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Post-infection chronic fatigue following coronavirus disease-19: cross sectional study

Faheem Mohammed Alanazi[1], **Waleed Khalid Alhowikan**[2*], **Dalia Ali Aljrary**[3], **Alanoud Abdullah Alqawili**[4], **Fahad Mohammed Algharbi**[5], **Hala Khamis Alghamdi**[6], **Hamad Bandar Alotaibi**[7], **Hamoud Shaya Alotaibi**[8], **Majed Maseer Almutairi**[9], **Rawan Hamdan Aljehani**[10], **Sarah Abdulhadi Algallaf**[11], **Saud Abdullah Alhasoun**[12]

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Authors' Affiliation:
[1]Emergency Consultant, Emergency Department, General Hospital King Saud Medical City, Riyadh, Kingdom of Saudi Arabia, cisco 011 - 837 1777, ext: 70012; Email: Faheem@ksmc.med.sa
[2]Emergency resident, Emergency department, General Hospital, King Saud medical city Riyadh, Kingdom of Saudi Arabia; Email: walhowikan@gmail.com: Orcid: 0000-0002-6505-1314
[3]Emergency resident, Emergency department, General Hospital, King Saud medical city Riyadh, Kingdom of Saudi Arabia
[4]General physician, Amaarefa University, Riyadh, Saudi Arabia
[5]Medical intern, Shaqra University, Saudi Arabia
[6]Medical intern, King Khalid University, Saudi Arabia
[7]General physician, Shaqra University, Saudi Arabia
[8]General physician, Taif University, Saudi Arabia
[9]Medical intern, Vision College of Medicine, Vision Colleges, Riyadh, Saudi Arabia.
[10]Medical intern, Alfaisal University, Saudi Arabia
[11]General physician, Imam Abdulrahman Ibn Faisal University, Saudi Arabia
[12]Medical intern, Imam Mohammed Ibn Saud Islamic University, Riyadh, Saudi Arabia

***Corresponding author**
Emergency resident, Emergency department, General Hospital, King Saud medical city Riyadh, Kingdom of Saudi Arabia
Saudi Arabia
Email: walhowikan@gmail.com

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ABSTRACT

Coronavirus disease has a wide range of symptoms, from asymptomatic infection to critical illness, which may even lead to death. Fatigue is the most prevalent symptom in COVID patients during and after the acute phase of the disease. Fatigue in COVID patients still with unknown etiology. This cross-sectional study used data from KSMC hospital records and direct interviews with patients affected by chronic fatigue following confirmed COVID. Data were analyzed using SPSS V24 and multiple regression analysis. Pearson correlation, chi square test were used in the analysis process. Our results found that vaccination status is strongly affecting chalder fatigue scale; also age, comorbidities and COVID severity affect the scale. Comorbidity was found to be high in older participants; also higher comorbidities associated with increased disease severity.

Keywords: Coronavirus disease, chronic fatigue, etiology, COVID patients

1. INTRODUCTION

SARS-CoV 2 virus is a cause of serious pandemic which was first originated in China, causing a disease of respiratory tract, coronavirus disease can range through a wide diversity of symptom from mild disease or even unrecognized infection which is only detected by laboratory investigations without apparent symptoms to severe infection which may need hospital admission, ICU admission, mechanical ventilation, or even lead to death. Most countries in the world were affected by the virus including 190 countries.

Recently it has been known that COVID may be followed with symptoms even after the recovery from the acute phase (Nehme et al., 2021). Post-acute phase symptoms of COVID can persist for a long period ranging from days to

months (Malik et al., 2022). "Long haulers" is a term which has been used to describe those patients who experienced these long term symptoms, it's sometimes called "long COVID" or "Post-acute COVID". According to the National Institute for Health and Care Excellence (NICE) guidelines on long COVID, long COVID is defined as the onset of symptoms during or after an infection consistent with COVID-19 that lasts for more than 4 weeks. When symptoms persist beyond 12 weeks after infection and cannot be attributed to another cause, NICE advises using the term post-COVID syndrome (Sivan and Taylor, 2022).

Fatigue, dyspnea, depression, arthralgia, headache, and sleeplessness were the most commonly reported symptoms, respectively (Malik et al., 2022). Chronic fatigue is a major problem for those who suffer from neurological diseases. Significant efforts have been made to understand the pathogenic mechanisms of weariness; yet, only a small amount of knowledge exists at the present time. For one thing, it's not always easy to pinpoint exactly what's going wrong and bringing on feelings of exhaustion. Possible causes of weariness include shifts in neurotransmitter levels, inflammation, psychiatric diseases, psychosocial strain, cognitive dysfunction, and metabolism abnormality (Rudroff et al., 2020). Reduced physical or mental performance after recovering from COVID-19 is characterized by a combination of variables, including alterations in central, psychological, and periphery (Rudroff et al., 2020). In this study, we assessed chronic fatigue in patients who were tested positive for COVID 19 at KSMC. Also, we correlated fatigue severity with COVID severity, comorbidities, and other demographic characteristics.

2. METHOD

From hospital records data, patients who were tested positive for COVID 19 RT-PCR in KSMC during the period from (1 Jan to 1 May 2021) whether they were admitted or not, were included in the study. Only patients with chronic fatigue of more than 6 months (National Academies Press, 2015) and who agreed to participate were included in the study. Data was collected in the period from (1 Aug to 15 Sep 2022) first from patients files in KSMC, the by direct interview or with voice call to assess patients fatigue status using Arabic-translated version of chalder fatigue scale (Chalder et al., 1993). The scale has convergent validity (Pace et al., 2013) and good internal consistency (Cella & Chalder. 2010). Likert scale from 0 to 3 was used with a range of total score from 0 to 33, only patients with chronic fatigue were included in the study (more than 6 months of fatigue after COVID 19 infection).

Comorbidity was assessed using charlson comorbidity index (Katz et al., 1996) which contains 18 physician-diagnosed diseases and categorized as (0, 1, ≥ 2). The severity of coronavirus disease was assessed using CDC guidelines for classifying COVID severity (National Institutes of Health, 2022). The range of disease spectrum from asymptomatic infection to critical illness depending on symptoms; (cough, fever, malaise, sore throat, vomiting, nausea, loss of smell or taste and diarrhea), SpO2, PaO2/FiO2 ratio, respiratory rate, lung infiltrate, respiratory failure and multiple organ failure. SPSS V24 was used for data analysis; frequency and percent analysis were performed on categorical variables, while descriptive statistics were performed for continuous variables. Multiple regression analysis was done to show the impact of (age, COVID severity, comorbidity, and vaccination status) on a chalder fatigue scale. To assess the correlation of disease severity with demographic variables and comorbidities Pearson correlation was used. Also, we used chi-square with fisher exact test to assess the relation of categorized age with categorized comorbidities.

The KSMC review board granted ethical approval and waivers of permission with the reference number (H1R1-23-Aug22-01). First the consent has been taken from KSMC to give the permission for data collection from patient's files. All data was collected and stored in optimum level of confidentiality, and no one had access to data only research authors and statisticians will do. Informed verbal consent was taken from the participants and we told them about the research process and no direct benefits they will get from this study, everyone who refused to participate was excluded.

3. RESULTS

289 subjects participated in this cross sectional study, the mean age is 45.5 with the majority of females 61%. Illiterate participants comprise little of the study sample (only 7%). While participants with a university degree are 52.9%. Regarding immunization status, 35% were fully vaccinated before development of Coronavirus disease, while 15% were not vaccinated (Table 1).

Table 1 Characteristics of participants (n = 289). N (%)

Age, mean (the range)	45.5 (18 – 79.9)
Gender, female	178 (61)
Educational level	
Illiterate	21 (7)
Primary school	41 (14.1)

Secondary school	74 (25.6)
University	153 (52.9)
Immunization	
Fully vaccinated	102 (35)
Received second dose of the Pfizer or Moderna or single dose of a Johnson & Johnson vaccine less than two weeks ago	86 (30)
Received first dose of Moderna or Pfizer	56 (19)
Not vaccinated	45 (15)
Comorbidity	
0	148 (51)
1	68 (23)
≥ 2	73 (25)
Lung disease	38 (13)
Cardiovascular disease	46 (16)

According to group analysis we categorized age into 4 groups (18-30, 31-40, 41-50, more than 50) then the mean of Chalder fatigue scale was calculated for each group as follows (13.5, 16.7, 21.9, 27.5) respectively. Classification of COVID severity according to CDC guidelines ranging from asymptomatic infection to critical illness depending on symptoms and other parameters was shown on table 2 & figure 1.

Table 2 Classification of COVID severity

COVID severity	Frequency (%)
Mild illness	95 (33)
Moderate illness	94 (32)
Severe illness	73 (25)
Critical illness	37 (13)

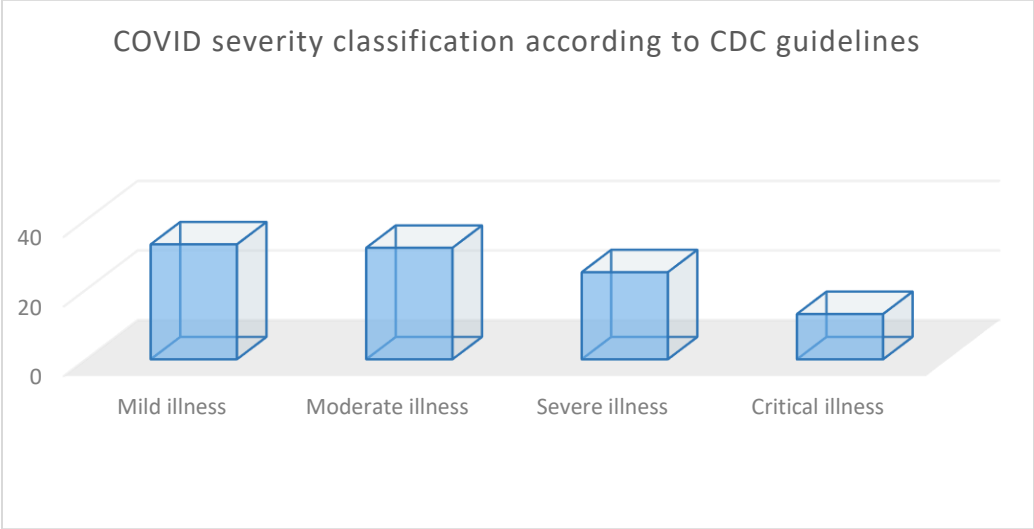

Figure 1 COVID severity

Multiple regression analysis was performed to see the impact of various factors including demographic variables and comorbidity on the chalder fatigue score. Significant results were detected with age, vaccination status, COVID severity and comorbidity (P correlation, 0.451, 0.623, 0.341, 0.523) respectively. The independent variables were tested for multicollinearity assumptions and all VIF was greater than 1.0. Normal probability plot was performed for chalder fatigue scale, and according to the

figure the variable follows a normal distribution manner, figure (2). The model which includes (age, vaccination status, COVID severity and comorbidity) show 52% of the variance in chalder fatigue scale (R = 0.523). The most independent variable which affects the scale is the vaccination status (beta = .412 p value 0.001) followed by comorbidity, age and COVID severity (Beta = .214, .186, .021) respectively (Table 3).

Table 3 Multiple regressions

	USD		SD	Sig.	Collinearity Statistics
	B	Std. Error	Beta		VIF
Age	.003	.037	.186	.041	1.028
Vaccination status	1.264	.785	.412	.003	1.054
COVID severity	2.792	.795	.021	.450	1.129
Comorbidity	.770	.575	.214	.023	1.116

a. Dependent Variable: Chalder fatigue scale

b. Abbreviations: B; regression coefficient, USD; Unstandardized Coefficients SD; Standardized Coefficients, CI; Confidence Interval, VIF; variance inflation factor.

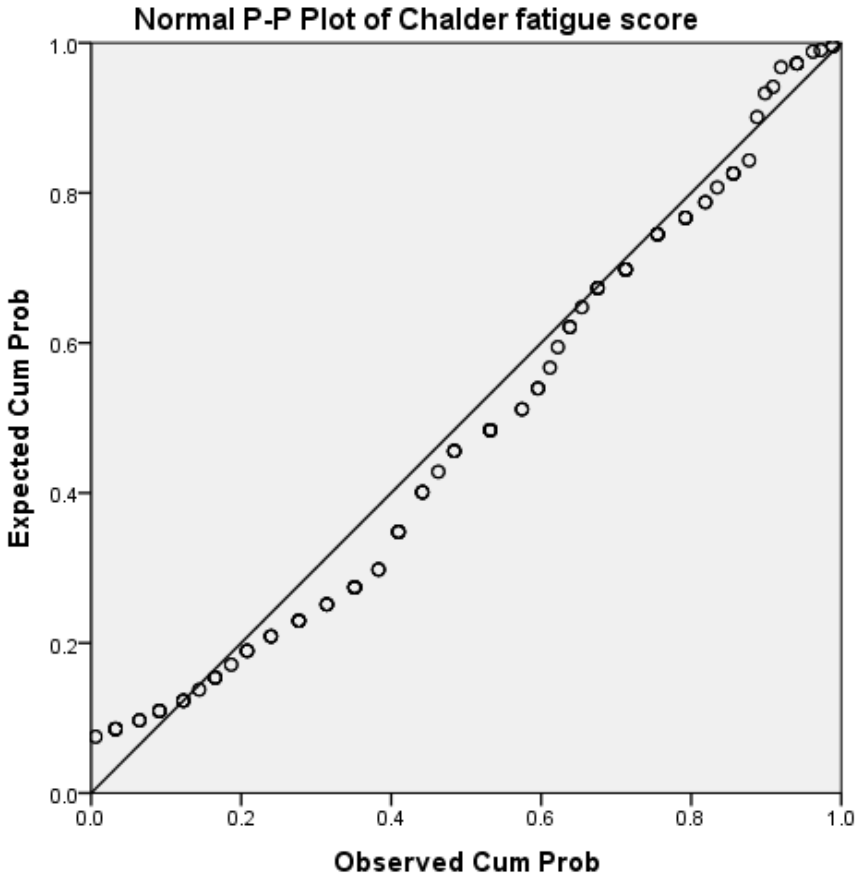

Figure 2 Pearson correlation

Pearson correlation was used to assess the correlation between disease severity and other demographic variables. Gender doesn't show significant relation with disease severity, while age was positively associated with COVID severity (P correlation .578, P value .014)

Classified comorbidity was correlated with demographic variables and disease severity according to CDC classification guidelines, using chi squire and fisher exact test (Table 4).

Table 4 Cross-tabs for charlson comorbidity index (classified)

Age groups	Comorbidity			P value
	0 comorbidity N (%)	1 comorbidity N (%)	2 and more comorbidity N (%)	
18-30 years	67 (79)	24 (24)	6 (7)	0.021
31-40 years	31 (67)	10 (21)	5 (12)	
41-50 years	36 (60)	13 (21)	11 (22)	
51 years and above	14 (23)	21 (35)	24 (68)	

4. DISCUSSION

Fatigue was recorded as a common persistent symptom in patients who were COVID 19 positive; it may occur in association with other COVID symptoms during the acute phase of disease or after recovery. Bio-psychological nature of disease is expected to be an origin for post-COVID-19 chronic fatigue (Weingartner and Stengel, 2021). Also, it can be caused by other factors such as physical or biological dysfunction. Cytokines which are released by the Coronavirus, affect psychological mechanisms and so it may cause fatigue. Graham et al., (2021) cohort study highlighted that autoimmune disorders play a role in the pathophysiology of fatigue in COVID 19 patients. Feeling of hopelessness, avoidance behavior in addition to financial problems as a result from unemployment, all these might be factors which contribute to post COVID 19 fatigue (Weingärtner and Stengel, 2021). Finally, Townsend et al., (2021) excluded significant dystonia in patients with post-COVID-19 chronic fatigue.

Our study concluded that the fatigue scale was higher in older patients with post-COVID chronic fatigue syndrome. According to a systematic review study conducted in 2021, age and multiple comorbidities were regarded as factors affecting severity of post-COVID-19 fatigue (Cabrera et al., 2021). Our study also found that, severity of COVID during the acute phase has an influence on severity of post COVID-19 chronic fatigue. This goes in the same direction with Cabrera et al., (2021) study.

According to multiple regression analysis results, vaccination is the most independent variable affecting the scale, with non-vaccinated participants having the highest score on the chalder fatigue scale if compared to known vaccinated. According to a study conducted in China by Li et al., (2022), vaccination is associated with a lower risk of developing pneumonia from COVID 19. Another case control study conducted in the United States concluded that full vaccination significantly decreased the risk of hospitalization from COVID 19 (Brown et al., 2021). Booster shots are necessary to maintain protection against SARS-CoV-2 because humoral immunity produced by the vaccination gradually wanes over time. Researchers have looked into how different factors, including vaccination, prior SARS-CoV-2 infection, and a combination of the two, affect humoral immunity against novel SARS-CoV-2 strains. Over time, the protective effects of boosters and previous infections wore off, making reinfection more likely, particularly during Omicron predominance. Serious COVID-19 symptoms, such as hospitalization or death, were still mitigated by humoral immunity (Lin et al., 2022).

Classification of disease severity using frequency analysis highlighted that the most prominent group in disease severity classification was the moderate illness group 28% of participants. According to chi square results, 68% of participants in the older age group (51 and above) have 2 or more comorbidities, according to charlson comorbidity index. In general, the prevalence of chronic diseases increases with age. By the age of 75–79, the odds of having two or more major conditions rise to 60%; by the age of 85–89, that number rises to almost 75% (Day, 2017).

5. CONCLUSION

We concluded that fatigue in COVID patients is affected by vaccination status, disease severity, age and comorbidities. Additionally studies in the same topic are required because fatigue is a problem of high impact on quality of life it also affects community integration and participation of affected individuals.

Author's contribution

Research idea - Faheem Mohammed alanazi Alanoud abdullah alqawili, Fahad Mohammed Algharbi, Hala Khamis Alghamdi, Hamad Bandar Alotaibi

Proposal writing - Faheem Mohammed alanazi, Fahad Mohammed Algharbi, Hala Khamis Alghamdi, Hamad Bandar Alotaibi

Questionnaire preparation - Faheem Mohammed alanazi, Hala Khamis Alghamdi, Hamad Bandar Alotaibi, Hamoud Shaya Alotaibi, Majed Maseer Almutairi

Data collection - Faheem Mohammed alanazi, Majed Maseer Almutairi, Rawan Hamdan Aljehani, Sarah Abdulhadi Algallaf, Saud Abdullah Alhasoun

Data entering and analysis - Faheem Mohammed alanazi, Majed Maseer Almutairi, Rawan Hamdan Aljehani, Sarah Abdulhadi Algallaf, Saud Abdullah Alhasoun

Result writing - Faheem Mohammed alanazi, Rawan Hamdan Aljehani, Sarah Abdulhadi Algallaf, Saud Abdullah Alhasoun, Fahad Mohammed Algharbi, Hala Khamis Alghamdi, Hamad Bandar Alotaibi

Discussion writing - Faheem Mohammed alanazi, Hamoud Shaya Alotaibi, Majed Maseer Almutairi9, Rawan Hamdan Aljehani, Sarah Abdulhadi Algallaf, Saud Abdullah Alhasoun

Preparing reference style - Faheem Mohammed alanazi, Hamoud Shaya Alotaibi, Majed Maseer Almutairi, Rawan Hamdan Aljehani, Sarah Abdulhadi Algallaf, Saud Abdullah Alhasoun

Searching for appropriate journal - Hamoud Shaya Alotaibi, Majed Maseer Almutairi, Rawan Hamdan Aljehani, Sarah Abdulhadi Algallaf, Saud Abdullah Alhasoun

Final report editing - Faheem Mohammed alanazi, Majed Maseer Almutairi, Rawan Hamdan Aljehani, Sarah Abdulhadi Algallaf

Financial connections

All writers have declared that they have no financial connections to any organizations that might be interested in the work that has been submitted, either right now or in the past. Each author has further affirmed that "they have no additional affiliations or activities that could be viewed as having influenced the work that has been submitted.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data associated with this study are present in the paper.

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