

## ORIGINAL ARTICLE

# THE ASSESSMENT OF POST-COVID-19 MANIFESTATIONS IN RECOVERED PATIENTS AND THE FACTORS ASSOCIATED WITH HIGH SYMPTOMS BURDEN

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### Abstract:

**Background:** Persistent COVID-19 symptoms and post-COVID chronic diseases have received more attention rather than the infection itself. This study's goal was to evaluate the health status of recovered COVID-19 patients and analyze the factors associated with a high burden of symptoms. **Methods:** This was a cohort study among hospital-released and recovered COVID-19 patients after three to six months of infection. Data was collected through a structured interview and analyzed by IBM SPSS (version 25). **Results:** Fatigue (74.2%) followed by anxiety (38.9%) and joint pain (34.7%) were the most common symptoms of post-COVID period. Among participants, 21.34% had low dietary adherence and 17.2% had high adherence. A statistically significant correlation of high symptoms burden with dietary adherence and age was observed. People with low dietary adherence are at risk of high symptom burden and chronic diseases (AOR: 3.56, 95%CI:1.46-8.69). Habit of smoking, Asthma, Hypothyroidism, Ischemic heart disease are significant predictors ( $P < 0.05$ ). Patients those did not require ICU also had a lower risk of burden. **Conclusion:** Effective control of post-COVID symptoms is important to confirm a healthy life. Therefore, it is important to maintain good dietary practice, avoid bad habits and control of chronic diseases for a good quality of life.

**Keywords:** COVID-19; Long COVID; Symptoms; Dietary adherence; Chronic disease.

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### Introduction:

The SARS-CoV-2 usually cause an acute multisystem disease which can have symptoms that last for up to two weeks.<sup>1-3</sup> According to the WHO, some symptoms may persist for a long period, some may start to show up three months after the onset of COVID-19 and may linger for at least two

months.<sup>4</sup> Patients with serious infections are more likely to require hospitalization and hence are more likely to experience persistent symptoms.<sup>5</sup> The post COVID-19 symptoms are recent public health concern that has drawn a lot of attention. The duration of these symptoms is not well understood.<sup>3</sup>

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As of December 2022, almost 6.7 million people had died from COVID-19 infection worldwide. In Bangladesh, there have been over two million confirmed illnesses and about 30000 recorded fatalities (6). While most afflicted individuals recovered and resumed their regular lives, many patients reported health issues after beating the sickness.<sup>2,7</sup> Genetic variations, viral load exposure, and immune system reactions to the virus are just a few examples of the elements that might cause an individual to display a wide range of clinical symptoms.<sup>5</sup> Numerous known and improbable reasons can be used to account for individual clinical discrepancies. Age, coexisting disorders (such diabetes, cardiovascular disease, chronic lung diseases, etc.), genetic variances, and others can all contribute to disease severity.<sup>8,9</sup>

After the recovery of COVID-19, the presence of any remaining symptoms is regarded as Long COVID.<sup>10,11</sup> Persistent symptoms might be associated with variety of factors (disease related, demographic, immune system, cardiovascular system, brain, lungs, and other organs). The frequent Long COVID symptoms include fatigue, dyspnea, chest pain, muscle/joint pain, heart palpitations, hair loss, loss of taste and smell, digestive issues, cognitive symptoms, and psychosocial issues. High burden of post-COVID-19 symptoms is more common in people with coexisting medical conditions and increases with age. But it's important to keep in mind that it can also affects young patients and those with comorbidities most.<sup>12,13</sup>

The rates of COVID-19 symptomatic persistence were found to be 13.3% at 1 month and 4.5% at 2 months in a prior study involving 4118 participants.<sup>14</sup> Another study in the UK found that, after 12 weeks, 13.7% of 20000 participants still had a symptom.<sup>15</sup> More recently, research using commercial electronic health record data found that 1 in 5 people (aged 18 to 64) and as many as 1 in 4 people (aged 65 or older) had an illness that was newly diagnosed using a diagnosis code.<sup>16</sup>

A plant-based diet known as the Mediterranean diet (MD) is linked to a lower risk of COVID-19 comorbidities and manifestations, which lessens the burden of symptoms in the post-COVID-19 period.<sup>17</sup> In earlier research, it was discovered that the MD score was negatively correlated with the severity of COVID-19 symptoms such as dyspnea, cough, fever, chills, weakness, myalgia, nausea and vomiting, and sore throat. Higher adherence to the MD was also

associated with a shorter period of hospitalization and convalescence, and inflammatory biomarkers.<sup>18</sup> According to previously conducted studies the MD adherence has been reported an increase in various countries due to the raised awareness.<sup>19</sup> There is a scarcity of studies that clearly reveal the impact of high MD adherence on reducing the burden of post-COVID-19 symptoms. The recommendation of a complete Mediterranean dietary pattern is more effective than that of its individual food groups in preventing the infection and symptoms of COVID-19.<sup>20</sup>

The patients' quality of life is negatively impacted by the COVID-19 disease and post COVID symptoms. The factors those contribute to Long COVID have also been discussed in various studies. However, studies those evaluated the symptoms those arises after recovery of COVID-19 and discussed the association with dietary adherence is not available. A deeper comprehension of the risk factors that contribute to the development of new symptoms or diseases after recovery from infection is also required. We set out to evaluate the symptoms that manifested and persisted in people who had been hospitalized after three to six months of COVID-19 infection.

## **Methods:**

### **Study design:**

This was a cross-sectional study among recovered adult COVID-19 patients in Dhaka city. The study population were people who were infected by COVID-19 during January to March 2022, admitted to the hospital, survived and released from hospital after recovery. The hospital registrar was the source of the sample population, which was used to select study participants. The patient list was collected from the targeted hospital with contact details. The Data collection period was May to June, 2022. The article is developed following the strengthening the reporting of observational studies in epidemiology (STROBE) checklist for cross sectional studies. All the patients were confirmed COVID-19 positive by reverse transcription polymerase chain reaction (RT-PCR) assay and had available health records for the study.

### **Study setting and site:**

The study site was Dhaka City and the sampling frame was the patient registrar of Ad-din Medical College Hospital, which is one of the largest privately facilitated tertiary level hospitals in Dhaka City. Data was collected through phone call interview and face

to face interview between May to June 2022 by experienced physicians.

**Study participants, sampling and data collection**

The participants were confirmed COVID-19 patients admitted to the Ad-din Medical College Hospital between January and March 2022 and who recovered. During the study period, around 30 or more COVID-19 patients were admitted each day in the targeted facility. To control the selection bias, systematically one of every five patients from the register was selected for the interview. If we were unable to connect the targeted study sample, the immediate sample was interviewed. Participants who were aged less than 20 years, did not have any symptoms or complexity, infected with COVID-19 during later days, and those who were not interested were excluded from the study. Data with incomplete information were also excluded from the analysis. Finally, 314 complete interviews of surviving patients were included in the analysis.

**Tools and variables:**

During the hospitalization period, the clinical records were documented and checked by experienced medical doctors. We had asked the participants about their current health condition and the status of symptoms and co-morbidities those have taken place after the recovery from COVID-19. Dietary adherence was measured by the Mediterranean Diet Adherence Screener (MEDAS) tool for MD adherence assessment. The 14-item MEDAS tool categorized the adherence level into three categories (low adherence: d”5 points, moderate adherence: 6–9 points, and high adherence: e”10 points).<sup>21</sup> MEDAS was validated in various countries, including Italy, Macedonia, Spain, Greece, Portugal, Bulgaria, etc.<sup>22</sup>

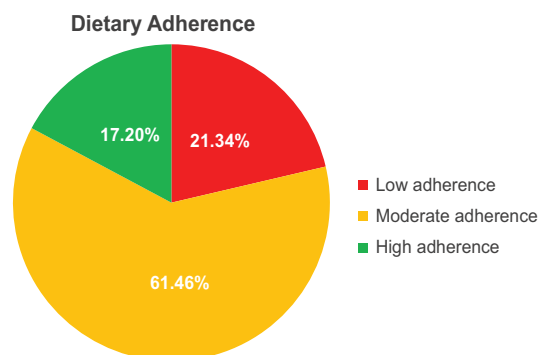
**Statistical analysis:**

Based on the burden of symptoms and chronic conditions, study participants were categorized as (i) d”4 manifestations and (ii) >4 manifestations. The collected data were entered in Microsoft Excel-2013 and statistical analysis was performed by IBM Statistical Package for the Social Sciences (SPSS) version-25 software. The descriptive analysis of categorical variables was performed by frequency, percentage and continuous variables were reported as means with standard deviation. Association between dependent and independent variables were analyzed by Pearson’s Chi-square test or Fisher’s exact test when appropriate. Statistically significant variables were subjected to multiple logistic regression analysis to identify the predictors high manifestation burden.

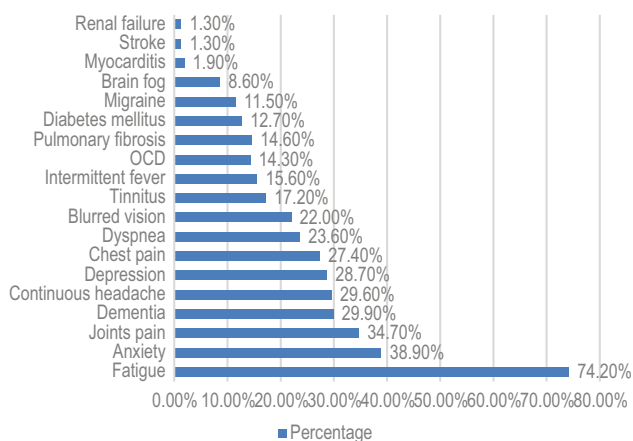
**Results:**

The mean age of the study participants was 55.4 (±13.6) years, ranged between 24 to 90 years. Majority of our study participants (51.3%) were between 41-60 years old as a smaller number of young people usually admitted to hospital for COVID-19 and male were predominant (66.2%). More than 32% of our study participants had smoking habit. During the time of infection, a large proportion had comorbidities including, hypertension (37.7%), Asthma (17.5%), Hypothyroidism (14%), Cardiovascular problem (23.6%), Anemia (23.6%), Acute kidney infection (14.3%). ICU was required for 20.7% of our study participants and 88.5% said they are already vaccinated (Table I).

The mean Dietary adherence score 7.36(±2.1) ranged between 3 to 12 out of 14. We have categorized the adherence level into three categories following (low adherence, moderate adherence, and high adherence). Among study participants, 21.34% showed low adherence to MD and only 17.2% showed high adherence (Figure 1).



**Fig.-1.** Dietary adherence of recovered COVID-19 patients



**Fig.-2.** Symptoms of COVID-19 recovered patients in post-COVID period

The median number of manifestations arises after infected with COVID-19 is 4 and maximum 10 manifestation. The frequency of various manifestations is shown in figure 2. Fatigue (74.2%) followed by the anxiety (38.9%) and joints pain (34.7%) are the most common manifestations faced during the after COVID-19 period.

We have analyzed the association between dietary adherence and manifestations appeared after recovered from COVID-19 by Spearman co-relation. According to test statistic, number of manifestations increases with the decrease of MD adherence level ( $r=-0.34$ ,  $p<0.01$ ), thus have medium and statistically significant negative correlation between these two variables. The age of the participants also has statistically significant positive correlation ( $r=0.31$ ,  $p<0.01$ ) with number of manifestations. Binary linear regression analysis also identified MD adherence as the statistically significant predictor for number of manifestation (OR: 7.25, 95% CI: 6.39-8.11).

The association between disease/symptoms burden and independent variables were determined by chi-square analysis. Age, smoking habit, Asthma, Hypothyroidism, Cardiovascular problem, Acute kidney infection, ICU requirement, and Dietary adherence has statistically significant association with disease burden ( $p<0.05$ )(Table 1).

The multiple logistic regression analysis indicates, participants those does not have the habit of smoking (AOR: 0.43, 95% CI: 0.24-0.77), did not have Asthma during hospitalization (AOR: 0.34, 95% CI: 0.17-0.68), Hypothyroidism (AOR: 0.37, 95% CI: 0.15-0.93), ischemic heart disease (AOR: 0.33, 95% CI: 0.15-0.74), did not required ICU (AOR: 0.31, 95% CI: 0.15-0.64) are associated with lowering the symptom burden during post COVID period. Participants with low dietary adherence are at higher risk of more disease burden during the post COVID period (AOR: 3.56, 95% CI: 1.46-8.69) (Table II).

**Table-I**  
*Frequency distribution and bivariate analysis*

Variables	Category	Frequency (%)	No of Manifestation		P value
			≤4 (%)	> 4 (%)	
Age in years	24-40	39 (12.4)	33 (84.6)	6 (15.4)	0.02*
	41-60	161 (51.3)	110 (68.3)	51 (31.7)	
	61-90	114 (36.3)	68 (59.6)	46 (40.4)	
Gender	Female	106 (33.8)	69 (65.1)	37 (34.9)	0.57
	Male	208 (66.2)	142 (68.3)	66 (31.7)	
Habit of Smoking	No	213 (67.8)	155 (72.8)	58 (27.2)	<0.01*
	Yes	101 (32.2)	56 (55.4)	45 (44.6)	
Hypertension	No	195 (62.1)	137 (70.3)	58 (29.7)	0.14
	Yes	37.9 (Yes)	74 (62.2)	45 (37.8)	
Asthma	No	259 (82.5)	185 (71.4)	74 (28.6)	<0.01*
	Yes	55 (17.5)	26 (47.3)	29 (52.7)	
Hypothyroidism	No	283 (90.1)	200 (70.7)	83 (29.3)	<0.01*
	Yes	44 (14.0)	11 (35.5)	20 (64.5)	
Cardiovascular problem	No	240 (76.4)	194 (71.9)	76 (28.1)	<0.01*
	Yes	74 (23.6)	17 (38.6)	27 (61.4)	
Anemia	No	240 (76.4)	164 (68.3)	76 (31.7)	0.44
	Yes	74 (23.6)	47 (63.5)	27 (36.5)	
Acute kidney infection	No	269 (85.7)	187 (69.5)	82 (30.5)	0.03*
	Yes	45 (14.3)	24 (53.3)	21 (46.7)	
ICU requirement	No	249 (79.3)	186 (74.7)	63 (25.3)	<0.01*
	Yes	65 (20.7)	25 (38.5)	40 (61.5)	
Vaccinated	No	36 (11.5)	25 (69.4)	11 (30.6)	0.76
	Yes	278 (88.5)	186 (66.9)	92 (33.1)	
Dietary adherence	Low	65 (20.7)	15 (23.1)	50 (76.9)	<0.01*
	Medium	193 (61.5)	151 (78.2)	42 (21.8)	
	High	56 (17.8)	45 (80.4)	11 (19.6)	

**Table-II**  
*Multiple logistic regression analysis*

Variables	Category	$\beta$	AOR (95% CI)	Significance
Age in years	24-40	-0.56	0.57 (0.19-1.66)	0.30
	41-60	-0.09	0.91 (0.49-1.71)	0.77
	61-90	Reference		
Habit of Smoking	No	-0.84	0.43 (0.24-0.77)	0.01*
	Yes	Reference		
Asthma	No	-1.07	0.34 (0.17-0.68)	<0.01*
	Yes	Reference		
Hypothyroidism	No	-0.98	0.37 (0.15-0.93)	0.04*
	Yes	Reference		
Ischemic heart disease	No	-1.11	0.33 (0.15-0.74)	0.01*
	Yes	Reference		
Acute kidney infection	No	-0.14	0.86 (0.38-1.96)	0.73
	Yes	Reference		
ICU requirement	No	-1.16	0.31 (0.15-0.64)	<0.01*
	Yes	Reference		
Dietary adherence	Low	1.27	3.56 (1.46-8.69)	0.01*
	Medium	-0.37	0.69 (0.32-1.48)	0.34
	High	Reference		

**Discussion:**

We have successfully completed a cross-sectional study targeting the health status of recovered COVID-19 patients. Here, we have assessed COVID-19 related manifestations and Mediterranean diet adherence. Our analysis has successfully revealed patterns of dietary adherence and other factors that are associated with a higher number of manifestations related to COVID-19.

The most common manifestation reported by the study participants is fatigue, followed by anxiety and joint pain. Fatigue was common among 74.2% of the study participants. A study previously conducted among Bangladeshi adults also reported a 63% prevalence of fatigue after two months of hospital discharge.<sup>23</sup> Joint pain was also highly prevalent in our study. The problem of muscle pain due to muscle weakness and skeletal muscle damage is very common for COVID-19 patients.<sup>24</sup> Both anxiety and depression were highly prevalent among our study participants. According to a previously conducted research, the COVID-19 pandemic has increased the prevalence of anxiety and depression worldwide by 25%.<sup>25</sup> Another study said that, the COVID-19 pandemic has led to a 27.6% increase of major depression.<sup>26</sup> Dementia and

brain fog are also two common manifestations of COVID-19. If left untreated, brain fog can impact the quality of life and lead to other conditions such as Parkinson’s disease, memory loss, and Alzheimer’s disease.<sup>27</sup>

Despite being a respiratory or lung condition, COVID-19 can also affect the heart. Our analysis has reported a high proportion of people with problems in their hearts. Recovery can be hampered for those who have COVID-19, especially if those issues persist. Like other viral illnesses, the coronavirus may directly infect and harm the heart’s muscular tissue. Thus, chest pain is experienced by 10% of patients after recovery.<sup>28-30</sup> A study reported the presence of chest pain among 27% of patients. Myocarditis has also been reported as a complication in patients with COVID-19. In April 2021, increased myocarditis incidence was reported in the United States after mRNA COVID-19 vaccination.<sup>31</sup>

Intermittent fever is also reported as one of the long COVID symptoms.<sup>32</sup> We have also seen a significant proportion of our study participants face this. The possibility of obsessive-compulsive disorder (OCD) being precipitated or brought on by COVID-19-related inflammatory stimuli. More than 14% of our study

participants also reported OCD after their recovery from infection. The prevalence of OCD has increased at a higher rate since the initiation of COVID-19 pandemic.<sup>33</sup>

Six months to a year after COVID-19, survivors often have persistent abnormalities on lung imaging. On pulmonary function tests, some people have chronic lung impairment.<sup>34</sup> Around 15% of our study participants also faced pulmonary fibrosis after their recovery from infection.

There were 12.7% newly diagnosed DM patients in our study, which is very alarming. Previous research also suggests that, those recovering from a severe SARS-CoV-2 infection may experience acute sequelae like newly diagnosed DM. Patients of all ages and genders are at risk of being newly diagnosed with diabetes following COVID-19.<sup>35-37</sup>

Cerebrovascular diseases are common among COVID-19 patients and also in the post COVID-19 period, especially in those who have existing vascular risk factors.<sup>38</sup> Studies have mentioned that, anticoagulation played an important role in the stroke during COVID-19. Even after the recovery from the infection, a high risk of stroke exists, which supports our study findings. When an acute ischemic stroke occurs in patients with COVID-19, the probability of death increases by two-fold.<sup>39</sup>

Patients with COVID-19 have a high prevalence of kidney illness at admission, and AKI frequently develops during hospitalization and is linked to higher fatality rates. Survived COVID-19 patients also have a high risk of kidney disease in the post-acute phase.<sup>40,41</sup> These findings corroborated our observations, and clinicians should be more aware of kidney disease during the post COVID period.

The anti-inflammatory properties of the Mediterranean diet are essential during the struggling health condition of the body during the post-COVID. Essential steps needed to be taken to improve the adherence to dietary recommendations among the COVID-19 recovered patients. Previous studies have observed that MD adherence has a negative association with COVID-19 related deaths in various countries. We also observed a negative association between MD adherence and post COVID-19 symptom burden.<sup>42,42</sup>

The association of age with the severity and outcome of COVID-19 is widely known, and this study has demonstrated the relation between advanced age and complexity after the recovery from infection (44,45). On the other hand, smoking is a well-recognized risk factor for progression of COVID-19, which is also

associated with a number of comorbidities (46). Our findings suggest the recovered patients those are smokers to immediately stop it even if they have no symptoms related to COVID-19.

#### **Conclusion:**

Persistent COVID-19 symptoms and post COVID chronic diseases are concerning public health issues in recent days. A large proportion of study participants showed low dietary adherence, which contributed to the high burden of symptoms during Post-COVID-19 for long term. People with low dietary adherence are also at higher risk for chronic diseases. Patients who did not require ICU also had a lower risk of long-term COVID symptoms burden. Effective control of post-COVID symptoms is important to confirm a healthy and good quality of life. Therefore, it is important to maintain good dietary practices, avoid bad habits, and control chronic diseases.

#### **Limitations of the study:**

This study was conducted in a single center. A complete thrombophilia evaluation could not be performed in every patient due to financial constraints and genetic study was not done.

#### **Data Availability:**

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

#### **Conflict of Interest:**

The authors stated that there is no conflict of interest in this study

#### **Funding:**

This research received no external funding.

#### **Ethical consideration:**

The study was approved by the Ethical Review Committee of Ad-din Medical College Hospital, Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

#### **Author Contributions:**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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