

# Length of hospital stay of COVID-19 patients and its relationship with liver function abnormalities

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## Article Info

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Received: 22 May, 2021  
Accepted: 27 June, 2021  
Available Online: 07 July, 2021

ISSN: 2224-7750 (Online)  
2074-2908 (Print)

DOI: <https://doi.org/10.3329/bsmmuj.v14i3.54674>

**Keywords:** COVID-19, Liver function,  
duration of hospital stay.

### Cite this article:

Sarker SS, Hasan SMA, Islam MS, Das N,  
Rahman KM, Alam MR, Kabir MA. Length of  
Hospital Stay of COVID-19 Patients and Its  
Relationship with Liver Function Abnormal-  
ities. *Bangabandhu Sheikh Mujib Med  
Univ J.* 2021; 14 (COVID-19 Supplement):  
8-12.

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### Available at:

[www.banglajol.info](http://www.banglajol.info)

A Journal of Bangabandhu Sheikh Mujib  
Medical University, Dhaka, Bangladesh



## Abstract

Corona Virus Disease (COVID-19), a threat to global public health, caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) has now spread to more than two hundred countries in the world. This ongoing pandemic has already exhausted our health care systems. So determining or predicting the need of healthcare resources has now become a number one priority and the length of hospitalization is a scale which represents the function of the health system of countries. Our objectives were to see the length of hospital stay of COVID-19 patients and its relationship with liver function abnormalities. This observational cross-sectional study was carried out in the COVID-19 inpatient department of BSMMU on 96 patients who are RT-PCR positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Liver function abnormalities (ALT, AST, ALP, PT, serum bilirubin and serum albumin) were recorded precisely. Length of hospital stay was documented. Occurrence of liver function abnormalities and their relation with length of hospital stay were assessed statistically. Total 96 patients were included. Mean hospital stay was found to be  $14.0 \pm 6.2$  with range from 5.0 to 33 days. Total 49(51.0%) patients required hospital staying  $\leq 14$  days and 47(49%) patients were found hospital stay  $> 14$  days. Mean length of hospital stay in case of mild COVID-19 patients was  $6.76 \pm 1.12$  days, in case of moderate Covid-19 patients was  $12.22 \pm 1.91$  days and in severe group it was  $19.18 \pm 4.81$  days. The mean length of hospital stay was statistically significant with raised ALT ( $18.9 \pm 6.2$ ), raised AST ( $18.9 \pm 5.9$ ) and low serum albumin ( $19.4 \pm 7.1$ ) group ( $p < 0.05$ ). No significant association was found between mean length of hospital stay and raised ALP, PT and S. bilirubin group. This study showed that length of hospital stay were significantly higher among severe COVID-19 patients and among liver function abnormalities raised ALT, raised AST and low serum albumin were associated with significant longer hospital stay. Assessing the length of hospital stay is helpful in understanding and predicting hospital bed demand and optimizing the use of healthcare resources.

## Introduction

A newly emerging infectious disease named Coronavirus disease 2019 (COVID-19) has become a global public health issue caused by severe acute respiratory syndrome corona virus (SARS-CoV-2). This ongoing pandemic which may develop to acute respiratory distress syndrome or multiple organ failure was first identified in December 2019 in Wuhan, Hubei, China.<sup>1</sup> According to current estimate up to 15-18% of patients may become severe or critically ill, less than 5% case become fatal, some of them require intensive care unit care.<sup>2</sup> Most commonly reported symptoms are respiratory tract manifestations

in patients with COVID-19.<sup>3</sup> Many case series have also been reported variable involvement of GI and hepatic involvement apart from respiratory system involvement.<sup>4</sup> Significantly higher risk of liver function abnormalities seen in those with severe disease than in those with non severe disease. Among the deceased persons the incidence of liver injury might reach as high as 78%.<sup>5</sup>

Due to rapid outbreak of COVID-19, health care facilities are now challenged by the huge number of patients influx into hospital. According to WHO, till 18th June, 2021 more than 178 million confirmed cases have been registered with a death toll of 3.86 million

worldwide. In Bangladesh till now total confirmed cases are 844,970 and the number of total deaths are 13,399. Even developed countries with their highly efficient health care facilities greatly stressed and suffered from high death tolls.

For decision making and proper planning, it is important to understand and predict hospital bed demand.<sup>6</sup> Length of hospitalization is a scale representing the function of the health system of countries. To determine the ongoing needs for healthcare resources (bed, staff, oxygen) has become the number one priority for many countries. In one study, median length of hospital stay ranged from 4 to 53 days within china and 4 to 21 days outside of China.<sup>6</sup> Guo et al. in their study found median length of hospital stay was 10-13 days.<sup>7</sup> Length of hospital stay differs due to various risk factors as well as the geographic setting due to varying COVID-19 care guidelines.<sup>6</sup> Among the number of risk factors, raised ALT and AST was addressed as an independent predictors of length of hospital stay.<sup>8</sup>

To find out the length of hospital stay and its relationship with liver function abnormalities, we conducted a cross sectional study on patients hospitalized with COVID-19 in COVID inpatient unit, Bangabandhu Sheikh Mujib Medical University, Dhaka.

## Methods

This is a cross sectional study carried out at dedicated COVID-19 unit of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. The study period was August, 2020 to January 2021.

### Inclusion Criteria:

Total 96 RT-PCR positive COVID 19 patients aged  $\geq 18$  years were included as study sample.

### Exclusion Criteria:

Patients with age less than 18 years and who does not understand or agree to comply with planned study procedure were excluded from our study.

### Study Procedure:

Patients suffering from SARS-CoV-2 infection confirmed by RT-PCR admitted in COVID-19 inpatient department were enrolled in the study after screening for inclusion and exclusion criteria. RT-PCR negative COVID-19 patients and those with known pre-existing liver disease were excluded. Demographic profile, precise date of initiation of symptoms of these patients was noted in data sheet. To assess liver function, ALT, AST, ALP, s. bilirubin, prothrombin time and s. albumin were done and noted precisely in data sheet. Liver function abnormalities were defined as: ALT > 40 U/L, AST > 40U/L, ALP > 120U/L, serum bilirubin > 1.2mg/dl, prothrombin time prolonged > 4 second and serum albumin < 35gm/L. COVID 19 disease severity was assessed and classified as mild, moderate, severe and critical cases by concerned Internal

Medicine & Pulmonology specialist consultant in accordance with the Interim Guidance, 27<sup>th</sup> May, 2020 on the Management of COVID 19 from WHO (WHO, 2020). Total duration of hospital stay was documented. We only included patients with normal discharge circumstances and excluded those with death outcomes. Occurrence of liver function abnormalities and their relation with duration of hospital stay was assessed statistically.

### Statistical analysis:

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Unpaired t-test was used for continuous variables. P values <0.05 were considered as statistically significant.

## Result:

Total 96 patients were included in this study. Two third (66.7%) patients were male and 32(33.3%) were female. Male female ratio was 2:1. Of them, 37(38.5%) patients belonged to age 51-60 years. The mean age was found  $57.2 \pm 12.1$  years with range from 20 to 86 years. (Table I)

Table-I		
Distribution of the study patients by demographic characteristics (n=96)		
Socio-demographic characteristics	Number of patients (n)	Percentage (%)
Age (years)		
≤30	2	2.1
31-40	8	8.3
41-50	14	14.6
51-60	37	38.5
61-70		22 22.9
71-80	11	11.5
>80	2	2.1
Mean±SD	57.2±12.1	
Range (min-max)	20-86	
Sex		
Male	64	66.7
Female	32	33.3

This study showed that 44 (45.8%) patients had severe, 27 (28.1%) patients had moderate and 25 (26.0%) had mild COVID-19 disease. (Table II)

Table-II		
Distribution of the study patients according to severity of COVID-19 diseases (n=96)		
COVID-19 diseases	Number of patients (n)	Percentage (%)
Mild	25	26.0
Moderate	27	28.1
Severe	44	45.8

In our study mean hospital stay was found to be  $14.0 \pm 6.2$  with range from 5.0 to 33 days. Total 49(51.0%) patients required hospital staying  $\leq 14$  days and 47(49%) patients were found hospital stay  $> 14$  days. (Table III).

Table-III		
Distribution of the study patients according to hospital stay (n=96)		
Hospital stay (days)	Number of patients (n)	Percentage (%)
$\leq 14$	49	51.0
$> 14$	47	49.0
Mean $\pm$ SD	14.0	$\pm 6.2$

Mean length of hospital stay in case of mild COVID-19 patients was  $6.76 \pm 1.12$  days, in case of moderate Covid-19 patients was  $12.22 \pm 1.91$  days and in severe group it was  $19.18 \pm 4.81$ . (Table IV)

Table-IV		
Length of Hospital Stay according to severity of COVID-19 diseases (n=96)		
COVID-19 diseases	Length of hospital stay	
	Mean $\pm$ SD	Range
Mild	$6.76 \pm 1.12$	5-10
Moderate	$12.22 \pm 1.91$	10-16
Severe	$19.18 \pm 4.81$	6-33

In our study median ALT was 36.0 U/L (range 13-355), AST was 35.0 U/L (range 17-170), ALP was 87.5 U/L (range 56-15), prolonged prothrombin time was 0.8 second (range 0-7.2), serum bilirubin was 0.64 mg/dL (range 0.30-3.1) and serum albumin was 37.0 g/L (range 25-43). Raised ALT ( $> 40$  U/L) was found in 37.5%, Raised AST ( $> 40$  U/L) was found in 39.6%, Raised ALP ( $> 120$  U/L) was found in 1%, Raised Serum Bilirubin ( $> 1.2$  mg/dL) was found in 2.1%, Low Serum Albumin ( $< 35$  g/L) was found in 18.8% cases. (Table V)

Table-V			
Distribution of the study patients according to liver function abnormality (n=96)			
Laboratory variables		Number of patients (n)	Percentage (%)
ALT			
	Raised ( $> 40$ U/L)	36	37.5
	Normal (0-40 U/L)	60	62.5
Median		36.0	
Range (min-max)		13.0-355.0	
AST			
	Raised ( $> 40$ U/L)	38	39.6
	Normal (0-40 U/L)	58	60.4
Median		35.0	
Range (min-max)		17.0-170.0	
ALP			
	Raised ( $> 120$ U/L)	1	1.0
	Normal (40-120 U/L)	95	99.0
Median		87.5	
Range (min-max)		56.0-145.0	
Prothrombin Time (PT)			
	Raised ( $> 4$ sec)	9	9.4
	Normal (0-4 sec)	87	90.6
Median		0.8	
Range (min-max)		0.0-7.2	
Serum Bilirubin			
	Raised ( $> 1.2$ mg/dL)	2	2.1
	Normal (0.3-1.2 mg/dL)	94	97.9
Median		0.64	
Range (min-max)		0.30-3.1	
Serum Albumin			
	Low ( $< 35$ g/L)	18	18.8
	Normal (35-55 g/L)	78	81.3
Median		37.0	
Range (min-max)		25.0-43.0	

Our study shows that mean hospital stay was  $18.9 \pm 6.2$  days in patients with raised ALT and  $11.0 \pm 4.0$  days in patients with normal ALT. The difference was statistically significant ( $p < 0.05$ ) between two groups. (Table VI)

**Table-VI****Association between ALT with hospital staying (n=96)**

	ALT		p value
	Raised (n=36)	Normal (n=60)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Hospital staying (days)	18.9 $\pm$ 6.2	11.0 $\pm$ 4.0	0.011
Range (min-max)	6.0-33.0	5.0-18.0	

This study observed that mean hospital stay was found 18.9 $\pm$ 5.9 days in patients with raised AST and 10.7 $\pm$ 4.0 days in patients with normal AST. The difference was statistically significant ( $p < 0.05$ ) between two groups. (Table VII)

**Table-VII****Association between AST with hospital staying (n=96)**

	AST		p value
	Raised (n=38)	Normal (n=58)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Hospital staying (days)	18.9 $\pm$ 5.9	10.7 $\pm$ 4.0	0.001
Range (min-max)	6.0-33.0	5.0-18.0	

In our study mean hospital stay was 6.0 $\pm$  days in patients with raised ALP and 14.1 $\pm$ 6.2 days in patients with normal ALP which is not statistically significant. In case of raised prothrombin group mean hospital stay was 17.2 $\pm$ 7.0 days and 13.7 $\pm$ 6.1 days in patients with normal prothrombin time. The difference was not statistically significant ( $p > 0.05$ ) between two groups. ( Table VIII & IX )

**Table-VIII****Association between ALP with hospital staying (n=96)**

	ALP		p value
	Raised (n=1)	Normal (n=95)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Hospital staying (days)	6.0 $\pm$	14.1 $\pm$ 6.2	-
Range (min-max)	6.0-6.0	5.0-33.0	

**Table-IX****Association between prothrombin time with hospital staying (n=96)**

	Prothrombin time		p value
	Raised (n=9)	Normal (n=87)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Hospital staying (days)	17.2 $\pm$ 7.0	13.7 $\pm$ 6.1	0.618
Range (min-max)	6.0-27.0	5.0-33.0	

This study shows that mean hospital stay was 15.5 $\pm$ 13.4 days in patients with raised serum bilirubin and 14.0 $\pm$ 6.1 days in patients with normal serum bilirubin group. The difference was not statistically significant ( $p > 0.05$ ) between two groups. ( Table X)

**Table-X****Association between serum bilirubin with hospital staying**

	(n=96)		p value
	Serum bilirubin		
	Raised (n=2)	Normal (n=94)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Hospital staying (days)	15.5 $\pm$ 13.4	14.0 $\pm$ 6.1	0.731
Range (min-max)	6.0-25.0	5.0-33.0	

In this study mean hospital stay was 19.4 $\pm$ 7.1 days in patients with low serum albumin and 12.7 $\pm$ 5.3 days in patients with normal serum albumin. The difference was statistically significant ( $p < 0.05$ ) between two groups. (Table XI)

**Table-XI****Association between serum albumin with hospital staying (n=96)**

	Serum albumin		p value
	Raised (n=18)	Normal (n=78)	
	Mean $\pm$ SD	Mean $\pm$ SD	
Hospital staying (days)	19.4 $\pm$ 7.1	12.7 $\pm$ 5.3	0.001
Range (min-max)	6.0-33.0	5.0-26.0	

**Discussion:**

The objective of the study was to see the length of hospital stay of COVID-19 patients and its relationship with liver function abnormalities. We included 96 patients for this study from COVID-19 inpatient unit of BSMMU.

In our study 37 (38.5%) patients belonged to age 51-60 years. The mean age was found 57.2 $\pm$ 12.1 years with range from 20 to 86 years. 64 (66.7%) patients were male and 32 (33.3%) were female. Male female ratio was 2:1. This study showed that 44 (45.8%) patients had severe, 27 (28.1%) patients had moderate and 25 (26.0%) had mild COVID-19 disease.

In our study mean hospital stay was found to be 14.0 $\pm$ 6.2 with range from 5.0 to 33 days. Total 49(51.0%) patients required hospital staying  $\leq$ 14 days and 47(49%) patients were found hospital stay  $>$  14 days. In case of mild COVID-19 patients mean length of hospital stay was 6.76  $\pm$  1.12 days, in case of moderate Covid-19 patients it was 12.22  $\pm$  1.91 days and in



severe cases it was  $19.18 \pm 4.81$  days. Rees et al showed in their study that median hospital length of stay ranged from 4 to 53 days within china and 4 to 21 days outside of china.<sup>6</sup> Guo et al conducted a retrospective cohort study about risk factors associated with hospital length of stay in patients with COVID-19.<sup>7</sup> They observed median length of stay in hospital was 17 days. Chen et al. showed median length of stay was 18 days in their study.<sup>9</sup>

In this study we found that median ALT was 36.0 U/L, AST was 35.0 U/L, ALP was 87.5 U/L, prolonged prothrombin time was 0.8 second, serum bilirubin was 0.64 mg/dL and serum albumin was 37.0 g/L. Raised ALT (>40 U/L) was found in 37.5% cases, raised AST (>40 U/L) was found in 39.6% cases, raised ALP (>120 U/L) was found in 1%, raised s. bilirubin (>1.2 mg/dL) was found in 2.1%, low s. albumin (<35 g/L) was found in 18.8% cases. Su et al. in 2020 reported that the incidence of liver injury in patients with COVID-19 was reported as 39.6% to 43.4%, manifested mainly by the elevation of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, as well as hypoalbuminemia [10]. A few patients had a slight increase in total bilirubin (TBIL) level. This finding is almost consistent to our findings.

In this study mean hospital stay was found  $18.9 \pm 6.2$  days in raised ALT group and  $11.0 \pm 4.0$  days in normal ALT group. The difference was statistically significant ( $p < 0.05$ ) between two groups. The mean hospital stay was found  $18.9 \pm 5.9$  days in raised AST group and  $10.7 \pm 4.0$  days in normal AST group. The difference was statistically significant ( $p < 0.05$ ) between two groups. The mean hospital stay was found  $6.0 \pm$  days in raised ALP and  $14.1 \pm 6.2$  days in normal ALP group. The mean hospital stay was found  $17.2 \pm 7.0$  days in raised prothrombin time and  $13.7 \pm 6.1$  days in normal prothrombin time group. The difference was not statistically significant ( $p > 0.05$ ) between two groups. The mean hospital stay was found  $15.5 \pm 13.4$  days in raised serum bilirubin and  $14.0 \pm 6.1$  days in normal serum bilirubin group. The difference was not statistically significant ( $p > 0.05$ ) between two groups. The mean hospital stay was found  $19.4 \pm 7.1$  days in low serum albumin and  $12.7 \pm 5.3$  days in normal serum albumin. The difference was statistically significant ( $p < 0.05$ ) between two groups. Among the number of risk factors, raised ALT and AST was addressed as an independent predictors of length of hospital stay in a study conducted by Li et al.<sup>8</sup> This observation is consistent with findings in our study.

## Conclusion :

This study showed that length of hospital stay were significantly higher among severe COVID-19 patients and among liver function abnormalities raised ALT, raised AST and low serum albumin were associated with significant longer hospital stay. Assessing the length of hospital stay is helpful in

understanding and predicting hospital bed demand and optimizing the use of health care resources. Though it was a single centered study and sample size was small, further studies should be done including large number of patients and involving multiple center.

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