205 (46.49)	1.17	0.71 to 1.93	0.54			
Obese	76 (17.23)	0.84	0.45 to 1.58	0.59			
Stress of COVID-19 before infection							
Never*	283 (63.45)	1.0					
Low to moderate	79 (17.71)	2.35	1.18 to 4.68	0.02			
High	84 (18.83)	2.08	1.09 to 3.97	0.03			
Stress of COVID-19 after infection							
Never*	244 (54.71)	1.0					
Low to moderate	104 (23.32)	1.76	1.00 to 3.12	0.05			
High	98 (21.97)	2.37	1.26 to 4.45	0.01			

Psychological distress, positive	75 (17.05)	4.93	1.93 to 12.57	0.001	3.51	1.31 to 9.39	0.01
Exercise [c] before COVID-19 infection, no	208 (47.06)	1.29	0.83 to 2.02	0.26			
Exercise [c] after COVID-19 infection, no	316 (71.82)	2.07	1.33 to 3.29	0.002	1.48	0.89 to 2.48	0.13

OR: Odds Ratio; *Reference groups; ** Univariable logistic regression; ***Multivariable logistic regression; a. Unemployed or housewife or retired; b. Return to work or daily chores after complete recovery from COVID-19; c: Moderate to vigorous exercise or physical activity at least once a week for at least 10 minutes (moderate to vigorous activity is meant to make a person breathe faster).

reported dyspnea as the most prevalent one following COVID-19.[21]

We found statistical significance of symptomatic patients' older mean ages compared to asymptomatic ones. As we know, elderly patients have higher mortality rates of COVID-19 and are more likely to progress to severe forms of the disease, so monitoring this group of patients for persistent symptoms has a momentous importance.[22]

In our study, women suffered from at least one of the persistent/late-onset COVID-19 complications more than men, this is in the same line with an Italian study,[14] but in contrast with a retrospective Nigerian study in which there was not any association between persistent symptoms and sex.[20] However, as we know from the past studies, men are more hospitalized;[23] we also found that persistent/late-onset COVID-19 complication were more frequent in those with a history of hospitalization. This statement is consistent with the results of a previously mentioned systematic review.[21]

We found that not having adequate rest after initiation of the illness and going back to work before recovery phase are significant factors for presence of persistent/late-onset complications. On the other hand, prevalence of persistent COVID-19 complications among patients who had regular physical exercises before their illness was lower than others, but the difference was not statistically significant. It seems that physical activity after illness may be associated with lower prevalence of all persistent COVID-19 complications, showing that starting physical practices after illness could be a part of homecare advice for patients.[4, 24, 25]

We also found that psychological stress is a significant variable of persistent/late-onset complications development, as patients with higher level of psychological stress before their illness had more prevalence of persistent/late-onset complications. Some have suggested that chronic stress is a major risk factor for adverse COVID-19 outcomes and advise for stress reducing strategies in order to subside the inflammatory response, which is responsible for adverse complications.[26]

In the multivariable regression analysis, we found that female sex, non-adequate rest, and psychological distress were significantly associated with the presence of at least one of the persistent/late-onset complications of COVID-19. In a cohort study with a 4-month follow up, female sex was a predictor factor of persistent COVID-19 complications.[27] These all emphasize the importance of paying attention to adequate rest in the recovery phase and also management of psychological distress during the illness; therefore, team working with social workers, psychologists and psychiatrists in the follow up care of COVID-19 patients could play a significant role in lightening the load of persistent/late-onset complications.

This study was conducted in a large scale and included a considerable study population from the whole Tehran city; this is the strength of this study in comparison with previous studies conducted on the same population; this study still suffers from several limitations. It should be mentioned that although we evaluated the relationship between the occurrence of the complications and hospital

length of stay and ICU admission, we did not evaluate the impact of the disease severity based on the amount of lung involvement on long-term symptoms of COVID-19 which could be beneficial in future studies. Also, the interval between the interview and initiation of the disease was dissimilar among patients in our study, which could affect the analysis.

Conclusion

The findings of this study indicate that a significant number of patients will experience persistent/late-onset complications, both physically and mentally, after recovering from acute phase of COVID-19. Thus, physicians should have adequate resources and support to care for the patients to help them cope with the condition. Also, physicians should be aware of the long-term symptoms and complications in order to stop or reduce the chronic effects of the disease. It is suggested that the efficacy of multidisciplinary COVID-19 management strategies to track, diagnose, and perform rehabilitation and psychological programs should be assessed in future studies.

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