



Renal Involvement in Hospitalized COVID-19 Patients without Pre-existing Kidney Disease

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Abstract

Introduction: COVID 19, caused by the highly contagious SARS CoV 2 virus, has resulted in over 6 million deaths worldwide since December 2019. While primarily affecting the pulmonary system, the infection also impacts kidneys. Increasing evidence shows increasing renal impairment among hospitalized COVID-19 patients, highlighting the importance of monitoring renal functions and its association with COVID-19 disease severity.

Materials & Methods: This prospective observational study was conducted at Bangladesh Medical University (BMU), from September 2020 to August 2021, involving 231 adult COVID-19 patients with normal baseline serum creatinine. Patients with pre-existing conditions or unwilling to consent were excluded. Relevant data were collected and statistical analysis was conducted.

Results: The study population had a mean age of 53.5 ± 14.5 years, with 48.1% participants aged 51–70 years; males comprised 57.1%, and mean BMI was 23.3 kg/m^2 . Fever was the predominant symptom (93.9%), followed by cough (68.8%), loss of smell (50.2%), shortness of breath (45%), diarrhea (37.7%), and body ache (22.5%). Mean SpO₂ was $93.17 \pm 4.21\%$. Hypertension (29.9%) and diabetes (22.1%) were the most common comorbidities. HRCT revealed 26–50% lung involvement in 44.5% and 51–75% in 35.5% of patients. Average time from symptom onset to admission was 5.9 ± 2.3 days, with hospital stay averaging 13.1 ± 5.3 days. COVID-19 disease severity was moderate in 66.2%, severe in 16.9%, and critical in 5.2%. Renal complications were frequent: AKI occurred in 11.7%, proteinuria and hematuria each in 25.1%, and overall renal involvement in 55.8%. Critical cases showed the highest renal involvement (77.8%), followed by severe (76.9%) and moderate (51%).

Conclusion: There is significant impact of COVID-19 on renal function and monitoring renal involvement in hospitalized COVID-19 patients is vital for good prognosis.

Keywords: COVID-19, AKI, Renal Involvement.

Introduction

COVID-19, caused by the highly contagious SARS-CoV-2 virus, has had a devastating global impact, leading to over 6 million deaths since its emergence in late December 2019¹. COVID-19 infection presents in various clinical forms and

is recognized as a multisystem inflammatory syndrome, creating significant challenges for primary physicians. It can range from asymptomatic cases to those requiring outpatient treatment or hospitalization. While the disease primarily impacts the pulmonary system, leading to

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respiratory distress and hospital admissions, it also affects other systems, including the kidneys^{2,3}. Several studies have observed and documented an increasing incidence of renal involvement (elevated serum creatinine, hematuria and proteinuria) in COVID-19 patients, particularly among those admitted in hospital⁴⁻⁷. Studies have indicated that COVID-19 impacts the kidneys' vascular, tubular, and glomerular compartments⁸. Acute kidney injury (AKI) has also been found to correlate with complications and clinical outcomes. In a systematic review, AKI was found to be associated with increased mortality (relative risk: 13.38), severe disease (RR: 4.43), and the need for ICU support for hospitalized COVID-19 patients (RR: 5.90)⁶. Recent study has also shown in COVID-19 patients, renal involvement to be highly correlated with disease severity and increased risk of mortality during treatment⁷.

The SARS-CoV-2 uses the angiotensin II-converting enzyme (ACE2) and the transmembrane serine 2 protease (TMPRSS2) to enter cells. These enzymes are expressed in kidney cells, making them targets for infection⁷. This can lead to alterations in renal function tests and acute renal failure. The presence of virus antigens in kidney tissue and urine of COVID-19 patients supports this theory^{9,10}. In addition to its direct cytopathic effects, SARS-CoV-2 triggers a severe immune response, causing macrophage and lymphocyte infiltration, fibrosis, and microvascular changes, leading to acute tubular necrosis and AKI⁹. The virus also disrupts the renin-angiotensin-aldosterone system by occupying ACE2, increasing angiotensin II levels, which may cause nephron vasoconstriction and reduced glomerular filtration rate. This process also raises blood volume and sodium levels due to increased aldosterone activity and decreased angiotensin¹¹.

Bangladesh was hit by COVID-19 at March 2020, and ever since we have witnessed a high rate of renal involvement and related complications in COVID-19 patients. In depth data regarding renal involvement among hospitalized COVID-19 patients is needed to ensure better prognosis, but there is scarce evidence that evaluate renal involvement among such patients. Therefore, present study aimed to focus on the epidemiology of renal involvement among COVID-19 hospitalized patients, the predictors of this involvement and its association with disease severity.

Materials and Methods

This prospective observational study was conducted in the COVID unit of BMU, Dhaka from September 2020 to August 2021, among adult (age ≥ 18 years) admitted COVID-19 patients with normal baseline serum creatinine. Patients with pre-existing proteinuria, pre-existing hematuria, on maintenance hemodialysis, renal transplant

recipient, pregnant and lactating women, with structural kidney disease like stone or tumor, patients with urinary tract infection or unwilling to give written consent for the study, were excluded. Using purposive sampling technique, 231 respondents were enrolled in the study as per selection criteria. Before starting the study, formal ethical approval was taken from the Institutional review board (IRB) of BMU. Patients' history and clinical examination were done with proper personal protection by wearing personal protective equipment (PPE). Drug history, laboratory and radiological findings, disease course and pre-existing comorbidities were obtained and recorded in data sheet.

The severity of COVID 19 was classified according to BMU clinical case management guidance (2020) into four categories. Mild cases presented with nonspecific symptoms such as fever, cough, sore throat, malaise, headache, myalgia, anosmia, conjunctival redness, or rash, without dyspnea or radiological evidence of pneumonia. Moderate cases included patients with mild symptoms plus radiological findings of pneumonia, respiratory distress with a rate < 30 breaths/min, or oxygen saturation $> 93\%$ on room air. Severe cases were defined by respiratory distress with a rate ≤ 30 breaths/min, oxygen saturation $\leq 93\%$ at rest, or arterial partial pressure of oxygen (PaO₂)/fraction of inspired oxygen (FiO₂) ≤ 300 mmHg. Critical cases encompassed patients with respiratory failure requiring mechanical ventilation, shock, acute respiratory distress syndrome (ARDS), or other organ dysfunction necessitating intensive care. AKI was diagnosed according to the definition by the KDIGO 2012 Clinical Practice Guidelines¹².

Baseline serum creatinine and previous urine analysis reports were collected if available. When not available prior to the diagnosis of COVID-19, serum creatinine measured on admission was used as the baseline value. Routine investigations including renal function test were done. Patients were followed up at regular interval. For all the respondents, repeat renal function test including urine routine microscopic examination and serum creatinine was done at 48 hours, on day 7 and at discharge. Three months after discharge patients with renal involvement (proteinuria, hematuria, AKI) were followed up. Data were collected using a preformed semi structured data collection sheet (questionnaire). Demographic data of the patients including their age and gender were collected. All information regarding clinical features was recorded. All the reports of the investigations were recorded in the data sheet.

Statistical analysis was performed using Windows® based software program Statistical Packages for Social Sciences 25 (SPSS-25) (Chicago, IL, USA). After collection, all the

data were checked and cleaned. Quantitative data were expressed as percentage, mean and standard deviation and qualitative data were expressed as frequency distribution and percentage. To determine statistical significance, Chi-squared test and Independent Sample T-test were considered according to applicability. P value of < 0.05 was considered statistically significant.

Results

Mean age of the study population was 53.5 ± 14.5 years, with 26.0% respondents from age group 51 – 60 years, followed by 22.1% respondents from 61 – 70 years (Table I). Study population was male (57.1%) predominant. Mean BMI was 23.3 ± 3.2 kg/m². Most of the respondents (93.9%) had fever on presentation. Other complaints included cough (68.8%), shortness of breath (45.0%), loss of smell

(50.2%), diarrhea (37.7%) and body ache (22.5%). Mean SpO₂ was $93.17 \pm 4.21\%$. Hypertension was the most prevalent comorbidity at 29.9% respondents, followed by DM at 22.1% respondents. In HRCT reports, 44.5% respondents had 26 - 50% lung involvement, followed by 35.5% having 51 - 75% lung involvement. Average time from symptoms onset to admission was 5.9 ± 2.3 days. Average length of hospital stay was 13.1 ± 5.3 days.

COVID-19 disease severity was assessed and 66.2% had moderate disease, followed by 16.9% with severe disease (Figure 1a). AKI status of the study population was assessed (Figure 1b). AKI was found among 27 (11.7%) respondents, of which stage 1 AKI was found among 14 (51.9%) respondents, stage 2 AKI was found among 6 (22.2%) respondents and stage 3 AKI was found among 7 (25.9%) respondents.

Table-I
Descriptive statistics of the study population. (n = 231)

Characteristics	Data	
Age (in years)	53.5 ± 14.5	
Age group (in years)	<30	15 (6.5%)
	31 – 40	33 (14.3%)
	41 – 50	48 (20.8%)
	51 – 60	60 (26.0%)
	61 – 70	51 (22.1%)
	>70	24 (10.4%)
Gender	Male	132 (57.1%)
	Female	99 (42.9%)
BMI (kg/m ²)	23.3 ± 3.2	
Comorbidities	Diabetes Mellitus (DM)	51 (22.1%)
	Hypertension (HTN)	69 (29.9%)
	Ischemic Heart Disease (IHD)	34 (14.7%)
	Cerebrovascular Disease (CVD)	9 (3.9%)
	Obstructive Airway	19 (8.2%)
	Clinical presentation during admission	Fever
	Cough	159 (68.8%)
	Shortness of breath	104 (45.0%)
	Body ache	52 (22.5%)
	Diarrhoea	87 (37.7%)
	Loss of smell	116 (50.2%)
HRCT findings (percentage of lung involvement)	SpO ₂ (%)	93.17 ± 4.21
	0%	8 (3.5%)
	1 - 25%	17 (7.4%)
	26 - 50%	103 (44.5%)
	51 - 75%	82 (35.5%)
	>75%	21 (9.1%)
Time from symptoms onset to admission (in days)	5.9 ± 2.3	
Length of hospital stay (in days)	13.1 ± 5.3	

Data presented as n (%) or mean \pm SD.

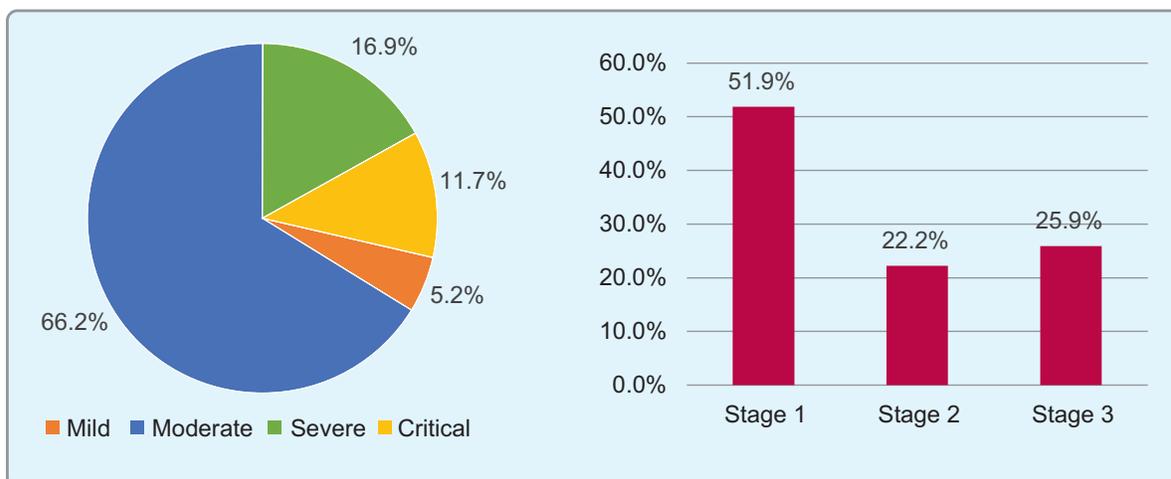


Figure 1: a: Distribution of study population according to COVID-19 severity. (n = 231). b: Distribution of study population according AKI Stages. (n = 27)

Respondents were found to suffer from proteinuria, hematuria, AKI and renal involvement (Table II). Proteinuria +1 was found among 58 (25.1%) respondents, of which 37 (16.0%) had moderate disease. Proteinuria +2 to +3 was found among 23 (10.0%) respondents, of which 11 (4.8%) had moderate disease. Hematuria was found among 58 (25.1%) respondents, of which 30 (13.0%) had moderate disease. Among the 27 (11.7%) respondents with AKI, 11 (4.8%) had moderate disease. Renal involvement was found among 129 (55.8%) respondents, of which 78 (33.8%) had moderate disease.

Study population was assessed according to renal involvement relative to disease severity (Table III). Among the study population, respondents with critical COVID-19

disease showed highest (77.8%) renal involvement, followed by 76.9% severe COVID-19 patients with renal involvement and 51.0% moderate COVID-19 patients with renal involvement.

Among the study population, 129 (55.84%) respondents had renal involvement (Table IV). Mean age of patients with renal involvement was 55.3 ± 16.1 years and patients without renal involvement was 51.3 ± 12.0 years, but this difference was not statistically significant. No statistically significant difference was found in terms of gender distribution related to renal involvement. Statistically significant (p < 0.05) difference was also observed regarding diabetes status and hypertension among patients with renal involvement

Table-II
Clinical findings according to COVID-19 severity. (n = 231)

Variables	Severity of COVID-19				Total
	Mild	Moderate	Severe	Critical	
Proteinuria 1+	0	37 (16.0%)	11 (4.8%)	10 (4.3%)	58 (25.1%)
2+ to 3+	0	11 (4.8%)	7 (3.0%)	5 (2.2%)	23 (10.0%)
Hematuria	0	30 (13.0%)	15 (6.5%)	13 (5.6%)	58 (25.1%)
AKI	0	11 (4.8%)	7 (3.0%)	9 (3.9%)	27 (11.7%)
Renal involvement	0	78 (33.8%)	30 (13.0%)	21 (9.1%)	129 (55.8%)

Data presented as n (%).

Table III*Distribution of study population according to renal involvement. (n = 231)*

Disease severity	Renal Involvement	
	Frequency	Percentage
Mild (n = 12)	0/12	0
Moderate (n = 153)	78/153	51.0%
Severe (n = 39)	30/39	76.9%
Critical (n = 27)	21/27	77.8%
Total (n = 231)	129/231	55.8%

Table-IV*Distribution of study population according to renal involvement. (n = 231)*

Variables	Renal Involvement		P Value
	Present (129, 55.84%)	Absent (102, 44.16%)	
Age (in years)	55.3 ± 16.1	51.3 ± 12.0	0.036 ^b
Gender	Male	81 (35.1%)	51 (22.1%)
	Female	48 (20.8%)	51 (22.1%)
Diabetes mellitus	35 (27.1%)	16 (15.7%)	<0.05 ^a
Hypertension	48 (37.2%)	21 (20.6%)	<0.05 ^a

Data presented as n (%) or mean ± SD.

^a Chi-squared test was conducted, P < 0.05 was considered statistically significant.

^b Independent Sample T-test was conducted, P < 0.05 was considered statistically significant.

Discussion

Mean age of the study population was 53.5 ± 14.5 years. Study population was 57.1% male and 42.9% female. These results are consistent with Pei et al., 2020 study showing mean age of hospitalized COVID-19 patients to be 56.3 years with 54.7% male predominance¹³. Hachim et al., 2021 also showed similar finding among hospitalized COVID-19 patients, which further supports present study findings¹⁴. Highest prevalence of COVID-19 was observed among respondents in age group 51 – 60 years at 26.0%. This is consistent with Kalantari, Tabrizi and Foroohi, 2020 study showing highest prevalence of COVID-19 patients from the age group of 50–59 years¹⁵. Present study showed fever (93.9%), cough (68.8%), dyspnoea (45%) and diarrhea (32.4%) to be the most common clinical presentations during admission for COVID-19 patients. Other studies have also shown similar findings^{13,16}. Mean SpO₂ in present study was 93.2 ± 4.2% which is consistent with the SpO₂ value (93%) shown in Pei et al., 2020 study¹³. Hypertension (29.9%) and diabetes mellitus (22.1%) were the most frequent comorbidities in present study. Other studies have also revealed hypertension and diabetes mellitus to be the most prevalent comorbidities among

COVID-19 hospitalized patients, which supports present study findings^{13,17,18}. Present study showed time from symptoms onset to admission to be 5.9 ± 2.3 days, which is consistent with d" 7 days found for most patients in other studies^{19,20}. mean length of hospital stay in present study was 13.1 ± 5.3 days, slightly higher than Figueroa et al., 2024 showing 9 days²⁰.

Among the study population, 66.2% had moderate disease, 16.9% had severe and 5.2% had critical disease. Hong et al., 2020 showed among COVID-19 patients, 60.1% had moderate disease, 14.3% had severe and 6% had critical disease, which is consistent with current study finding²¹. Present study showed 35.1% respondent developed proteinuria and 25.1% developed hematuria during their stay at hospital. Among hospitalized COVID-19 patients, incidents of proteinuria were shown to be 18.4-65.8% and incidents of hematuria were shown to be 17.4-41.7% in other studies^{13,21,22}. In present study, 11.7% developed AKI, which is consistent with other studies showing 10.5% to 20.7% COVID-19 patients developing AKI^{13,23}. Present study showed 51.9% of the respondents with AKI to have stage 1 disease, followed by 25.9% with stage 3 and 22.2% having stage 3 disease. Alfano et al., 2021 showed similar

findings of 57.9% of the AKI patients having stage 1 disease, 24.6% having stage 2 and 17.3% having stage 3 disease²⁴.

Present study showed 55.8% of the respondents having renal involvement. Other studies among hospitalized COVID-19 patients have also shown renal involvement to develop among 60-75.4% respondents, supporting present study finding (13,25). In present study, among respondents with critical COVID-19 disease, 77.8% had renal involvement, followed by 76.9% severe COVID-19 patients with renal involvement and 51.0% moderate COVID-19 patients with renal involvement. This is higher than Yang et al., 2020 findings, showing 29% renal involvement among critically ill COVID-19 patients, which is lower than present study findings²⁶. Zheng et al., 2020 also suggested increasing prevalence of renal involvement with increasing disease severity among hospitalized COVID-19 patients²⁷. Among the study population, statistically significant ($p < 0.05$) difference was observed regarding diabetes status and hypertension among patients with renal involvement. This is corroborated by Abdulaziz Al-Muhanna et al., 2022 study showing substantial increase in disease severity for diabetes mellitus and hypertension among COVID-19 patients with renal involvement²⁸.

Conclusions

Present study findings highlight the significant impact of COVID-19 on renal function and the importance of monitoring renal involvement in hospitalized COVID-19 patients. Although this was a single center based prospective study, since COVID-19 pandemic is over at the time of publication of this study, a multicenter based retrospective study on the admitted COVID-19 patients' data could be conducted for better understanding the impact of COVID-19 on renal system.

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