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Association Between Functional Status and Fatigue Among Individuals Recovering from COVID-19 Infection

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ABSTRACT

Background: Fatigue is one of the most common and disabling symptoms after COVID-19. The relationship between fatigue severity and post-COVID functional status is not well studied. This study examined how fatigue relates to functional status and what factors affect these outcomes in people recovering from COVID-19.

Objective: To examine the link between post-COVID-19 fatigue and functional status. Additionally, the study aims to explore other factors tied to fatigue in people recovering from COVID-19.

Methodology: We conducted a cross-sectional study with 344 post-COVID-19 participants. Demographic data, comorbidities, hospitalization, and exercise habits were collected. We used the PCFS scale for functional limitation, FSS for fatigue, mMRC for dyspnea, and EQ-5D-5L for quality of life. Correlations and multivariate regression identified predictors of fatigue and limitation.

Results: The median PCFS grade was 1 (range 0–4). The mean FSS score was 4.5 ± 1.5. PCFS and FSS showed a moderate positive correlation ($r = 0.48$, $p < 0.001$). An FSS cutoff of 4.8 predicted moderate-to-severe limitation (AUC = 0.82). Female sex, COPD, high comorbidity, dyspnea, hospitalization, and low EQ-5D-5L mobility and anxiety/depression scores were linked to more fatigue and poorer status. Regular exercise before infection protected against fatigue and functional impairment.

Conclusion: Fatigue impacts functional recovery after COVID-19, regardless of time since infection. Including fatigue and functional assessments in post-COVID care may help early identification and target rehabilitation.

Keywords: COVID-19; Fatigue; Functional Status; Post-COVID Syndrome; Rehabilitation

Introduction

SARS-CoV-2 causes COVID-19, which continues to burden public health, even after acute infection. While many recover, a significant number develop lasting symptoms, known as post-COVID condition or long COVID, including fatigue, dyspnea, cognitive dysfunction, muscle or joint pain, and reduced quality of life.[1,2] Fatigue is particularly common and is likely the most disabling symptom for patients after COVID.[3,4]

Fatigue after COVID-19 arises from multiple sources, including persistent inflammation, mitochondrial dysfunction, dysregulation of autonomic controls, deconditioning, microvasculature injury, and neuroimmune changes.[5,6] Fatigue can impact physical, cognitive, and social participation, and may reduce the ability to perform activities of daily living (ADLs) and maintain independence. Although both fatigue and functional impairment are present in post-COVID populations, their relationship remains less well-examined.

Several tools evaluate functional status after COVID-19. The Post-COVID-19 Functional Status (PCFS) scale is increasingly used. PCFS is a patient-reported, ordinal tool that captures functional limitation after COVID-19, including changes in lifestyle, usual activities, and socialization.[7,8] Studies show PCFS is valid and correlates with dyspnea, quality-of-life scales, exercise capacity, and other PROMs (patient-reported outcomes).[9,10] Its simplicity and widespread use make PCFS practical for longitudinal follow-up and research.[11,12]

Related research has examined fatigue in post-COVID cohorts. For example, one multicenter evaluation found that fatigue, measured with various scales, was closely linked to decreased quality of life, mood symptoms, post-exertional malaise, and female sex.[13] In another single-center study, fatigue emerged as the biggest determinant of functional status, surpassing lung impairment.[14] People who survived severe COVID report long-term fatigue, decreased exercise capacity, and lower functional status one year after ICU discharge [15,16]

Still, there are many gaps in the literature. First, many studies have small sample sizes or focus only on hospitalized or severely affected patients. This limits generalization to larger recovering populations. Second, few studies have examined the statistical association between fatigue severity and functional limitation, including correlation and regression analyses, while controlling for demographic and clinical covariates. Third, little research examines variables like comorbidities, time since infection, BMI, age, sex, or pre-morbid exercise habits. These may mediate or moderate the relationship between fatigue and functional limitation. Fourth, few studies have examined the PCFS scale in adequately powered samples to determine if it differentiates fatigue severity.

Long-term fatigue and functional limitations are common among COVID-19 survivors. It is important to understand how these two areas interact when predicting, planning rehabilitation, and monitoring. If fatigue is associated with functional status even after controlling for other variables, our research may justify prioritizing fatigue-based treatment. Studying a large sample may help identify fatigue cut-offs that predict significant functional limits. This study aims to address an important research gap by systematically correlating fatigue severity and functional recovery. It will also identify factors linked to fatigue in a moderately powered, large sample size.

Objective

To examine the relationship between post-COVID-19 fatigue and functional status, and to explore additional factors associated with fatigue among individuals recovering from COVID-19 infection.

Methodology

This cross-sectional analytical study was conducted from January 2022 to June 2023 at Sheikh Zayed Hospital, Rahim Yar Khan. Adult participants (aged 18 years and older) were included if they had confirmed COVID-19 (by RT-PCR or antigen test) and had recovered from the acute phase. To select participants, we screened medical records to identify eligible patients, who were then invited to participate. Individuals were excluded if they had been diagnosed previously with a major neurological illness, a severe psychiatric disorder, were unable to complete questionnaires due to cognitive impairment, or refused consent. A sample size of 344 was determined based on an anticipated moderate association between fatigue severity and functional status, with a power of 80% and $\alpha = 0.05$, also accounting for possible non-responses.

Eligible participants were recruited via outpatient clinics, COVID-19 up services, and community outreach. Those who met the criteria and gave consent completed data collection using a standardized questionnaire and participated in a structured interview conducted by trained health workers. Demographic characteristics (age, sex, marital and occupational status), anthropometric measurements (height, weight, BMI), smoking history, and pre-infection physical activity were recorded. Clinical details such as the date of COVID-19 diagnosis, hospitalization status (including any ICU admission), duration of hospital and ICU stays, need for home oxygen after discharge, relevant comorbidities (including respiratory diseases like COPD and asthma, or other systemic illnesses), and the Charlson Comorbidity Index (CCI) score were also obtained.

We assessed people's well-being after COVID-19 using a simple scale from 0 (no problems) to 4 (severe problems). This scale covered changes in lifestyle, daily activities,

and social participation. We also recorded how long it had been since diagnosis. To assess tiredness, we used a 9-item scale where higher scores meant greater tiredness. Patients rated their breathing difficulties on a simple scale, and their quality of life was measured with a questionnaire about mobility, self-care, daily activities, pain, and mood.

All data were double-entered into a secure database and verified for accuracy and consistency. Data were double-entered into a secure database and checked for accuracy and consistency. Continuous variables were summarized as median (IQR) or mean ± SD, according to distribution, and categorical variables as counts and percentages. The Shapiro-Wilk test assessed normality. Correlations between continuous variables were examined using Pearson or Spearman coefficients as appropriate. Comparisons across groups were made with t-tests or Mann-Whitney U tests (two groups), ANOVA or Kruskal-Wallis test (more than two groups), and chi-square tests for categorical data.

Multivariate analyses identified predictors of functional limitation (PCFS grade) and fatigue severity (FSS score). Ordinal logistic regression was used for functional status with significant univariate factors ($p < 0.10$) as predictors. Multiple linear regression was used for fatigue. Assumptions such as multicollinearity, linearity, and proportional odds were checked. Significance was set at $p < 0.05$. ROC curve analysis assessed FSS's ability to predict moderate-to-severe functional limitation (PCFS ≥ 3).

Ethics approval was obtained from the Institutional Review Board of Sheikh Zayed Hospital, and all participants provided informed written consent. Data confidentiality was maintained with deidentification before analysis.

Table 1. Demographic and clinical characteristics of participants (n = 344)

Variable	Mean ± SD / n (%) / Median (IQR)
Age (years)	49.6 ± 13.8
Sex (M/F)	188 (54.7%) / 156 (45.3%)
BMI (kg/m²)	27.9 ± 4.8
Marital status	Single 78 (22.7%); Married 266 (77.3%)
Employment status	Employed 178 (51.7%); Unemployed 92 (26.7%); Retired 74 (21.6%)
Smoking status	Never 190 (55.2%); Former 97 (28.2%); Current 57 (16.6%)
Chronic respiratory disease	42 (12.2%)
Systemic (non-respiratory) disease	92 (26.7%)
Hospitalized during COVID-19	144 (41.9%)
ICU admission	31 (9.0%)
Home oxygen after discharge	24 (7.0%)
Regular exercise before infection	102 (29.7%)
CCI score	1 (0–6)
Time since COVID-19 diagnosis (months)	5 (1–15)

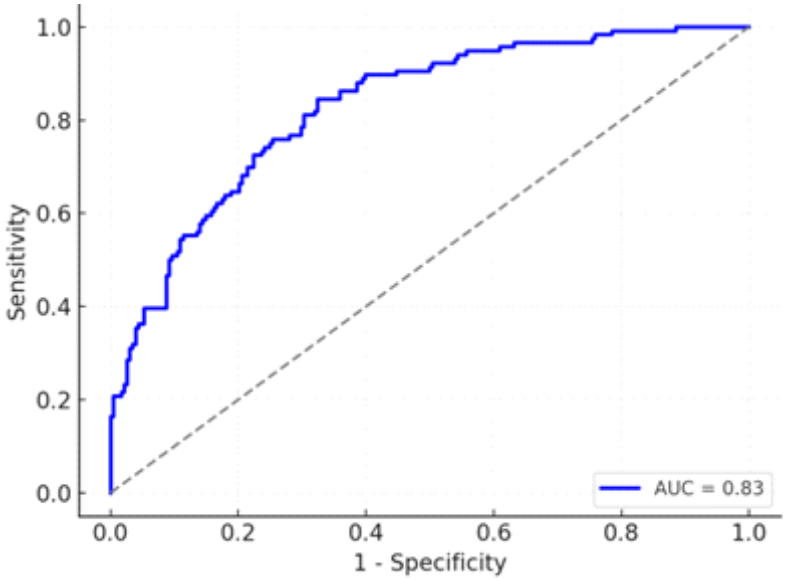

Figure 2. ROC curve showing predictive ability of FSS for moderate-to-severe functional limitation (PCFS ≥ 3)

Results

A total of 344 participants with a confirmed history of COVID-19 infection were enrolled. Among study cases, 188 (54.7%) were male and 156 (45.3%) were female (Figure 1).

The mean age of the study cases was 49.6 ± 13.8 years, and the mean BMI was 27.9 ± 4.8 kg/m². The median time since diagnosis was 5 months (range = 1–15 months). Among study participants, 42% had been hospitalized, and 9% required ICU admission. Chronic respiratory diseases were present in 12% of participants, most commonly COPD (7%) and asthma (4%), while 27% reported non-respiratory systemic diseases. The median Charlson Comorbidity Index (CCI) was 1 (range = 0–6)(Table 1).

The median Post-COVID Functional Status (PCFS) grade was 1 (0–4), and the median Fatigue Severity Scale (FSS) score was 4.5 (1–7). A significant positive correlation was found between PCFS grade and FSS score ($r = 0.48$, $p < 0.001$), indicating that greater fatigue was associated with worse functional limitation.

Participants with PCFS grades ≥ 3 had a mean FSS score of 5.2 ± 1.4, while those with grades ≤ 2 had mean FSS = 3.8 ± 1.6 ($p < 0.001$). The ROC curve for FSS in predicting moderate-to-severe functional limitation (PCFS ≥ 3) yielded an AUC = 0.82 (95% CI 0.77–0.87) with an optimal cutoff of FSS ≥ 4.8 (sensitivity 74.5%, specificity 78.2%) (Figure 2).

Higher PCFS grades were associated with being married ($p = 0.01$), chronic systemic disease ($p < 0.001$), chronic respiratory disease ($p = 0.002$), positive CT findings ($p <$

Table 2. Predictors of higher PCFS grade (ordinal regression, n = 344)

Parameter	p-value	Odds Ratio (95% CI)
mMRC score ≥ 2	< 0.001	2.45 (1.72–3.49)
Positive CT findings	0.004	1.98 (1.24–3.16)
Presence of systemic disease	0.012	1.71 (1.13–2.58)
EQ-5D-5L mobility limitation	< 0.001	2.03 (1.46–2.82)
EQ-5D-5L anxiety/depression	0.021	1.59 (1.07–2.37)
Regular exercise (Yes)	0.006	0.64 (0.46–0.88)

Table 3. Predictors of Fatigue Severity Scale (FSS) score (multiple linear regression)

Variable	β (Standardized)	p-value
Sex (female)	0.132	0.003
COPD	0.096	0.024
EQ-5D-5L mobility	0.152	< 0.001
EQ-5D-5L anxiety/depression	0.103	0.009
EQ-5D-5L VAS	–0.214	< 0.001
$R^2 = 0.36$, $p < 0.001$		

0.001), and a history of hospitalization, ICU admission, or home oxygen therapy (all $p < 0.01$). Additionally, higher grades were also observed in those with dyspnea ($p < 0.001$), cough ($p = 0.01$), and lack of regular exercise ($p = 0.002$). In contrast, there were no significant differences in PCFS grades according to sex ($p = 0.18$), smoking status ($p = 0.12$), or participation in rehabilitation ($p = 0.65$). Furthermore, PCFS showed a positive correlation with age ($r = 0.31$), BMI ($r = 0.14$), mMRC dyspnea score ($r = 0.62$), and length of hospital stay ($r = 0.38$), while a negative correlation was observed with EQ-5D-5L VAS quality of life score ($r = –0.51$). Finally, ordinal regression analysis indicated that mMRC dyspnea score, CT findings, and EQ-5D-5L mobility, usual activities, and anxiety/depression domains were independent predictors of worse functional status (Table 2).

Results showed that FSS scores were significantly higher among women ($p = 0.002$), unemployed participants ($p = 0.01$), those with respiratory or systemic disease ($p < 0.001$), and those with dyspnea or hospitalization history ($p < 0.01$). FSS correlated positively with age ($r = 0.12$, $p = 0.02$), BMI ($r = 0.09$, $p = 0.04$), and CCI ($r = 0.18$, $p < 0.001$). Linear regression showed that female sex, COPD, EQ-5D-5L mobility, and anxiety/depression domains were independent predictors of higher fatigue (Table 3).

Discussion

In 344 post-COVID-19 patients, we found a moderate positive correlation between fatigue severity (FSS) and functional limitation (PCFS) ($r \approx 0.48$). An FSS cutoff of about 4.8 discriminated moderate-to-severe functional impairment (PCFS ≥ 3). Fatigue and functional limitation were linked to female sex, respiratory disease (especially COPD), higher CCI, dyspnea (mMRC), hospitalization/ICU admission, and worse EQ-5D-5L scores in mobility, usual activities, and anxiety/depression. Regular pre-infection exercise was protective. We compare these findings to international literature and note clinical implications for follow-up and rehabilitation.

Our finding of a high prevalence of fatigue and its strong association with impaired function aligns with large longitudinal cohorts and systematic reviews identifying fatigue as a common post-COVID symptom. Huang et al. reported that at 6 months post-discharge, fatigue or muscle weakness remained the most prevalent symptom and that survivors had notable impairments in health-related quality of life and physical performance.[17] While their study included hospitalized patients, our findings extend these associations to a mixed-severity cohort. Community and outpatient studies, such as Townsend et al., also report persistent fatigue not directly linked to the severity of acute illness, supporting the idea that persistent fatigue is multifactorial.[18] In our cohort, time since infection did not significantly predict fatigue or PCFS grade, and both remained consistent across categories, further suggesting that the causes of persistent fatigue are multifaceted.

Population studies that link risk factors to prolonged symptoms help provide context for our identified predictors. For instance, Sudre et al. used community symptom-tracking app data and found that being female, older age, and having more symptoms in the first week were all predictors of long-lasting symptoms (long COVID). Our observation that female sex independently predicts higher FSS scores and that older age is associated with both fatigue and worse PCFS supports the generalizability of these risk factors. Notably, Sudre's broader community-based sample contrasts with our clinic-based study. The fact that similar associations between demographic factors and fatigue outcomes are seen in both settings underscores the robustness of these demographic predictors, regardless of recruitment methods or illness severity.[19]

Studies have examined how functional status tools relate to fatigue. Klok et al. developed the PCFS scale to assess

post-COVID-19 functional limitations.[20] Other research shows PCFS relates to fatigue and health-related quality of life. Leite et al. found PCFS distinguishes patients by fatigue, quality of life, and function.[21] Our results support this: the moderate correlation between PCFS and FSS, AUC of 0.82, and an FSS threshold around 4.8 are useful for identifying moderate-to-severe impairment.

Comparing our results with other regional studies refines our understanding of post-COVID symptom persistence in different patient groups. For example, Carvalho-Schneider and colleagues from France monitored noncritical adult outpatients two months post-symptom onset, finding that a significant proportion continued to report persistent symptoms, including fatigue.[22] This highlights that the risk of long-term health issues is not confined to hospitalized patients. Similarly, Tenforde et al. conducted a multistate U.S. outpatient study, identifying that many outpatients had not returned to normal health within 2 to 3 weeks, with persistent recovery difficulties affecting people of all ages.[23] By observing ongoing fatigue and functional challenges several months post-infection in both outpatient and inpatient groups, our findings parallel these prior community and outpatient reports, underscoring that prolonged impairment is widely distributed across severity and settings.

Comorbid respiratory diseases, mainly COPD, worsen post-COVID disability, as other studies show. Pre-existing lung problems predict poorer recovery and more severe symptoms.[24,25] In our analysis, COPD significantly raised FSS scores, suggesting people with lung disease may need more follow-up and earlier rehabilitation. Quality of life and mood were closely linked to fatigue and PCFS. This fits with the idea that post-infectious fatigue reflects biological, psychological, and social factors. Links between anxiety/depression (EQ-5D) and both FSS and PCFS show that mental health assessment is crucial for post-COVID fatigue and limitation. Our moderate correlation and FSS cutoff of 4.8 provide actionable insights, indicating that patients at or above this threshold require further assessment and may benefit from early rehabilitation. Our multivariable models confirm fatigue relates to function regardless of age, BMI, and some severity indices, but is also influenced by comorbidities and quality of life. This suggests interventions should be multifaceted, combining physical, psychological, and symptom management. Our results match findings from Asia, Europe, and North America, supporting generalizability. Larger, multi-site studies with long-term follow-up would provide a clearer picture of the temporal trends and causal relationships.

Conclusion

The present study concluded that among individuals recovering from COVID-19, fatigue emerged as a significant and persistent symptom closely associated with poorer functional status. The moderate positive correlation we found between the Fatigue Severity Scale (FSS) and the Post-COVID Functional Status (PCFS) scale indicates that as fatigue worsens, so does the likelihood and extent of functional limitations. Notably, an FSS score of around 4.8 effectively identified patients experiencing moderate to severe functional impairment, suggesting it could be a valuable benchmark for assessing post-COVID conditions. Our research also revealed that factors such as being female, having a higher burden of comorbidities, suffering from respiratory diseases like COPD, being hospitalized or admitted to the ICU during the acute phase, and experiencing severe dyspnea were all independent predictors of both fatigue and functional limitations. On the flip side, engaging in regular exercise before infection seemed to offer some protection, highlighting the importance of staying active and maintaining cardiorespiratory fitness. Additionally, a reduced quality of life, especially in areas related to mobility and anxiety/depression as measured by the EQ-5D-5L was strongly associated with fatigue and hindered functional recovery, emphasizing the complex nature of post-COVID effects that involve both physical and mental health aspects. Overall, these findings suggest that fatigue is not just a lingering symptom but a key factor influencing recovery after COVID-19. Identifying and addressing fatigue early on through a range of interventions, like pulmonary rehabilitation, psychological support, and structured exercise programs could lead to improved functional outcomes and a better quality of life.

Future longitudinal studies are warranted to explore causal pathways between fatigue and functional decline, to monitor long-term trajectories of recovery, and to evaluate the efficacy of rehabilitation strategies aimed at mitigating post-COVID fatigue. Integrating fatigue screening and PCFS grading into post-COVID clinical follow-up could provide an efficient framework for identifying high-risk individuals and guiding targeted interventions toward holistic recovery.

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