


Six-Month Post-Acute COVID-19: High Self-Reported Morbidity Among Adults Younger Than Sixty Years and Females

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To the Editor

The outbreak of novel coronavirus disease 2019 (COVID-19) has infected over 254 million people, causing 5.1 million deaths worldwide. Symptomatic COVID-19 patients who present with acute hypoxemic respiratory failure require hospital care where acute lifesaving measures can be implemented. The health consequences, however, go well beyond hospitalization [1]. Long-term sequelae across multiple medical domains, including the respiratory, psychiatric, infectious, rheumatologic, and neurocognitive have been reported after COVID-19 [2, 3]. Prevalence of these long COVID conditions vary from 5% to 80% depending upon the case definitions and population studied [4].

We aimed to describe the self-reported occurrence of symptoms and their effect on patient's functioning 6 months after their acute hospitalization for COVID-19.

From a historical cohort study of hospitalized COVID-19 patients in our hospital, we identified patients discharged home, between March 8 and June 14, 2020 [5]. COVID-19 was confirmed via reverse transcriptase-polymerase chain reaction assay of a nasopharyngeal swab. Patients were contacted by telephone 6 months after discharge. The purpose of the study was explained, and they were asked to consent to a telephone questionnaire. We used a modified version of a previously validated general symptom questionnaire (GSQ-30) to assess multi-system symptom burden among patients with post-treatment Lyme disease syndrome [6]. It is easy to administer and strongly correlates with the functional impairment among patients with multi-system disease. The Patient Health Questionnaire-2 (PHQ-2) was also used to screen for major depression. GSQ-30 questionnaire measures somatic, neurological and neuropsychiatric symptom burden. Each question had five options: "not at all", "a little bit", "somewhat", "quite a bit", and "very much", which

during analysis were converted into "yes" and "no" categories. Category "no" reflected option, "not at all". Demographic and clinical characteristics were available from the original study. The study was approved by the Institutional Review Board.

Of the original 565 patients, 258 patients were discharged home (45%) and had a telephone number on record. Of these, 57 (22%) patients were able to be contacted and agreed to participate in the survey. The mean (standard deviation (SD)) age of the respondents was 55.1 (14.8) years, 50 (87.7%) were black, and 37 (64.9%) were female. Of these patients, 37 (64.9%) patients had hypertension, 24 (42.1%) had diabetes and 43 (75.4%) were obese. Pneumonia was diagnosed in 35 (61.4%) patients at the index hospitalization. The most common symptoms at the time of follow-up were fatigue (60.0%), dyspnea (57.1%), feeling irritable, sad or decreased pleasure (56.4%), and memory difficulty (56.4%). The mean (SD) GSQ-30 score for the cohort was 30.1 (25.1). Females had a significantly higher mean (SD) GSQ-30 score than males (35.1 (26.5) versus 20.2 (19.3), $P = 0.02$).

We further stratified our cohort based on their age (Table 1) and sex (Table 2). Mean (SD) GSQ-30 score among patients ages < 60 year was 29.1 (25.4) compared to 32.1 (25.1), $P = 0.68$ among patients ages ≥ 60 years. Patients ages < 60 years tended to experience similar, if not worse, impaired functioning ($P = 0.07$) compared with those ages 60 years and above. Patients ages ≥ 60 years had more balance problems ($P = 0.02$). Severity of illness, need for intubation or intensive care unit (ICU) stay and length of hospitalization at the time of index hospitalization were not statistically different among patients ages less than 60 years compared to those over 60 years and above. Females were more vulnerable to the symptoms of fatigue, neurologic and neuropsychiatric domains than males (Table 2). Females had an increased incidence of needing more sleep than usual ($P = 0.05$), not feeling rested on awakening ($P = 0.04$), shooting, stabbing and burning pain ($P = 0.02$), discomfort with normal light and sound ($P = 0.04$), feeling irritable or sad ($P = 0.007$), feeling panicky, anxious or worried ($P = 0.001$), and memory difficulty ($P = 0.03$) than males.

Our study describes the clinical burden of post-acute COVID-19 (PAC-19) in four core domains: fatigue, neurological, neuro-psychiatric and viral-like symptoms using GSQ-30 questionnaire. GSQ-30 had been previously validated to assess the functional impairment post-treatment Lyme disease syndrome. Our findings, like previous studies, showed fatigue, and neu-

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Table 1. Self-Reported Post-Acute COVID Syndrome in Adults Younger Than 60 Versus Adults at or Older Than 60 Years

Modified GST-30 questionnaire	Age < 60 years, n = 38 (%)	Age ≥ 60 years, n = 19 (%)	P value
Sex			0.05
Male	10 (26.3)	10 (52.6)	
Female	28 (73.7)	9 (47.4)	
Insurance-public	16 (42.1)	17 (89.5)	< 0.01
Comorbidities			
Hypertension	20 (52.6)	17 (89.5)	< 0.01
Diabetes	15 (39.5)	9 (47.4)	0.57
Obesity	33 (86.8)	10 (62.5)	0.04
Mean Charlson score (SD)	0.61 (1.2)	1.6 (2.1)	0.03
COVID-19 symptoms at the time of hospitalization			
Altered mental status	2 (5.3)	2 (10.5)	0.46
Shortness of breath	28 (73.7)	15 (78.9)	0.66
Cough	33 (86.8)	14 (73.7)	0.22
Fever	30 (78.9)	8 (42.1)	0.005
Fatigue	22 (57.9)	11 (57.9)	1.0
Muscle aches	16 (42.1)	9 (47.4)	0.71
Nausea/vomiting	9 (23.7)	7 (36.8)	0.30
Headaches	3 (7.9)	4 (21.1)	0.15
Severe COVID-19 pneumonia	7 (18.4)	2 (10.5)	0.56
Outcomes at the time of hospitalization			
Ventilation	3 (7.9)	1 (5.3)	0.71
ICU admission	3 (7.9)	1 (5.3)	0.71
Length of hospitalization (SD)	7.0 (6.9)	5.7 (4.7)	0.40
Post COVID-19 sequelae			
Mean time to survey (SD)	7.5 (0.47)	7.4 (0.47)	0.49
Any ED visit	5 (13.2)	3 (15.8)	0.79
Any hospital readmission	4 (10.5)	2 (10.5)	1.00
Any new symptom	15 (44.1)	12 (70.6)	0.07
Viral-like symptoms			
Shortness of breath	21 (56.8)	11 (57.9)	0.94
Fever	5 (13.5)	5 (26.3)	0.24
Nausea and/or vomiting	6 (16.2)	4 (21.1)	0.66
Headaches	13 (35.1)	8 (42.1)	0.61
Fatigue symptoms			
Back pain	15 (40.5)	10 (52.6)	0.39
Stiff or painful neck	11 (29.7)	9 (47.4)	0.19
Muscle aches or pain	19 (52.8)	9 (47.4)	0.70
Joint pain or swelling	15 (41.7)	9 (47.4)	0.69
Muscle weakness	10 (27.8)	9 (47.4)	0.15
Feeling fatigue or having low energy	21 (58.3)	12 (63.2)	0.73
Feeling worse than before after exercise or after normal physical exertion	14 (37.8)	11 (57.9)	0.15
Insomnia/trouble falling or staying asleep	11 (30.6)	6 (31.6)	0.94

Table 1. Self-Reported Post-Acute COVID Syndrome in Adults Younger Than 60 Versus Adults at or Older Than 60 Years - (continued)

Modified GST-30 questionnaire	Age < 60 years, n = 38 (%)	Age ≥ 60 years, n = 19 (%)	P value
Needing more sleep than usual	15 (41.7)	7 (38.9)	0.85
Not feeling rested on awakening	17 (47.2)	8 (42.1)	0.72
Neurological symptoms			
Numbness and tingling	11 (30.6)	10 (55.6)	0.08
Shooting, stabbing and burning pains	11 (30.6)	6 (31.6)	0.94
Skin or muscle twitching	6 (16.7)	5 (26.3)	0.40
Discomfort with normal light and sound	5 (13.9)	2 (10.5)	0.72
Balance problems or sense of room-spinning	13 (36.1)	13 (68.4)	0.02
Change in visual clarity or trouble focusing	15 (41.7)	7 (36.8)	0.73
Bladder discomfort or change in urination	5 (13.9)	5 (26.3)	0.26
Light-headed or uncomfortable on standing	13 (36.1)	7 (36.8)	0.96
Hot or cold sensations in extremities	5 (13.9)	4 (21.1)	0.50
Irregular or rapid heart beats	13 (36.1)	8 (42.1)	0.66
Neuropsychiatric symptoms			
Feeling irritable, sad or decreased pleasure	22 (61.1)	9 (47.4)	0.33
Feeling panicky, anxious or worried	22 (61.1)	7 (36.8)	0.09
Trouble finding words or retrieving names	14 (38.9)	7 (36.8)	0.88
Trouble with memory	19 (52.8)	12 (63.2)	0.46
Slower speed of thinking	17 (47.2)	11 (57.9)	0.45
Symptoms Impaired functioning	17 (45.9)	4 (21.1)	0.07
Major depression per PHQ-2	11 (29.7)	5 (26.3)	0.79

COVID-19: coronavirus disease 2019; SD: standard deviation; ICU: intensive care unit; ED: emergency department; PHQ-2: Patient Health Questionnaire-2.

Table 2. Self-Reported Post-Acute COVID Syndrome in Female Versus Male Adults

Modified GST-30 Questionnaire	Males, n = 20 (%)	Females, n = 37 (%)	P value
Race			
White	2 (10)	5 (13.5)	0.7
Black/African-American	18 (90)	32 (86.5)	
Insurance-public	14 (70.0)	19 (51.4)	0.17
Comorbidities			
Hypertension	14 (70%)	23(62.2)	0.55
Diabetes	10 (50.0)	14 (37.8)	0.38
Obesity	10 (55.6)	33 (91.7)	0.002
COVID-19 symptoms at the time of hospitalization			
Altered mental status	2 (10.0)	2 (5.4)	0.52
Shortness of breath	13 (65.0)	30 (81.1)	0.18
Cough	15 (75.0)	32 (86.5)	0.28
Fever	11 (55.0)	27 (73.0)	0.17
Fatigue	11 (55.0)	22 (66.7)	0.75
Muscle aches	8 (40.0)	17 (45.9)	0.67
Nausea/vomiting	4 (20.0)	12 (32.4)	0.32
Headaches	2 (10.0)	5 (13.5)	0.70
Outcomes at the time of hospitalization			

Table 2. Self-Reported Post-Acute COVID Syndrome in Female Versus Male Adults - (continued)

Modified GST-30 Questionnaire	Males, n = 20 (%)	Females, n = 37 (%)	P value
Ventilation	1 (5.0)	3 (8.1)	0.66
ICU admission	1 (5.0)	3 (8.1)	0.66
Length of hospitalization (SD)	6.1 (4.2)	6.9 (7.2)	0.60
Post COVID-19 sequelae			
Any ED visit	2 (10.0)	6 (16.2)	0.52
Any hospital readmission	2 (10.0)	4 (10.8)	0.92
Any new symptom	8 (44.4)	19 (57.6)	0.37
Mean GSQ score (SD)	20.2 (19.3)	35.1 (26.5)	0.02
Viral-like symptoms			
Shortness of breath	8 (42.1)	24 (64.9)	0.10
Fever	3 (15.8)	7 (18.9)	0.77
Nausea and/or vomiting	1 (5.3)	9 (24.3)	0.08
Headaches	4 (21.1)	17 (45.9)	0.07
Fatigue symptoms			
Back pain	6 (31.6)	19 (51.4)	0.16
Stiff or painful neck	4 (21.1)	16 (43.2)	0.10
Muscle aches or pain	11 (57.9)	17 (47.2)	0.45
Joint pain or swelling	6 (31.6)	18 (50.0)	0.19
Muscle weakness	6 (31.6)	13 (36.1)	0.74
Feeling fatigue or having low energy	10 (52.6)	23 (63.9)	0.42
Feeling worse than before after exercise or after normal physical exertion	7 (36.8)	18 (48.6)	0.40
Insomnia/trouble falling or staying asleep	4 (21.1)	13 (36.1)	0.25
Needing more sleep than usual	4 (22.2)	18 (50.0)	0.05
Not feeling rested on awakening	5 (26.3)	20 (55.6)	0.04
Neurological symptoms			
Numbness and tingling	7 (38.9)	14 (38.9)	1.00
Shooting, stabbing and burning pains	2 (10.5)	15 (41.7)	0.02
Skin or muscle twitching	2 (10.5)	9 (25.0)	0.20
Discomfort with normal light and sound	0 (0.0)	7 (19.4)	0.04
Balance problems or sense of room-spinning	7 (36.8)	19 (52.8)	0.26
Change in visual clarity or trouble focusing	6 (31.6)	16 (44.4)	0.35
Bladder discomfort or change in urination	3 (15.8)	7 (19.4)	0.74
Light-headed or uncomfortable on standing	4 (21.1)	16 (44.4)	0.09
Hot or cold sensations in extremities	1 (5.3)	8 (22.2)	0.11
Irregular or rapid heart beats	4 (21.1)	17 (47.2)	0.06
Neuropsychiatric symptoms			
Feeling irritable, sad or decreased pleasure	6 (31.6)	25 (69.4)	0.007
Feeling panicky, anxious or worried	4 (21.1)	25 (69.4)	0.001
Trouble finding words or retrieving names	5 (26.3)	16 (44.4)	0.19
Trouble with memory	7 (36.8)	24 (66.7)	0.03
Slower speed of thinking	8 (42.1)	20 (55.6)	0.34
Symptoms impaired functioning	7 (35.0)	14 (38.9)	0.77
Major depression per PHQ-2	3 (15.0)	13 (36.1)	0.09

COVID-19: coronavirus disease 2019; SD: standard deviation; ICU: intensive care unit; ED: emergency department; GSQ: General Symptom Questionnaire; PHQ-2: Patient Health Questionnaire-2.

ropsychiatric symptoms as the most common complaints in COVID-19 survivors [2, 7]. Notably, the younger participants reported significant morbidity, if not worse, than older patients. Over 45% of patients ages < 60 years suffered impaired functioning, compared with 21.1% of patient's ages 60 years and above. This difference approached statistical significance, but larger studies can validate these results. Therefore, early rehabilitation may be targeted for all the COVID-19 survivors.

Females have been reported to be disproportionately affected by psychiatric sequela [7, 8]. Women and severity of illness has been described as predictors for persistent psychological symptoms [9]. Higher levels of anxiety and depression have been reported earlier among COVID-19 survivors [3, 7, 9]. In our study, females more likely felt sad, irritable, anxious and troubled with memory problems. Our study findings of significantly higher GSQ-30 scores in females compared to men strongly correlates with the functional impairment among the females. Thus, there is utmost urgency to develop a framework and strategy to address this post infectious condition which is causing a great degree of morbidity among younger and female COVID-19 survivors [10].

This study was limited by the relatively low response rate and lack of comparative baseline data on depression. The low response rate, however, was primarily because of not being able to contact people, versus people not agreeing to the survey. Many people who responded to the survey expressed gratitude that the hospital had reached out to see how they were doing. Nevertheless, we provide new information to better understand the full spectrum of PAC-19. Larger studies are needed to further validate our findings.

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Conflict of Interest

We presented this work at ID week 2021 as poster presentation.

Informed Consent

Not applicable.

Author Contributions

AB contributed to the study design, analysis and manuscript

writing. WZ contributed to the preparation of data and manuscript preparation. MS contributed in study design, and manuscript editing. SS did data analysis, and manuscript preparation and editing. LS contributed in study design, and manuscript editing.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author

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