

METHODS

The study of clinical profile of acute kidney injury in COVID-19 patients

Shraddha Goswami¹, Mohit Mahajan^{1*}, Naresh Pahwa¹, Vijay Malviya², Vishnu Shukla³ and Trishala Chhabra³

¹Nephrology Department, SAIMS Indore, Indore, MP, India

²Department General Medicine, Consultant ESI Hospital Indore, Indore, India

³SAIMS Medical College, Indore

***Correspondence:**

Mohit Mahajan,
mohitmahajan1110@gmail.com

Received: 29 June 2022; **Accepted:** 27 July 2022; **Published:** 27 August 2022

Aim: All prior studies have demonstrated that acute renal damage in People who have the coronavirus disease of 2019 (COVID-19) are often diagnosed and have a dismal prognosis. Acute renal injury in COVID-19 patients has not been well reported in developing countries like India. Examining the clinical traits, biochemistry, and prognosis of acute kidney injury (AKI) in COVID-19 patients is the aim of this article.

Methods: The Department of Nephrology at the Sri Aurobindo Medical College and Graduate Institute (M.P.) in Indore, India, conducted this study from April 1, 2020, to January 31, 2021. We examined 130 COVID-19 cases of AKI recorded by SAMC and PGI in Indore. Included 18 year-old and older COVID-19 patients verified by real-time reverse polymerase chain reaction (RT-PCR). The term “sepsis” was employed in its conventional sense. The Kidney Disease Improving Global Outcomes (KDIGO) guidelines of AKI were adhered to. Patients under the age of 18 undergoing renal replacement therapy for CKD in stages I to IV and ESRD were not eligible.

Results: A total of 12,438 COVID patients were admitted to our hospital during this period. The incidence of AKI was 1.04% (130). The mean age was 51.2 years. The male-to-female ratio was 1.4:1 (76:54). Commonest symptoms were fever in 71.5% (93) of patients, headache in 62% (81) of patients, and cough in 51.5% (67) of patients, followed by breathlessness in 37.5% (49) patients. The typical creatinine values at the time of admission were 3.57 mg/dl. AKI stage 1 was seen in 30% (39) cases, stage 2 in 45.5% (59) cases, and stage 3 in 24.5% (32) cases. The most common etiology was sepsis in 65% (84) and drugs in 14% (18). T2DM was the most common comorbidity in 42% (55) of patients, HTN in 41.5% (54) of patients, Coronary Artery Disease (CAD) in 9.2% (12) of patients, and malignancy in 5% (7) of patients. Oxygen by nasal mask/nasal prongs was required in 59% (77) of patients, BIPAP in 16% (21) of patients, and ventilatory support in 12.5% (16) of patients. The average hospitalization was 12.3 days. Dialysis was required in 16% (21) of patients. Notably, 87% (113) of patients recovered completely, and 13% (17) of patients expired. The majority of patients had elevated inflammatory markers. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated in 81% (105) of patients, and ferritin was raised in 71% (92) of patients.

Conclusion: Hospitalized COVID-19 patients commonly get AKI, which is associated with a poor prognosis and high mortality. In COVID-19 patients, increased inflammatory markers, type 2 diabetes, sepsis, older age, and male sex were the main risk factors for developing acute renal injury.

Keywords: AKI, acute kidney injury, CKD, chronic kidney disease, ESRD, end-stage renal disease, SOFA, sequential organ failure assessment

Introduction

Since 2019, Coronavirus infection in 2019 (COVID-19; also known as SARS-CoV-2) has spread over the world from one city in Hu Bay, China (1). A pandemic has been proclaimed by the Acute respiratory distress syndrome, which COVID-19 patients experience, is recognized by the World Health Organization (WHO) illness, is a frequent complication (ARDS). According to a recent study, more than 40% of patients hospitalized with severe and life-threatening COVID-19 developed ARDS, and more than 50% of diagnosed patients died of the disease (2). In a Chinese cohort study of 1,099 patients admitted with COVID-19, 93% were admitted, 91% had pneumonia, 5% were admitted to the intensive care unit (ICU), 3% had ARDS, and less than 1% had acute respiratory distress [acute kidney injury (AKI)] (3). In this study, the prevalence of AKI in COVID-19 patients appears to be low.

AKI occurrences have been documented in studies from Asia, the United States, and Europe to vary from 2 to 50%. 4 Studies published so far have shown that the incidence of AKI is very different. T2DM was the most common comorbidity, and hypertension, CAD, and malignancies were other comorbidities (4). In a Spanish study, all patients admitted to the ICU had a death rate of 38% and a prevalence of AKI needing dialysis of 17%. In New York, 35% of patients experienced AKI, and 14% of AKI patients needed dialysis (5).

On March 31, 2021, India reported 1,21,48,602 confirmed (COVID-19) positive cases, while Indore had the highest number of 69,671 cases in Madhya Pradesh (6).

According to recent research, the literature (3, 5, 7, 8) developed nations' COVID-19 AKI outcomes. There is a dearth of information from emerging nations. We examined the incidence, risk factors, clinical symptoms, biochemical profiles, and outcomes of 120 COVID-19-positive patients who developed AKI while being hospitalized for COVID-19 at the SAMC and PG Institute Indore in order to close this evidence gap.

Materials and methods

Real-time reverse polymerase chain reaction (RT-PCR) was used to diagnose COVID-19 using nasopharyngeal (throat) and oropharyngeal (nasal) swabs (6). Retrospective evaluation of adults was done in COVID-19 study group from April 1, 2020, to March 31, 2021.

Inclusion criteria

Patients verified by RT-PCR to be positive for COVID-19 above the age of 18

Sepsis was defined in a standard manner.

The AKI criteria set out by Kidney Disease Improving Global Outcomes (KDIGO) were adhered to.

Exclusion criteria

Patients with CKD from stages I to V, ESRD on maintenance hemodialysis, peritoneal dialysis, renal transplant patients, and age less than 18 years were excluded.

AKI, defined as a 0.3 mg/dl rise in serum creatinine over a period of 48 h or a 50% increase in baseline creatinine, was the primary outcome determined using KDIGO criteria (9). The AKI stage was described using the KDIGO AKI staging definition.

When the Sequential Organ Failure Assessment (SOFA) score increases by two or more points, this indicates that one organ is dysfunctional a clinical indicator of sepsis (10). Patients with a suspected infection are likely to require a lengthy stay in the ICU or die there. Hospitals with qSOFA (i.e., 2 or more of the following) can be quickly detected at the bedside.

- o Hypotension: Systolic blood pressure of 100 mmHg or below.
- o A change in mental state [any (Glasgow Coma Score (GCS) less than 15].
- o Tachypnea: A respiration rate of at least 22.

Discharge policy (11):

The Indian Department of Health and Family Welfare released a new COVID-19 discharge policy in 2020. Prior criteria for COVID-19 patients' release were based on (a) standard chest X-rays and (b) two RT-PCR test results that are negative in a row.

Specific additional recommendations included:

- a. Patients may be discharged 10 days after onset of symptoms, 3 days without fever, with mild/very mild/presymptomatic signs.
- b. Patients with moderate symptoms may be discharged in case of (1) 3 days asymptomatic and (2) 10 days after onset of symptoms, and (3) patients with severe symptoms need to recover clinically as well as have a negative RT-PCR-COVID test (after symptom resolution).

Statistical analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 17.0 (SPSS Inc., Chicago, IL).

Continuous data are defined by the words median, mean, SD, and interquartile range (IQR). Students take a test to compare the two groups.

Results

Over the study period, 130 people who tested positive for both COVID-19 infection and AKI were evaluated. The median age of transplant recipients was 51.9 years, with men making up the bulk of the patient population. A hospital stay lasted an average of 12.3 days.

Most common comorbidities included diabetes (42%; $n = 55$), arterial hypertension (41.5%; $n = 54$), both hypertension and diabetes (32%; $n = 42$), ischemic heart disease in (15.6%; $n = 12$), malignancy (5.3%; $n = 7$), and sickle cell disease (0.76%; $n = 1$), as shown in **Table 1**.

Clinical features

Symptoms presented by the patients included fever (72%, $n = 87$), headache (65%, $n = 78$), cough (64%, $n = 53$), breathlessness (28%, $n = 34$), and sore throat (27%, $n = 33$), as summarized in **Table 2**.

TABLE 1 | Various comorbidities in AKI with patients of COVID-19.

S.no	Comorbidities	Number of patients (total 130)	Percentage (%)
1	Hypertension	55	42
2	Diabetes mellitus	54	41.5
3	Hypertension and diabetes mellitus	42	32
4	Ischemic heart disease	12	15.6
5	Solid malignancy	7	5.3
6	Sickle cell disease	1	0.76

TABLE 2 | Clinical features in AKI with COVID-19.

Clinical feature	Number	Percentage (%)
Fever	93	80
Headache	81	52
Cough	67	46
Breathlessness	49	46
Nausea	17	13
Nasal discharge	13	10
Chest pain	12	9
Vomiting	11	8
Abdominal pain	9	6
Diarrhea	6	4.5
Hemoptysis	2	1.5

Inflammatory markers

inflammatory markers such as erythrocyte sedimentation rate (ESR) were elevated in 81% ($n = 105$), C-reactive protein (CRP) in 81% ($n = 105$), and ferritin in 71% ($n = 92$), as shown in **Figure 1**.

Oxygen requirement

A total of 114 patients required oxygen supplementation out of which through nasal mask (59%, $n = 77$), BIPAP (16%, $n = 21$), and ventilatory support (12.5%, $n = 16$), as shown in **Figure 2**.

Laboratory findings

The total white blood cell count was 10,830 at the time of the presentation, and the average hemoglobin was 11.1 g/dl (IQR, 11.5–15.5 g/dl) (IQR, 4,000 to 11,000 mm). The platelet count was 1,36,000 (IQR, 1.5 to 4.5 lacs mm), serum urea was 106 mg/dl (IQR, 15–40 mg/dl), serum creatinine was 3.6 mg/dl (IQR, 0.7–1.2 mg/dl), ESR was 31 (IQR, 0–20), CRP was 2.4 (IQR, < 0.6), and mean serum ferritin was 898 (IQR, 10–291).

Medical management

Specific therapies included azithromycin treatment, hydroxychloroquine, favipiravir, remdesivir, tocilizumab, steroids, and convalescent plasma.

Patients did not receive any conventional pharmaceuticals, such as colchicine, oseltamivir, chloroquine, interferon, or plasmapheresis and antiretroviral medications (ribavirin and lopinavir/ritonavir).

Hospital experience and clinical results

A total of 38.2% ($n = 49$) of patients needed to be sent to the critical care unit (ICU). A total of 16% ($n = 21$) patients required hemodialysis, which is primarily associated with AKI 3, and sepsis was observed in 65% ($n = 84$) of patients and was found to be the leading cause of AKI. Nearly, 12.5% ($n = 16$) of patients needed ventilation and all succumbed to the disease. Patients were not followed up after discharge. The overall mortality rate of the patient was 15% ($n = 17$). Risk factors for death included age, male gender, type 2 diabetes, sepsis, high levels of inflammatory markers including CRPs, the need for hemodialysis, and the need for ventilation.

Discussion

COVID-19 is rapidly spreading to populations across the globe. Almost everyone is susceptible to infection, either

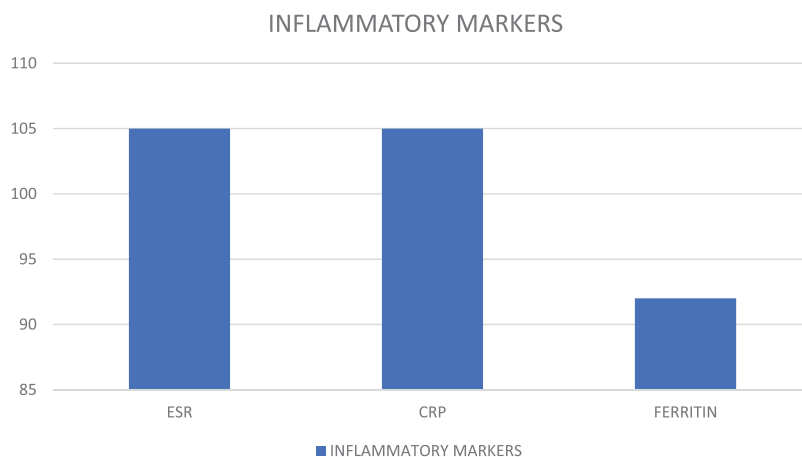


FIGURE 1 | Inflammatory markers of the patients with AKI in COVID-19.

directly or indirectly. We present 130 cases of AKI with COVID-19 infection.

Despite the fact that our cohort is extremely small, it is evident that COVID-19 can present in a variety of ways and that individuals with AKI can have a wide range of prognoses.

We have described a retrospective institutional investigation of COVID-19 patients at our hospital who were AKI-positive. During the national blockade, many patients with COVID-19 received simple home treatment for mild to moderate illness when testing locally was impossible because of testing and resource constraints. It is crucial to use caution. A wide range of clinical symptoms was present at the time of presentation, including fever, sore throat, body aches, coughing, and nausea or vomiting. The incidence of AKI in this study was comparable with another examination of the New York hospital system (12) and lower than that reported in China and Italy. In our study, there were no differences, including a high proportion of patients with comorbid hypertension and diabetes, which contributes as risk factors for developing AKI (3). Diabetes, hypertension, and coronary artery disease were the major comorbidities observed in patients with COVID-19.

The mechanism of renal lesions is multifactorial (13). Vulnerable patients, especially the elderly and those with comorbidities, are at a risk of developing a serious illness. The possible mechanism of AKI is similar to other viral diseases that cause kidney damage. This hypothesis is supported by the presence of CoV viral nucleic acid substances in the body fluids (urine and blood) of SARS-CoV-infected and COVID-19 patients.(14) Virus detection in the urine may continue even after respiratory excretion has stopped; urine virus can be detected for a longer duration than sputum (15).

According to molecular studies, the angiotensin-converting enzyme 2 (ACE2) receptor is used by the coronavirus (SARS-CoV 2), which is related to SARS-CoV, to enter cells. It has been discovered that the binding partner receptors for SARS-CoV and MERS-CoV are present in

OXYGEN REQUIREMENT

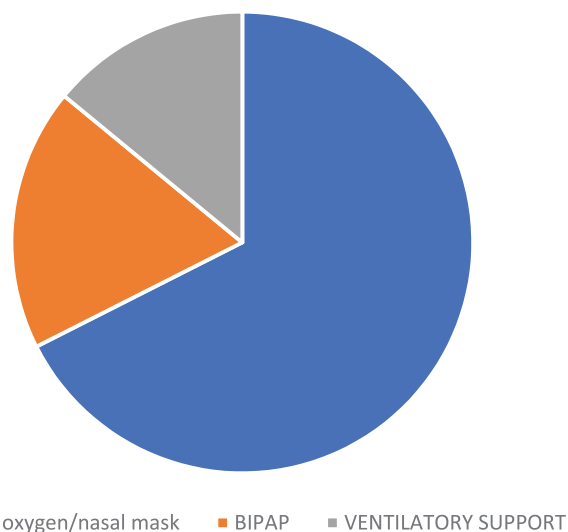


FIGURE 2 | oxygen requirement of COVID-19 patients with AKI.

dipeptidyl peptidase-4 (DPP4) and ACE2, respectively (16, 17).

Damage directly mediated by effector T cells may be another hypothesized mechanism. The hypothesis of glomerular damage mediated by the immune complex was not supported by normal glomerular pathology on microscopy in patients with SARS-CoV and lack of electron-dense deposition on microstructure microscopy (19). Another important mechanism is virus-induced sepsis and the release of cytokines into the circulation, as shown in **Image 1**, (18) which causes severe inflammatory reactions, shock, hypotension, shock, and severe target organ damage, including kidney damage. The clinical picture of COVID-19 patients with sepsis supports this hypothesis.

The average age of our study cohort was 59 years, compared to 63 years in the US and Chinese studies (20, 21). As we operate as a tertiary care center, almost 45% of patients enroll in AKI Stage 2. This is higher than the corresponding

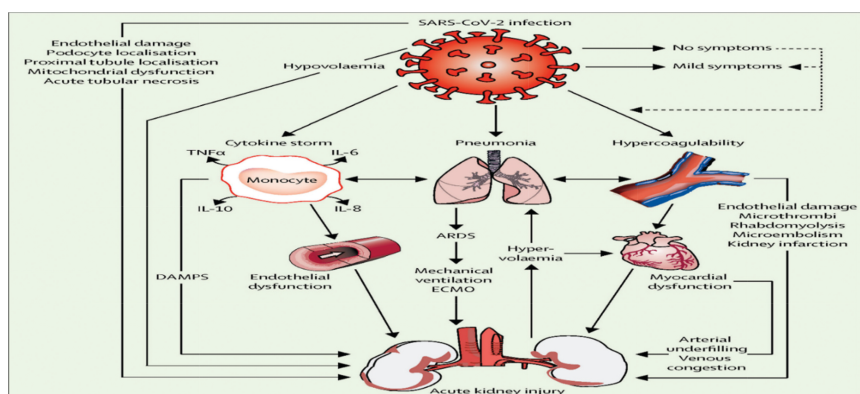


IMAGE 1 | Multisystem involvement in COVID-19 (18).

rate of 30% as was seen in China's population. Prerenal factors with fever and volume loss due to inadequate oral absorption, hyper-inflammatory syndrome leading to cytokine-mediated tubular damage, and ventilator-related renal damage were identified as contributors to AKI.

Furthermore, inflammatory markers were significantly elevated in those who succumbed. A cytokine storm with multifold elevations of ESR, CRP, and ferritin is potential contributors to mortality as reported earlier.(22)Evolutionary links to both innate immunity and thrombosis may explain such a phenomenon in COVID-19 (23).

Only 21% of our patients underwent dialysis therapy. This is in contrast to several studies from China, the US, and Europe where the proportion of dialysis requirement varied from 35 to 70% (20, 21). Only 12.5% of our patients were treated by invasive mechanical ventilation, whereas the rates were 70% in Chinese and US cohorts with AKI (24). It is well known that ventilator-associated renal injury contributes to adverse outcomes. As international experience emerged, our intensivists were more in favor of non-invasive ventilatory strategies that could explain our improved survival rates. When both invasive breathing and dialysis were necessary, all 16 patients passed away. Azithromycin, favipiravir, plasma therapy, tocilizumab, and remdesivir are examples of supportive care that is now used in therapies.

Mortality rates were associated with various risk factors like patients with older age (>60 years), serum creatinine, decreased lymphocyte count, elevated IL-6 levels (cutoff value: 65 ng/L), elevated D-dimer > 960 ng/ml, higher serum lactic acid dehydrogenase (>300 μ /L), CRP (cutoff value: 100 mg/L), high procalcitonin, oxygen demand above 6 L/min, ventilator, increased before COVID-19, disease severity at presentation, and multiple comorbidities, as described in various studies from developed countries. These risk factors were similar in our study. There are limits to our study due to the lack of consistent therapy guidelines for COVID-19-positive patients, as well as treatment modifications based on fresh information and proof from the

growing body of published COVID-19 reports, which, from what I gather, will continue to develop.

Conclusion

AKI was seen in 1% of COVID-19 participants. Among patients, death occurred in 15% of cases. AKI, which is occurs often in hospitalized COVID-19 patients and is linked to a poor prognosis and greater death. Increased inflammatory markers, type 2 diabetes, sepsis, advanced age, and male sex were the most frequent risk variables for the occurrence of acute renal damage in COVID-19 patients.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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