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Predictors of impaired functioning among long COVID patients

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Abstract.
BACKGROUND: There is limited information on which acute factors predict more long-term symptoms from COVID-19.
OBJECTIVE: Our objective was to conduct an exploratory factor analysis of self-reported symptoms at two time points of Long COVID-19.
METHODS: Data from patients with Long COVID-19 were collected at the initial two weeks of contracting SARS CoV-2 and the most recent two weeks, with a mean duration of 21.7 weeks between the two-time points. At time point 2, participants also completed the Coronavirus Impact Scale (CIS), measuring how the COVID-19 pandemic affected various dimensions of their lives (e.g., routine, access to medical care, social/family support, etc.).
RESULTS: At time 1, a three-factor model emerged consisting of Cognitive Dysfunction, Autonomic Dysfunction and Gastrointestinal Dysfunction. The analysis of time 2 resulted in a three-factor model consisting of Cognitive Dysfunction, Autonomic Dysfunction, and Post-Exertional Malaise. Using factor scores from time 1, the Autonomic Dysfunction and the Gastrointestinal Dysfunction factor scores significantly predicted the CIS summary score at time two. In addition, the same two factor scores at time 1 predicted the occurrence of myalgic encephalomyelitis/chronic fatigue syndrome at time 2.
CONCLUSION: Cognitive and Autonomic Dysfunction emerged as factors for both time points. These results suggest that healthcare workers might want to pay particular attention to these factors, as they might be related to later symptoms and difficulties with returning to pre-illness family life and work functioning.

Keywords: Long COVID-19, SARS CoV-2 virus, PASC, exploratory factor analysis, myalgic encephalomyelitis/chronic fatigue syndrome

1. Introduction

The typical symptoms of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) are fatigue, fever or chills, shortness of breath, and the new loss of taste or smell. Other common symptoms can include trouble breathing and persistent pain or pressure in the chest [1–3]. Many of those infected with SARS-CoV-2 have not fully recovered and exhibit continuing and new symptoms [4]. Some of the continuing symptoms include fatigue, muscle aches, cardiac issues, and rashes. In addition, some patients have developed lung scarring, blood clots, renal failure, neurological complications [5], and heart damage [6]. This continuation and development of new symptoms, once the presence of the SARS-CoV-2 virus no longer exists in the person, has been referred to as "long COVID" or Post-Acute Sequelae of SARS CoV-2 infection (PASC) [7, 8].

Estimates vary in terms of how many have PASC after being infected with SARS CoV-2 [9]. In one of the more comprehensive reviews, Chen et al.'s [10] meta-analysis found that the worldwide prevalence of the post COVID-19 condition was 37% at 1 month after infection, 25% at 2 months, 32% at 3 months, and 49% at 4 months. The most commonly reported symptoms of post-COVID-19 infection include, in

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rank order, fatigue, muscle or body aches, shortness of breath, and difficulty concentrating or focusing [11, 12]. In a systematic review of 15 studies involving 47,910 patients examining the long-term effects of COVID, Lopez-Leon and colleagues [13] found that 80% of the infected patients developed one or more long-term symptoms, with the five most common symptoms being fatigue, headache, attention disorder, hair loss, and dyspnea. In another study of patients, the most frequent symptoms after month 6 were fatigue, post-exertional malaise, and cognitive dysfunction [14]. Nehme et al. [15] found 39% reported residual symptoms 7 to 9 months after COVID-19 diagnosis. Fatigue was the most common symptom reported, followed by loss of taste or smell, dyspnea, and headache. Huang et al. [16] found that 55% of COVID-19 survivors reported at least one sequelae symptom 2 years later, with fatigue and muscle weakness as the most commonly reported symptoms. In their review article, Whittaker et al. [17] found that headache and anosmia were common neurological manifestations of SARS-CoV-2.

Sudre et al. [18] found that experiencing more than five symptoms during the first week of illness was associated with Long COVID. Sue et al. [19] followed over 200 patients for two to three months after their COVID diagnoses and found four factors that helped predict if a person will develop Long COVID (i.e., level of coronavirus RNA in the blood early in the infection, the presence of certain autoantibodies, the reactivation of Epstein-Barr virus, and having Type 2 diabetes).

Other studies have tried to group the symptoms into categories. Giszas et al. [20] recruited a sample of 909 participants at a median interval of 367 days after acute SARS-CoV-2 infection, and 71% complained of having experienced persistent symptoms at a median interval of 367 days after acute SARS-CoV-2 infection. Two subgroups emerged, with quality of life being normal in 71% and markedly diminished in 29%. D'Cruz and colleagues [21] identified seven domains for PASC symptoms, which are neurocognitive, autonomic, gastrointestinal, respiratory, musculoskeletal, psychological, and "others." Other investigators have used statistical strategies to identify phenotypes. Kenny et al. [22] used multiple correspondence analysis and hierarchical clustering to find 3 clusters. The first had predominantly pain symptoms, the second had a preponderance of cardiovascular symptoms, and the third cluster had significantly fewer symptoms than the others. Hughes et al. [23] developed a symptom burden questionnaire for Long COVID with promising psychometric methods, but it is somewhat long with 17 independent scales tapping 131 items. Luo et al. [24] recruited patients from outpatient and inpatient hospitals and used a principal components analysis that resulted in a five factor model. They labeled these factors as respiratory-digestive-related, nervous system-related, cough-related, upper respiratory tract-related, and digestive-related factors. A limiting factor in this study was that there were only 60 participants. In another study, Yifan et al. [25] provided 140 nurses with a questionnaire measuring somatic symptoms. A positive aspect of their questionnaire was that it measured the symptoms' frequency and severity. They found three factors: "breathing and sleep disturbance", "gastrointestinal complaints and pain", and "general symptoms." A drawback of their study was the Kaiser-Meyer-Olkin Test indicated the sample size was not adequate.

Guo et al. [26] recently performed two Principal Component Analyses (PCA), with the first involving the initial symptoms and the second involving symptoms experienced since the initial phase. Their first PCA, revealed five components of Neurological/Psychiatric, Fatigue/Mixed, Gastrointestinal, Respiratory/Infectious, and Dermatological. Their second PCA found Neurological, Gastrointestinal/Autoimmune, Cardiopulmonary/Fatigue, Dermatological/Fever, Appetite Loss, and Mood. In addition, neurological/psychiatric and fatigue/mixed symptoms during the initial illness and neurological, gastrointestinal, and cardiopulmonary/fatigue symptoms during the ongoing illness, predicted the experience of cognitive symptoms. While PCA can reduce correlated observed variables to a smaller set of independent composite variables, factor analysis has the advantage to identify the latent or hidden constructs.

There are few factor analysis studies of Long-COVID symptoms, and they have rarely compared symptomatology at early points of illness to later points. The current study examined reported symptoms at two time points so as to identify factor analytic latent changes over time. The study also examined predictors of the impact of COVID-19 as well as whether patients met a myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) case definition. Key features of this ME/CFS are post-exertional malaise, cognitive impairment, and unrefreshing sleep, which also are found in Long COVID.

2. Method

2.1. Participants

In August of 2020, the authors obtained IRB permission to distribute questionnaires to long-haulers, those who had self-reported not recovering from COVID-19. The questionnaires were posted on several social media sites, which are devoted to the exchange of information among long-haulers. Participants were asked to complete two symptom questionnaires at one time point, with one describing current symptoms (time point 2) and one recounting experiences from an average of 21.7 weeks prior (time point 1). The participants were not provided incentives for filling out the questionnaires (For more details, see [27, 28]). Table 1 provides demographic characteristics of the sample.

2.2. Measures

2.2.1. The DePaul Symptom Questionnaire

Participants completed the DePaul Symptom Questionnaire (DSQ-1) [29], a 54-item self-report measure of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome symptomatology. Participants were asked to rate the frequency of each symptom over the past six months on a five-point Likert scale with 0 = none of the time, 1 = a little of the time, 2 = about half the time, 3 = most of the time, and 4 = all of the time. Likewise, participants were asked to rate the severity of each symptom over the past six months on a five-point Likert scale with 0 = symptom not present, 1 = mild, 2 = moderate, 3 = severe, and 4 = very severe. All frequency and severity scores were standardized to a 100-point scale. All frequency and all severity scores were multiplied by 25 to create scores from 0 to 100. These frequency and severity scores were averaged for each symptom to create a composite score.

Table 1
Sociodemographic information

	Demographic	N = 299 *M* (SD)
Age (years)	44.01 (12.9)	
Illness duration (weeks)	21.3 (8.0)	
Gender		% (n)
	Male	15.7 (47)
	Female	81.6 (244)
	Nonbinary	1.7 (5)
Race		
	White/Caucasian	90.3 (270)
	Other	7 (21)
	Asian/Pacific Islander	3.3 (10)
	Black/African American	1.7 (5)
	Latinx	7.4 (22)

The DSQ-1 has demonstrated high test-retest reliability among persons with ME/CFS and controls [30], shown strong internal consistency [31], and yielded valid, clinically useful results [32, 33]. Moreover, the DSQ-1 has been used to accurately differentiate those with ME/CFS from those with other chronic illnesses [34, 35]. The DSQ-1 is available in the shared library of Research Electronic Data Capture ([REDCap]; 36). The full questionnaire can be viewed at this url: https://redcap.is.depaul.edu/surveys/?s=tRxytSPVVw.

2.2.2. COVID-19 symptoms

The CDC lists several additional symptoms of COVID-19 on their website: https://www.cdc.gov/coronavirus/2019-ncov/downloads/COVID19-symptoms-24x36-en.pdf. These items included: dry cough, loss of taste/smell, difficulty breathing, diarrhea, nose congestion, and loss of hair. As these items were not on the DSQ, they were added to the survey that was completed by the COVID-19 sample.

2.2.3. Coronavirus Impact Scale (CIS)

Participants were asked to complete the CIS [37]. The 12-item questionnaire consists of 4-point Likert scale questions and one open-ended question that assesses how the COVID-19 pandemic has affected various dimensions of a person's life (e.g., routine, access to medical care, social/family support, etc.). The first eight questions assess the respondents' experiences while the rest ask about extended family members and friends. A CIS summary score was computed by taking the sum of the first eight questions. The instrument has demonstrated good reliability and validity [38].

2.2.4. Case definition for ME/CFS

The Canadian Consensus Criteria (CCC; [39]) requires the person to experience the following: (1) fatigue, (2) PEM, (3) sleep dysfunction, (4) pain, (5) two or more neurocognitive symptoms, and (6) symptoms that are within two areas of the following domains: autonomic, neuroendocrine, or immune. The ME/CFS case definition requires symptom persistence of six or more months and a substantial reduction in functioning. Substantial reduction in function was a self-report item in the DSQ in which

persons responded to a binary item: "Since the onset of your problems with fatigue/energy, have your symptoms caused a 50% or greater reduction in your activity level?" This item has been found to be as accurate as longer scales to identify patients with a substantial reduction in functioning [40]. 48.8% of participants at time point 2 met the Canadian diagnostic criteria for ME/CFS.

2.3. Statistical analysis and method for replacing missing values

301 participants missing 10% or more of items from the DSQ-1 were removed from analyses in the current study. For those remaining participants, missing values were replaced using a method dependent on the nature of the missing value. Participants could have missing data for either the frequency, the severity, or for both dimensions of a symptom. When a participant reported a "0" for either the frequency or the severity of a symptom (but not both), the corresponding missing score was replaced with a "0." For instance, if a participant reported "0" for the frequency of a specific symptom, we imputed a "0" for the severity of that symptom. We reasoned that a symptom should occur "none of the time" (frequency = 0) if the symptom is "not present" (severity = 0). Next, if a participant reported a frequency or severity score greater than "0" for a symptom but did not report a corresponding frequency or severity score, we reviewed every case from the total sample that matched the participant's reported score and used those cases to calculate the mode of the corresponding scores. The mode of the corresponding scores was used to replace the participant's missing value. For instance, if a participant responded "2" for the frequency of a symptom but was missing data for the severity of that symptom, the missing severity score would be imputed by calculating the mode severity score for every case that also reported a "2" for the frequency of that symptom. Finally, if a participant was missing scores for both frequency and severity of a symptom, both missing scores were replaced with the overall median scores for that symptom among the rest of the population.

2.4. Statistical analysis

IBM SPSS Statistics version 25 [41] and R 4.1.0 statistical software (R Foundation for Statistical Computing, Vienna, Austria) were used for all analyses. An exploratory factor analysis was performed on the 100-point symptom composite scores. A Promax rotation (kappa = 4) was used to allow the factors to correlate, and the principal axis factoring method was selected to determine the maximum amount of common variance between the factors. We determined the appropriate number of factors to retain by constructing a parallel analysis using 5000 iterations of our data using permutations and comparing the changes in eigenvalues across consecutive factors to those of our actual data. Factors from the actual data were retained so long as their respective eigenvalue exceeded that of the random data based on a 95% confidence interval. Of the factors that were retained, those preceding the Scree plot's point of inflection were assumed to be meaningful. Symptoms that did not load onto any of the factors (rotated loading <0.40) were dropped, and the analysis was repeated until all symptoms loaded onto a factor.

3. Results

3.1. Initial symptoms during first two weeks

Prior to running an exploratory factor analysis on the sample, the adequacy of the correlation matrix was examined for items with high (>0.9) and low (<0.3) correlations to ensure multicollinearity was not present. The item alcohol intolerance was removed as it correlated less than 0.3 with all items. Bartlett's test of sphericity was significant indicating the correlation matrix was not an identity matrix. Kaiser–Meyer–Olkin's measure of sampling adequacy (0.94) indicated that the matrix was appropriate for an exploratory factor analysis. Thereafter, the pattern matrix was evaluated, and items loadings below 0.4 were removed until all item loadings were 0.4 or above. Eigenvalues were then examined and three factors were identified based on the Scree plot. A parallel analysis was conducted and no additional factors needed to be added. Based on the Scree plot, a three-factor model was selected, and an exploratory factor analysis was conducted. The three factors were (1) "Cognitive Dysfunction", (2) "Autonomic Dysfunction", and (3) "Gastrointestinal Dysfunction" (See Table 2). Factors 1, 2, and 3 explained 43.2%, 7.8 %, and 5.9% respectively, a total of 56.8%.

3.2. Most recent two weeks

Before running an exploratory factor analysis on the sample, the adequacy of the correlation matrix

Table 2
Time 1 factor loadings for each symptom (N = 299)

	Factor scores		
	Cognitive dysfunction	Autonomic dysfunction	Gastrointestinal dysfunction
Absent-mindedness or forgetfulness	0.94		
Slowness of thought	0.94		
Problems remembering things	0.92		
Difficulty finding the right word to say or expressing thoughts	0.89		
Only able to focus on one thing at a time	0.86		
Difficulty paying attention for a long period of time	0.86		
Difficulty understanding things	0.85		
Unable to focus vision and/or attention	0.77		
Minimum exercise makes you physically tired		0.82	
Fatigue / extreme tiredness		0.78	
Physically drained or sick after mild activity		0.77	
Next day soreness or fatigue after non-strenuous, everyday activities		0.74	
Dead, heavy feeling after starting to exercise		0.73	
Need to nap daily		0.63	
Feeling unrefreshed after you wake up in the morning		0.63	
Dizziness or fainting		0.60	
Shortness of breath or trouble catching your breath		0.60	
Mentally tired after the slightest effort		0.56	
Feeling like you had a high temperature		0.55	
Pain or aching in your muscles		0.54	
Fever		0.53	
Feeling hot or cold for no reason		0.53	
Pain / stiffness / tenderness in more than one joint without swelling or redness		0.52	
Feeling chills or shivers		0.51	
Headaches		0.51	
Difficulty breathing		0.50	
Feeling unsteady on your feet, like you might fall		0.49	
Chest pain		0.47	
Abdomen / stomach pain			0.77
Irritable bowel problems			0.74
Bloating			0.69
Diarrhea			0.69
Nausea			0.54

Extraction method: Principal axis factoring. Rotation method: Promax with Kaiser normalization. Rotation converged in 8 iterations.

was examined for items with high (>0.9) and low (<0.3) correlations to ensure multicollinearity was not present. Two items, namely alcohol intolerance and sweating, that correlated less than 0.3 with all items were removed. Bartlett's test of sphericity was significant indicating the correlation matrix was not an identity matrix. KMO measure of sampling adequacy (0.94) also indicated that the matrix was appropriate. Thereafter, the pattern matrix was evaluated, and items loadings below 0.4 were removed until all item loadings were 0.4 or above. 25 items were removed. Eigenvalues were then examined and three factors were identified based on the Scree plot. A parallel analysis was conducted and no additional factor needed to be added. Based on the Scree plot, a three-factor model was selected, and an exploratory factor analysis was conducted. The three factors were labeled (1) "Cognitive Dysfunction" (2) "Autonomic Dysfunction" and (3) "Post-Exertional Malaise" (See Table 3). Factors 1, 2, and 3 explained 42.5%, 6.8 %, and 5.7% respectively, a total of 55.0%.

3.3. Factor scores

Factor scores for the first two weeks of symptoms (time 1) were computed by multiplying each variable

Table 3
Time 2 factor loadings for each symptom (N = 299)

	Factor scores		
	Cognitive dysfunction	Autonomic dysfunction	Post-exertional malaise
Problems remembering things	0.95		
Absent-mindedness or forgetfulness	0.91		
Difficulty understanding things	0.89		
Only able to focus on one thing at a time	0.87		
Slowness of thought	0.86		
Difficulty breathing	0.85		
Difficulty finding the right word to say or expressing thoughts	0.84		
Unable to focus vision and/or attention	0.69		
Feeling chills or shivers		0.64	
Feeling hot or cold for no reason		0.64	
Problems staying asleep		0.63	
Irritable bowel problems		0.63	
Cold limbs (e.g. arms, legs, hands)		0.62	
No appetite		0.59	
Waking up early in the morning (e.g. 3am)		0.59	
Nausea		0.55	
Diarrhea		0.50	
Feeling like you had a high temperature		0.47	
Some smells, foods, medication, or chemical make you feel sick		0.42	
Problems falling asleep		0.42	
Minimum exercise makes you physically tired			0.95
Physically drained or sick after mild activity			0.90
Dead, heavy feeling after starting to exercise			0.80
Next day soreness or fatigue after non-strenuous, everyday activities			0.73
Fatigue / extreme tiredness			0.66
Mentally tired after the slightest effort			0.50

Extraction method: Principal axis factoring. Rotation method: Promax with Kaiser normalization. Rotation converged in 6 iterations.

by its loading and summing them up. These factor scores were related to CIS and the Canadian Consensus Criteria at the most recent two weeks (time 2).

3.4. Predicting participant scores on the CIS

Multiple linear regression was used to test if the three factors (Cognitive Dysfunction, Autonomic Dysfunction and Gastrointestinal Dysfunction) at time 1 significantly predicted the CIS scores at time 2. The overall regression was statistically significant ($R^2 = 0.20$, $F(3, 284) = 23.78$, $p < .000$). The Autonomic Dysfunction factor score significantly predicted CIS ($\beta = 0.004$, $p < .000$), and the Gastrointestinal Dysfunction factor score significantly predicted CIS ($\beta = 0.008$, $p < .002$). The Cognitive Dysfunction factor score did not significantly predict CIS ($\beta = 0.001$, $p = .34$).

3.5. Predicting ME/CFS in COVID-19 participants

Logistic regression was used to analyze the relationship between three factors (Cognitive Dysfunction, Autonomic Dysfunction, and Gastrointestinal Dysfunction) at the time 1 and Canadian ME/CFS diagnosis at time 2. The resulting model explained 0.166 (Nagelkerke R Square) of the variation in meeting the Canadian Criteria Diagnosis. It correctly classified 65.9% of cases. The Autonomic Dysfunction factor score significantly predicted the occurrence of the Canadian Consensus ME/CFS case definition ($\beta = 0.002$, $p < .001$), and the Gastrointestinal Dysfunction significantly predicted the occurrence of the Canadian Consensus ME/CFS case definition ($\beta = 0.003$, $p < .04$). The Cognitive Dysfunction was not a significant predictor ($\beta = 0.000$, $p = .81$).

4. Discussion

This study assessed the latent constructs of Long COVID-19 at two time points with a statistically adequate sample size. Many prior studies have either not examined Long COVID over time, had small sample sizes, or did not use sophisticated classification methods. Our study found that two factors emerged during both time points, namely Autonomic and Cognitive Dysfunction, suggesting that these two domains represent important phenotypes of acute COVID and Long COVID. Equally important are our findings that a different third factor was present at each time point. At the onset of COVID-19, gastrointestinal symptoms emerged as a factor, while post-exertional malaise symptoms emerged at time 2. Finally, higher levels of autonomic and gastrointestinal symptoms during the onset of COVID-19 appear to be predictive of greater impairment at time 2, as measured by the CIS and case definition ME/CFS.

Our study found that Cognitive and Autonomic Dysfunction emerged as factors for both time points, suggesting they are promising symptom constructs for acute COVID and Long-COVID. This finding is in line with the several studies that measured COVID symptoms [23]. For example, D'Cruz and colleagues [21] identified neurocognitive and autonomic domains among the seven key domains of PASC. Of the limited number of factor and principal factor analyses conducted for two times, some similar findings did emerge with Guo et al.'s study [26], which found neurological/psychiatric symptoms at the first time point and neurological and gastrointestinal/autoimmune symptoms at the second time point. However, we used different statistical methods than Guo et al. [26], making comparisons more difficult. Still, our findings of Cognitive and Autonomic Dysfunction as key factors can serve as a focal point for further research so to help develop phenotypes of acute and Long COVID.

We also found that gastrointestinal symptoms may be predictive of later functioning as measured by the CIS and ME/CFS criteria. D'Cruz and colleagues [21] similarly found that gastrointestinal symptoms were a key domain of PASC. Additionally, Yifan and colleagues' [25] factor analysis of COVID symptoms resulted in three factors that included "gastrointestinal complaints and pain." Furthermore, Huber and colleagues [42] identified that ME/CFS could be differentiated into several subtypes, and two included gastrointestinal symptoms. Gastrointestinal symptoms early on may be associated with later problems in several studies. For example, Johnson and colleagues [43] found that 40% of adults with ME/CFS reported having gastrointestinal symptoms occurring in their youth. Similarly, Jason and colleagues [44] found that both before and at the onset of mononucleosis among college students, gastrointestinal symptoms were predictive of ME/CFS after six months of infection. The prominence of this symptom in several studies suggests that it might represent an early marker for those who do not recover from viral illnesses.

In addition, another interesting finding was that post-exertional malaise during time 2 emerged as a factor. Davis et al. [14] also found that one of the most common symptoms after six months of infection was post-exertional malaise. While gastrointestinal symptoms initially emerged as a factor at time 1, these symptoms became less prominent after the acute illness. Conversely, post-exertional malaise became more pronounced over time. It is certainly likely that this might be related to the phenotype changing as endurance and stamina problems, as witnessed by post-exertional malaise items, become more prominent over time.

Gastrointestinal and Autonomic time 1 factor scores were predictors of a higher risk of the later impact of COVID as well as ME/CFS. We have already alluded to the potential importance of gastrointestinal symptoms, and our findings also suggest that early autonomic symptoms could also be a predictor of later functional problems. Jason et al. [45] identified risk factors for adolescent post-infectious ME/CFS, utilizing a prospective, longitudinal design in which over 300 teenagers with Infectious Mononucleosis were identified through primary care sites and followed. Baseline autonomic symptoms as well as days spent in bed since mono, which reflect the severity of illness, were the only significant predictors of those who met ME/CFS criteria at 6 months. Jason et al.'s [45] and the current one suggest that early autonomic factors could help underlie some of the fundamental mechanisms that predispose some individuals to not recover from infectious illnesses such as COVID and Infectious Mononucleosis.

A limiting factor of this study is that a substantial number of participants were White/Caucasian. In future research, it is important to recruit participants from more diverse racial backgrounds so that the findings are more generalizable. For our time 1 data, our study utilized retrospective self-reporting; however, a better design would be to collect data during the initial infection. Also, the time point 2 data were col-

lected at various times from the initial infection, and future studies should have a more consistent time for the second assessment. Another limitation is that we did not include a control group of individuals who were infected with SARS-CoV-2 yet did not have persisting symptoms. Such a group would have allowed us to document differences between the people who recover and those who develop Long COVID. A final limitation is that data were collected from individuals who found out about the study through social media sites, and this might have produced a biased sample.

5. Conclusion

Our study contributes to understanding the latent factors of the acute and longer term symptomology of COVID-19 by conducting exploratory factor analyses at two time points. In addition, our study was able to identify possible early acute factors that might be related to the later development of substantial limitations in functioning as well as the development of ME/CFS. Others have also found that COVID-19 survivors' symptom burden remains high with substantially lower health status [16]. Therefore, identifying underlying factors of acute COVID and Long COVID is key to developing predictive models that will aid in better understanding the pathophysiology of this illness. These types of findings could also be helpful to healthcare workers, as they may be able to identify patients with these early predictors and help them deter a negative trajectory that could impede functioning in both family and work arenas.

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Author contributions

Both authors contributed to the study's conception and design. Material preparation, data collection and analysis were performed by both authors. The first draft of the manuscript was written by LJ and both authors commented on previous versions of the manuscript. Both authors read and approved the final manuscript.

Conflict of interest

None to report.

Ethics statement

Ethics approval was obtained from DePaul University on August 21, 2020. Consent was obtained from all patients.

References

[1] Lechien JR, Chiesa-Estomba CM, Place S, Van Laethem Y, Cabaraux P, Mat Q, et al. Clinical and epidemiological characteristics of 1420 European patients with mild-to-moderate coronavirus disease 2019. J Intern Med. 2020;288(3):335-44.

[2] Popov GT, Baymakova M, Vaseva V, Kundurzhiev T, Mutafchiyski V. Clinical characteristics of hospitalized patients with COVID-19 in Sofia, Bulgaria. Vector Borne Zoonotic Dis. 2020;20(12):910-5.

[3] Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020;75(7):1730-41.

[4] Alwan AN. A negative COVID-19 test does not mean recovery. Nature. 2020;584(170).

[5] Parshley P. The emerging long-term complications of COVID-19, explained. 2020 May 8 [cited in Vox [Internet] (2020, May 30). https://www.vox.com/2020/5/8/21251899/coronavirus-long-term-effects-symptoms [Accessed 8 December 2020].

[6] Shi S, Qin M, Shen B, Cai Y, Liu T, Yamg F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiology. 2020;5(7):802-10.

[7] Callard F. Very, very mild: COVID-19 symptoms classification. Somatosphere. 2020. http://somatosphere.net/2020/mild-covid.html/ [Accessed 10 January 2021].

[8] Löwy I. Ludwik Fleck where are you now that we need you? Covid-19 and the genesis of epidemiological facts? Somatosphere. 2020. http://somatosphere.net/2020/ludwik-fleck-where-are-you-now.html/ [Accessed 25 January 2021].

[9] Komaroff AL, Bateman L. Will COVID-19 lead to myalgic encephalomyelitis/chronic fatigue syndrome? Front Med. 2021;7:606824.

[10] Chen CMA, Spencer R, Haupert, BS, Lauren Z, Xu S, Lars GF, Bhramar M. Global prevalence of post COVID-19 condition or long COVID: A meta-analysis and systematic review. The Journal of Infectious Diseases. 2022;jiac136. https://doi.org/10.1093/infdis/jiac136

[11] Body Politic COVID-19 Support Group. What does COVID-19 recovery look like? An analysis of the prolonged COVID-19 symptoms survey by patient-led research team. 2020. https://patientresearchcovid19.com/research/report-1/

[12] Lambert NJ, Survivor Corps. COVID-19 "long haulers" symptoms survey report. Published online July 7, 2020. https://static1.squarespace.com/static/5e8b5f63562c031c16e36a93/t/5f459ef7798e8b6037fa6c57/1598398215120/2020+Survivor+Corps+COVID19+%27Long+Hauler%27+Symptoms+Survey+Report+%28revised+July+25.4%29.pdf [Accessed 19 March 2021].

[13] Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo PA, Cuapio, A, et al. More than 50 long-term effects of COVID-19: A systematic review and meta-analysis. Scientific Reports. 2021;30;2021.01.27.21250617.

[14] Davis, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, Redfield S, Austin JP, Akrami A. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. EClinicalMedicine. 2021;38:101019-101019. https://doi.org/10.1016/j.eclinm.2021.101019

[15] Nehme M, Braillard O, Chappuis F, Courvoisier DS, Guessous I, CoviCare Study Team. Prevalence of symptoms more than seven months after diagnosis of symptomatic COVID-19 in an outpatient setting. Annals of Internal Medicine. 2021;174(9):1252-60. https://doi.org/10.7326/M21-0878

[16] Huang L, Li X, Gu X, Zhang H, Ren L, Guo L, Liu M, Wang Y, Cui D, Wang Y, Zhang X, Shang L, Zhong J, Wang X, Wang J, Cao B. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: A longitudinal cohort study. The Lancet Respiratory Medicine. 2022;S2213-2600(22)00126-6. Advance online publication. https://doi.org/10.1016/S2213-2600(22)00126-6

[17] Whittaker A, Anson M, Harky A. Neurological manifestations of COVID-19: A systematic review and current update. Acta Neurol Scand. 2020;142:14-22. doi: 10.1111/ane.13266

[18] Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. Nat Med. 2021;27:626-31. https://doi.org/10.1038/s41591-021-01292-y

[19] Su Y, Yuan D, Chen DG, Ng RH, Wang K, Choi J, et al. Multiple early factors anticipate post-acute COVID-19 sequelae. Cell. 2022;185(5):881-95.e20.

[20] Giszas B, Trommer S, Schüßler N, Rodewald A, Besteher B, Bleidorn J, . . . Reuken PA. Post-COVID-19 condition is not only a question of persistent symptoms: Structured screening including health-related quality of life reveals two separate clusters of post-COVID. Infection. Published online, July 22, 2022. https://doi.org/10.1007/s15010-022-01886-9

[21] D'Cruz, RF, Waller MD, Perrin F, Periselneris J, Norton S, Smith L-J, et al. Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. ERJ Open Research. 2021;7(1):00655-2020.

[22] Kenny G, McCann K, O'Brien C, Savinelli S, Tinago W, Yousif O, Lambert JS, O'Broin C, Feeney ER, De Barra E, Doran P, Mallon PWG. All-Ireland Infectious Diseases (AIID) cohort study group, identification of distinct long COVID clinical phenotypes through cluster analysis of self-reported symptoms. Open Forum Infectious Diseases. 2022;9(4):ofac060. https://doi.org/10.1093/ofid/ofac060

[23] Hughes SE, Haroon S, Subramanian A, McMullan C, Aiyegbusi OL, Turner GM . . . Calvert MJ. Development and validation of the symptom burden questionnaire for long covid (SBQ-LC): Rasch analysis. British Medical Journal. 2022;377:e070230. doi: 10.1136/bmj-2022-070230

[24] Luo Y, Wu J, Lu J, Xu X, Long W, Yan G, Tang M, Zou L, Xu D, Zhuo P, Si Q, Zheng X. Investigation of COVID-19-related symptoms based on factor analysis. Ann Palliat Med. 2020;9(4):1851-8. doi: 10.21037/apm-20-1113

[25] Yifan T, Ying L, Chunhong G, Jing S, Rong W, Zhenyu L, Zejuan G, Peihung L. Symptom cluster of ICU nurses treating COVID-19 pneumonia patients in Wuhan, China. Journal of Pain and Symptom Management. 2020;60(1).

[26] Guo P, Benito Ballesteros A, Yeung SP, Liu R, Saha A, Curtis L, Kaser M, Haggard MP, Cheke LG. COVCOG 1: Factors predicting physical, neurological and cognitive symptoms in long COVID in a community sample. A first publication from the COVID and cognition study. Front Aging Neurosci. 2022;14:804922. doi: 10.3389/fnagi.2022.804922

[27] Jason LA, Islam M, Conroy K, Cotler J, Torres C, Johnson M, et al. COVID-19 symptoms over time: Comparing long-haulers to ME/CFS. Fatigue: Biomedicine, Health & Behavior. 2021;9(2):59-68.

[28] Jason LA, Islam MF. A classification system for post-acute sequelae of SARS CoV-2 infection. Cent Asian J Med Hypotheses Ethics. 2022:3(1):38-51. https://doi.org/10.47316/cajmhe.2022.3.1.04

[29] Jason LA, Sunnquist M. The development of the DePaul Symptom Questionnaire: Original, expanded, brief, and pediatric versions. Frontiers in Pediatrics. 2018;6:330.

[30] Jason LA, So S, Brown AA, Sunnquist M, Evans M. Test–retest reliability of the depaul symptom questionnaire. Fatigue: Biomedicine, Health & Behavior. 2015;3(1): 16-32.

[31] Jason LA, Sunnquist M, Brown A, Furst J, Cid M, Farietta J, Kot B, Bloomer C, Nicholson L, Williams Y, Jantke R, Newton JL, Strand EB. Factor analysis of the DePaul Symptom Questionnaire: Identifying core domains. Journal of Neurology and Neurobiology. 2015;1(4). doi http://dx.doi.org/10.16966/2379-7150.114

[32] Jason LA, Sunnquist M, Brown A, Evans M, Vernon SD, Furst J, Simonis V. Examining case definition criteria for chronic fatigue syndrome and myalgic encephalomyelitis. Fatigue: Biomedicine, Health & Behavior. 2014;2(1):40-56.

[33] Murdock KW, Wang XS, Shi Q, Cleeland CS, Fagundes CP, Vernon SD. The utility of patient-reported outcome measures among patients with myalgic encephalomyelitis/chronic fatigue syndrome. Quality of Life Research. 2017;26(4):913-21.

[34] Klebek L, Sunnquist M, Jason LA. Differentiating post-polio syndrome from myalgic encephalomyelitis and chronic fatigue syndrome. Fatigue: Bio Health Beh. 2019;7(4):196-206. https://doi.org/10.1080/21641846.2019.1687117

[35] Ohanian D, Brown A, Sunnquist M, et al. Identifying key symptoms differentiating Myalgic Encephalomyelitis and Chronic Fatigue Syndrome from Multiple Sclerosis. EC Neurol. 2016;4(2):41-5.

[36] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research lectronic Data Capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. Journal of Biomedical Informatics. 2009;42:377-81.

[37] Kaufman J, Stoddard J. Coronavirus impact scale. Unpublished Manuscript. 2020. https://www.phenxtoolkit.org/toolkit_content/PDF/CIS_Stoddard.pdf

[38] Stoddard J, Reynolds EK, Paris R, Haller S, Johnson S, Zik J, et al. The coronavirus impact scale: Construction, validation, and comparisons in diverse clinical samples. PsyArXiv. https://doi.org/10.31234/osf.io/kz4pg

[39] Carruthers BM, Jain AK, De Meirleir KL. Myalgic encephalomyelitis/chronic fatigue syndrome: Clinical working case definition, diagnostic and treatment protocols (Canadian case definition). Journal of Chronic Fatigue Syndrome. 2003;11(1):7-115.

[40] Wiedbusch E, Jason LA. Comparing operationalized approaches for substantial reduction of functioning in Chronic Fatigue Syndrome and Myalgic Encephalomyelitis. Archives of Community Medicine. 2022;4(1):59-63. https://doi.org/10.36959/547/653

[41] IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

[42] Huber KA, Sunnquist M, Jason LA. Latent class analysis of a heterogeneous international sample of patients with myalgic encephalomyelitis/ chronic fatigue syndrome. Fatigue: Biomedicine, Health & Behavior. 2018;6(3):163-78. DOI: 10.1080/21641846.2018.1494530

[43] Johnson M, Torres C, Jason LA. Adults with ME/CFS report surprisingly high rates of youth symptoms: A qualitative analysis of patient blog commentary. WORK: A Journal of Prevention, Assessment & Rehabilitation. 2022.

[44] Jason LA, Cotler J, Islam MI, Furst J, Katz BZ. Predictors for developing severe Myalgic Encephalomyelitis/Chronic Fatigue Syndrome following Infectious Mononucleosis. Journal of Rehabilitation Therapy. 2022;4(1):1-5. https://doi.org/10.29245/2767-5122/2021/1.1129

[45] Jason LA, Katz BZ, Shiraishi Y, Mears CJ, Im Y, Taylor RR. Predictors of post-infectious chronic fatigue syndrome in adolescents. Health Psychology and Behavioral Medicine: An Open Access Journal. 2014;2:41-51. PMCID: PMC3956649.