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Health-Related Quality of Life (HRQoL) and Its Associated Factors Among Post-COVID-19 Patients at Three Months in a Tertiary Hospital of Bangladesh

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ABSTRACT

COVID-19 is a burning issue brought on by the SARS-COV2 coronavirus. Many SARS-COV-2 survivors continue to experience a variety of symptoms, which negatively impact their standard of living. A total of 103 post-COVID patients participated in a prospective comparison study from July 2021 to December 2021 to assess the individual's health-related quality of life (HRQoL) and the elements that contribute to it. A control group with age and gender that matched 110 seemingly healthy individuals was also included for comparison. At three months, the EuroQol 5-dimensional 3-levels (EQ-5D-3L) questionnaire, which encompasses a brief expressive system questionnaire and an EQ-VAS visual analogue scale, was collected in a predesigned datasheet. The EQ index score was used to reflect all HRQoL data, which was then contrasted to a set of matched controls for ages and sexes. At three months, the mean EQ-5D index and EQ-VAS scores were lower than those of age and gender that matched the control group, at 0.810±0.208 and 73.240±11.36, respectively. Regarding dimensions of the questionnaire, mobility, self-care, usual activities, pain/discomfort, and depression/anxiety were assessed at three months follow-up. The mobility and usual activity parameters showed a statistically evident difference (p-value = 0.001) compared to the control group.

INTRODUCTION

COVID-19 is a distinctly transmissible ailment brought on by the SARS-COV2. Both an economic and a novel healthcare crisis emerged (Rubin et al., 2020). At the end of 2019, Wuhan city, in the Chinese province of Hubei, reported the first case of COVID-19. Since then, the illness rapidly spread over the world, affecting 220 nations (Worldometer, 2021). On 11 March 2020, the WHO designated it to be a pandemic illness (Cucinotta & Vanelli, 2020). The first three cases were made public by Bangladesh's Institute of Epidemiology Disease Control and Research (IEDCR) on 8 March 2020.

The broad family *Coronaviridae* contains encapsulated positive-sense single-stranded RNA viruses called coronaviruses. Along with other mammals and bird species, they can also infect humans. Coronavirus infections in both humans and animals can lead to respiratory and gastrointestinal disorders (V'kovski et al., 2021).

The SARS-CoV-2 is a member of the Beta coronavirus family, which includes the MERS and SARS viruses that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Many survivors of SARS-COV-2 infection present with impaired lung function that lasts for months to years after being released from the hospital (Xie et al., 2005). According to research, several variables, including age, smoking status, length of hospital stays and co-morbidities, such as diabetes, hypertension, and chronic lung diseases, may contribute to the blooming of post-COVID problems (Tsampasian et al., 2023). The potential medium- and long-term effects that COVID-19 survivors may endure are not well understood. Acute COVID-19 infection survivors experience a range of physical and mental health issues, including exhaustion, trauma-related stress disorder, despair, anxiety, and sleeplessness. These issues negatively impact a patient's well-being (Arab-Zozani et al., 2020).

Health-related quality of life (HRQoL) is receiving more attention as a result of social, economic, and healthcare service improvements. A multifaceted notion, the welfare of life often involves the subjective progression of parts of life, both good and bad. HRQoL is the concept of one's perceived physical and mental health over time. Furthermore, gaining new insights into the link between HRQoL and risk variables is important. Estimating HRQoL helps determine the impact of avoidable illness and infirmity (CDC, 2021).

Following hospital release, survivors of COVID-19 may have a variety of needs, including physical, neuro-psycho-social, and social needs, according to National Health Service (NHS) England (2020) (Halpin et al., 2021). A follow-up study discovered that hospitalized SARS and MERS survivors had reduced quality of life, indicating that the effects of COVID-19 were probably going to be comparable (Ahmed et al., 2020). A separate study on post-COVID patients conducted in Iran found a significant impairment of HRQoL (Arab-Zozani et al., 2020). There is a paucity of data available regarding post-COVID patients. So, this study aims to assess the health-related quality of life in post-COVID patients and to identify the association of factors contributing to this and, therefore, to ensure better health.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational research project was carried out in the COVID-19 unit and the Department of Respiratory Medicine from July 2021 to December 2021.

Sample Size Calculation

The following formula was used to determine the sample size:

$$n = \frac{(u+v)^2(\sigma_1^2+\sigma_0^2)}{(\mu_1-\mu_0)^2}$$

Where,

n = for measurement of different dimensions, the expected sample size
u = the predictable error, usually set at 1.96 at a 5% level, which correlates with 95% confidence level
v = 0.84 at 80% power
σ1 = 1.0 [SD for Comparison group]
σ0 = 0.2 [SD of EQ-5D-5L Index in study population] [Arab-Zozani et al., 2020]
μ1 = 0.9 [Mean of Comparison group] [Yang et al., 2018]
μ0 = 0.6 [Mean of EQ-5D-5L Index in study population] [Arab-Zozani et al., 2020]

So, the sample size for this study would be:

$$n = \frac{(1.96+0.84)^2 \times (1^2+0.2^2)}{(0.9-0.6)^2}$$

$$= 98$$

After using drop out formula, the sample size was:

N = 1 – d

Here, n = 98

d = 10% or 0.1 (Marginal error was taken 10%)

N = 98 / (1 – 0.1) = 108.9 ≈ 110

So, a total of 110 patients were selected as a case.

Another 110 age-sex matched apparently healthy people who did not have any symptoms of COVID-19 infection such as fever, cough, shortness of breath, fatigue, diarrhea etc. and were not known to have been in close contact with COVID patients from the community were selected as the control group after obtaining their consent.

Sample size: The total sample size was 220 according to selection criteria.

Study Participants

The subjects of the study were recruited according to the inclusion and exclusion criteria.

Inclusion Criteria

1. All patients who had a history of laboratory-confirmed SARS-CoV-2 infection by RT-PCR.
2. Age 18 years and above.
3. Previously hospitalized for COVID-19 disease.
4. At least three months after the onset of initial COVID-19 symptoms.
5. Patients who were willing to give informed written consent to participate in the study.

Exclusion Criteria

1. Under 18 years of age.
2. Learning impairment or other impartial or conveyance impairment.
3. Pregnancy

Sampling Technique

Sampling was done using a probability (random) sampling technique for both groups.

Data Collection

For this investigation, patients who were hospitalized in the COVID unit and had their SARS-CoV-2 infection confirmed in the lab by RT-PCR were taken into account. When a patient was discharged from the hospital, they were all evaluated for eligibility. Patients who were qualified for the trial and were open to taking part were enrolled. During discharge from the hospital, information about the demographic variables (age, sex, occupation, education, smoking status) was recorded in a

data sheet. The presence of any co-morbidities, like diabetes, hypertension, chronic kidney disease, ischemic heart disease, and pre-existing lung disease were also documented by history. Three months after the onset of their first symptoms, patients were contacted or urged to visit the Department of Respiratory Medicine at BSMMU. HRQoL was assessed using an EQ-5D-3L questionnaire (Rabin & Charro, 2001). The EQ-VAS was used to score overall health status from 0 (utmost state of health deterioration possible) to 100 (optimal state of health attainment). The data was collected based on the EQ-5D questionnaire. For the investigation, a total of 110 COVID-19 patients with RT-PCR confirmation were used. Two patients passed away, and five could not be reached during follow-up, which was conducted three months following the start of the first COVID-19 symptoms. Finally, 103 patients were taken as the case sample. Another 110 apparently healthy people who had not suffered from COVID-19 infection were selected from the general population as a control group with matched age and sex. Considering the COVID-19 pandemic, proper health hygiene was followed strictly in each step of the data collection procedure. Both investigator and participants wore masks and maintained a social distance of as much as possible. Hand hygiene was also appropriately maintained.

EQ-5D-3L Questionnaire

EQ-5D-3L questionnaire (Rabin & Charro, 2001) is a common benchmark tool for evaluating HRQoL. The EQ-5D is utilized globally and is available in the majority of world languages (over 180 languages), including the Bangla version, through a closely monitored translation process (Herdman et al., 2003). Each EQ-5D instrument comprises an EQ-VAS and a brief, detailed system questionnaire. Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression are the five aspects of the EQ-5D-3L. Each dimension contains three levels of responses, each of which is represented by a severity level-related number (1, 2 or 3). Thus, a 5-digit number between 11111 (having no difficulty in any of the categories) and 33333 (having serious problems in all aspects) is used to describe the health state profile of a person. A visual analogue scale that focuses on an upward trajectory is also part of the EQ-5D-3L questionnaire and ranges from 0 (the poorest possible health) to 100 (the best possible health) to determine the respondents' overall health condition. To determine a preference-based index (EQ-5D index score), the creators of the EQ-5D produced value sets using techniques like the time trade-off (TTO) valuation approach or the VAS valuation technique in various countries. This index score is calculated on a scale of 0.0 to 1.0, where 1.0 corresponds to full health. We adopted the widely used time TTO method created in the United Kingdom, UK TTO, because there was not a value set based on the TTO developed for the Southeast Asian population. Utilizing an online calculator, the EQ-5D index score was determined. A verified Bangla translation of the EQ-5D-3L and a translation certificate were obtained for this study by emailing the necessary information to EuroQol Research Foundation, Netherlands.

Ethical Permission

The Institutional Review Board of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, granted the ethical clearance (BSMMU/2021/4783) for this prospective observational research project.

Statistical Analysis

Data collected for the study were both quantitative (Age) and qualitative (gender, smoking status, severity). They were analyzed by using both descriptive and inferential statistics. SPSS Statistics 23 was used to organize, analyze, and present the data.

Descriptive statistical methods: The arithmetic mean, a trustworthy indicator of central tendency, and the standard deviation, a valid indicator of dispersion, were used

to evaluate continuous data. Frequency and percentages were used to summarize categorical data.

Inferential statistical analysis: Means for continuous variables were compared using unpaired t-tests. Categorical variables were compared using the chi-square test. Statistical significance between groups was assessed at a 5% level of significance.

Study of relationship: Using odds ratios (ORs) and a 95% Confidence Interval, binary logistic regression was performed to examine the relationship between the dependent and independent variables. Statistical significance was defined as a p-value of 0.05.

RESULTS

The distribution of the research subjects' demographic characteristics is shown in Table 1. The age range of participants in the post-COVID group comprised the majority was 31 to 40 years old, followed by 41 to 50 years old. In both the post-COVID patients' group and the control group, the distribution of participants by age group was statistically comparable (p = 0.999). Age and sex differences between participants in the two groups were not statistically significant.

Table 1 Distribution of the study participants according to demographic characteristics (N= 213)

Socio-demographic characteristics		Post-COVID patients n_1=103(%)	Control Group n_2=110(%)	p-value
Age	18- 30	18 (17.5)	20 (18.2)	[a]0.999[NS]
	31-40	22 (21.4)	24 (21.8)	
	41-50	19 (18.4)	20 (18.2)	
	51-60	18 (17.5)	20 (18.2)	
	61-70	17 (16.5)	16 (14.5)	
	≥71	9 (8.7)	10 (9.1)	
	Total	103 (100)	110 (100)	
	Mean± SD	48.25 ± 17.07	46.85 ± 16.90	[b]0.549 [NS]
Gender	Male	59 (57.3)	63 (57.3)	[a]0.999 [NS]
	Female	44 (42.7)	47 (42.7)	

[a] chi square test, [b] Independent sample t test
s = significant, ns = non-significant
Data were as expressed as mean ±SD, frequency, and percentage.

The distribution of the study participants according to co-morbidity is presented in Table 2. Hypertension and diabetes mellitus were the more prevalent co-morbidity in post–COVID patients. Based on their co-morbid condition, the participants in both groups were statistically indifferent.

Table 2 Distribution of the study participants according to co-morbidity

Comorbidity	COVID-19 survivors n_1=103	Control group n_2=110	p-value
Hypertension	33 (32.0)	27 (24.5)	0.224 [NS]
Diabetes mellitus	38 (36.9)	33 (30.0)	0.286 [NS]
Cardiovascular disease	9 (8.7)	14 (12.7)	0.384 [NS]
Chronic kidney disease	14 (13.6)	9 (8.2)	0.379 [NS]
Preexisting lung disease	15 (14.6)	11 (10.0)	0.221 [NS]

[a]Chi square test
s = significant, ns = non-significant
Data were as expressed as frequency and percentage.

At a three-month follow-up, the post-COVID patients' frequency distribution of EQ-5D-3L dimensions and levels is shown in Figure 1. Mobility issues and pain/discomfort dimensions were the most often mentioned dimensions, followed by some difficulties doing daily activities.

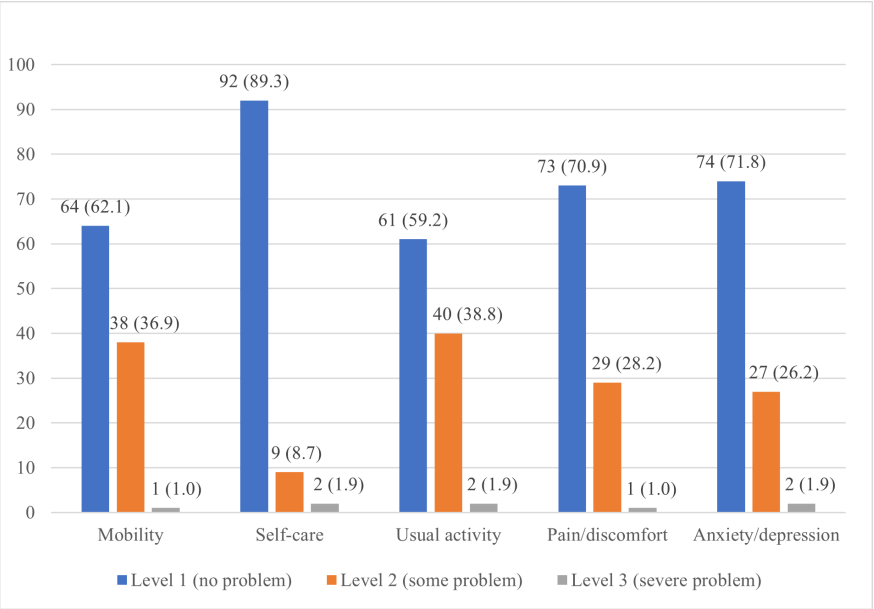

Figure 1 Frequency distribution of EQ-5D-3L dimensions and levels of post-COVID patients at three months follow-up.

The frequencies of the EQ-5D-3L dimensions and levels in the control group and post-COVID patients are shown in Table 3. There was a statistically significant difference in the participant distribution for various levels of mobility and the usual activity dimension between the post-COVID patient group and the control group (p = 0.001).

Table 3 Frequency distribution of EQ-5D-3L dimensions and levels in post-COVID patients and control groups

EQ-5D-3L		Post-COVID patients (3 months) $n_1 = 103$	Control Group $n_2 = 110$	p-value
Mobility	Level 1 (no problem)	64 (62.1)	104 (94.5)	<0.001[S]
	Level 2 (some problem)	38 (36.9)	6 (5.5)	
	Level 3 (severe problem)	1 (1.0)	0 (0.0)	
Self-care	Level 1 (no problem)	92 (89.3)	106 (96.4)	0.096[NS]
	Level 2 (some problem)	9 (8.7)	4 (3.6)	
	Level 3 (severe problem)	2 (1.9)	0 (0.0)	
Usual activity	Level 1 (no problem)	61 (59.2)	105 (95.5)	<0.001[S]
	Level 2 (some problem)	40 (38.8)	5 (4.5)	
	Level 3 (severe problem)	2 (1.9)	0 (0.0)	
Pain/discomfort	Level 1 (no problem)	73 (70.9)	74 (67.3)	0.884[NS]
	Level 2 (some problem)	29 (28.2)	35 (31.8)	
	Level 3 (severe problem)	1 (1.0)	1 (0.9)	
Anxiety/ depression	Level 1 (no problem)	74 (71.8)	77 (70.0)	0.949[NS]
	Level 2 (some problem)	27 (26.2)	31 (28.2)	
	Level 3 (severe problem)	2 (1.9)	2 (1.8)	

[a]Chi-square test
s = significant, ns = non-significant
Data were as expressed as frequency and percentage.

Table 4 presents the EQ-5D-3L index scores and the EQ-VAS scores of post-COVID patient group and control group data. The median EQ-5D-3L index score (TTO index score) varied significantly between the groups (p = 0.002). The median EQ-VAS value also varied significantly between the groups (p = 0.001).

Table 4 EQ-5D-3L index scores and EQ-VAS scores of post-COVID patients and control groups

EQ-5D-3L index		Post-COVID patients $n_1 = 103$	Control group $n_2 = 110$	p-value
TTO index	Mean ± SD	0.810 ± 0.208	0.883 ± 0.171	
	Median	0.848	1.00	0.002 [S]
	Range	-0.037 -1.00	0.193 – 1.00	
VAS	Mean ± SD	73.240 ± 11.367	81.950 ± 8.569	
	Median	70.00	80.00	<0.001 [S]
	Range	50 -100	55.00 – 100.00	

[a]*Mann-Whitney U test*
s= significant, ns= non-significant
Data were as expressed as mean ± SD, median, range.

Table 5, along with the EQ-5D-3L index scores, shows the post-COVID patients' (severe and non-severe) EQ-VAS scores at follow-up. The median EQ-5D-3L index score (TTO index score) showed a difference of statistical significance between persons who were severe and those who were not (p = 0.004). The median EQ-VAS value for patients with severe and non-severe diseases differed significantly (p = 0.002).

Table 5 EQ-5D-3L index scores and EQ-VAS scores of post-COVID patients (severe and non-severe COVID-19) at three months follow-up.

EQ-5D-3L index		Post-COVID patients (Follow-up) Non severe (n=87)	Severe (n=16)	p-value
TTO index	Mean ± SD	0.829±0.200	0.707 ±0.229	
	Median	0.850	0.743	0.004 [S]
	Range	-0.037- 1.00	0.082- 1.00	
VAS	Mean ± SD	74.62±10.75	65.75±12.041	
	Median	75	61	0.002 [S]
	Range	50- 100	50 -100	

[a]*Mann-Whitney U test*
s = significant, ns = non-significant
Data were as expressed as mean ±SD, median, range.

Demographic characteristics (sex, smoking), comorbidities (Hypertension, diabetes mellitus, cardiovascular disease, CKD, preexisting lung disease), severity and hospital stay were considered in the adjusted logistic regression analysis for five dimensions of HRQoL (Table 6). The presence of diabetes, pre-existing lung disease, cardiovascular disease, and severity of COVID-19 during infection, was significantly and independently associated with some degree of problem in different dimensions of EQ-5D-3L.

Table 6 Relationship between HRQoL dimensions and expected factors

Dependent variable	Independent variable	β	Odds Ratio	95% CI of ODDs Ratio		p-value
				Lower	Upper	
Mobility	Sex (male)	.152	1.165	0.434	3.123	0.762
	Hypertension	-.470	.625	0.189	2.062	0.440
	Diabetes mellitus	1.208	3.347	1.082	10.357	0.036[s]
	Cardiovascular disease	.919	2.507	0.376	16.725	0.342
	CKD	.403	1.496	0.239	9.385	0.667
	Pre-existing lung disease	.213	1.237	0.280	5.465	0.779
	Smoker	1.169	3.219	0.736	14.071	0.120
	Severity	2.141	8.506	0.803	90.064	0.075
	Length of hospital stay (>10 days)	-.612	.542	0.126	2.330	0.411
Self-Care	Pre-existing lung disease	1.753	5.772	1.159	28.741	0.032[s]
	Severity	3.161	23.590	1.948	285.598	0.013[s]
	Length of hospital stay (>10 days)	-2.681	.068	0.006	.800	0.032[s]
Usual activity	Diabetes mellitus	1.447	4.248	1.319	13.678	0.015[s]
Pain/Discomfort	Diabetes mellitus	1.665	5.286	1.733	16.117	0.003[s]
Anxiety/depression	Cardiovascular disease	1.667	5.298	1.074	26.141	0.041[s]

s = significant

DISCUSSION

The effect of COVID-19 infection on HRQoL and its contributing factors was investigated in this prospective observational analytical study. A total of 220 study participants aged 18 years and above were enrolled for this study from June 2021 to December 2021. Among them, there were two groups. One group consisted of 103 post-COVID patients (seven participants failed to follow-up); in another group, 110 healthy people, who did not suffer from COVID-19, were included for comparison.

In this study, patients aged 31 to 40 made up the largest proportion of participants (21.4%), followed by those aged 41 to 50 (18.4%). The majority of people in the control group (21.8%) were between the ages of 31 and 40. The two groups' average ages were 48.25 17.07 and 46.85 16.90 years, respectively. Because of this, both groups' means of age were nearly equal. In this study, males made up 57.3% of both groups while females made up 42.7%. These results matched those of studies by Shah et al. (2020), Sudre et al. (2021), and Zhou et al. (2020), among others.

Between the post-COVID and control groups, respectively, diabetes mellitus (36.9% versus 30%) and hypertension (32% versus 24.5%) were frequent co-morbid diseases. These results agreed with those of other research conducted by Huang et al. (2020) and Toussie et al. (2020). However, these results contradict with the study findings by Zhou et al. (2020), where hypertensive patients were 30% and diabetes was 19%. In this study, smoking was present in just 22.3% of post-COVID patients. Due to the lower percentage

of smokers, logistic regression analysis could not find a connection between smoking and decreased HRQoL in post-COVID patients. This result was in line with the research conducted by Farsalinos et al. in 2021. There was a hypothesis in Farsalinos' study that nicotine's ability to reduce inflammation via the nicotinic cholinergic system would make it protective against COVID-19. Smoking stimulates the synthesis of the angiotensin-converting enzyme-2 (ACE2) receptor, making smokers potentially more susceptible to this condition than non-smokers, according to Brake et al. in 2020. Smoking's impact on the severity of COVID-19 is still debatable.

In the study, the mean EQ-5D-3L index score of post-COVID patients during follow-up (at three months) was lower than that of the comparison group. Similarly, the mean EQ-VAS that represented the patient's own assessment of their health was lower than that of the control group. Both the difference in the median EQ-VAS value and the difference in the median EQ5D-3L index score between the two groups were statistically significant ($p < 0.002$ and $p < 0.001$, respectively). These findings were in agreement with another study of post-discharged COVID patients done by Garrigues et al. (2020).

The EQ-5D questionnaire is a reflective measurement of mobility, self-care, usual activities, pain or discomfort, and psychological symptoms like anxiety or depression, so the clinically significant decline seen in this study reflects the impact of the illness on HRQoL and the health burden on the country's economy. According to the percentage of people reporting issues affecting their HRQoL in each EQ-5D-3L component, typical activity (38.8%) was the most prevalent issue at the 3-month follow-up, followed by mobility (36.9%) and pain/discomfort (28.2%). However, the mobility and normal activity dimensions revealed statistically significant changes compared to the reference group ($p = 0.001$). These findings concur with those of a different study conducted by Meys et al. (2020) and Halpin et al. (2020).

In our study, univariate analysis revealed that co-morbid conditions such as diabetes, hypertension, chronic kidney disease, pre-existing lung disease, prolonged hospitalization (> ten days), and severe COVID infection were linked to poor mean EQ-5D-3L index scores ($p = 0.05$). The mean EQ-5D index score was different in patients with severe COVID-19 than in instances without severe COVID-19, perhaps because these patients had more severe COVID-19-related difficulties. In comparison to patients without diabetes mellitus, diabetic individuals had lower EQ-5D index scores. This may be because the disease progresses more rapidly in these patients, worsening their diabetes symptoms (Arab-Zozani et al., 2020). According to a different theory, hyperglycemia may play a part in the regulation of immunological and inflammatory responses, predisposing patients to severe COVID-19 and hence, potentially significant morbidity and mortality (Lim et al., 2021). That reveals that these factors may have a role in reduced HRQoL.

The presence of diabetes, pre-existing lung disease, cardiovascular disease, and the severity of COVID-19 during infection were all significantly and independently associated with some degree of problem in different dimensions of the EQ-5D-3L reflecting impairment HRQoL in our study ($p < 0.001$ and $OR > 1$), according to binary logistic regression analysis.

The current study had several limitations. First, this was a single-centered study. Second, there was a lack of information on HRQoL before acute COVID-19 illness. Third, during COVID-19 pandemic, the chance of asymptomatic COVID-19 infection in comparison group could not be ruled out completely. Finally, we used the UK crosswalk value set to estimate the EQ-5D-3L index score for post-COVID patients and comparison group. To our knowledge, a specific set of EQ-5D-3L for the Bangladeshi population has not been developed.

CONCLUSION

Our study showed that the HRQoL of post-COVID-19 patients was impaired at three months from their initial onset of symptoms compared to the average population. The most frequently reported problems were impairment in doing usual activities, followed by difficulties in mobility. Poor HRQoL was significantly related with the presence of several factors including severe COVID-19 infection and comorbidities like diabetes, pre-existing lung disease, and cardiovascular disease. Our findings would certainly spark interest among national and international communities of researchers and guide policymakers in developing and providing post-acute medical, psychological, and physical rehabilitation services to enable recovery from COVID-19 infection and, therefore, ensure the ability to return to work.

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