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ORIGINAL RESEARCH

Impact Of Acute Kidney Injury In Covid 19 Infected Patients

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Abstract

Background: Corona virus disease 2019 (covid-19) is a novel disease caused by a newly identified virus, severe acute respiratory syndrome corona virus 2 (sars-cov-2). The novel disease which begun in Wuhan, China in Dec 2019 was declared pandemic by world health organization on 11 march 2020. The most common reported reasons for intensive care unit admission for patients with severe corona virus disease 2019 (covid-19) are either hypoxemic respiratory failure leading to mechanical ventilation or hypotension requiring vasopressor support. Data on AKI are either lacking in this perspective, we emphasize that AKI can be a severe complication of covid-19 and highlight the importance of assessing, defining, and reporting the course of AKI in patients admitted in intensive care unit.

Methods: This is a single centre retrospective observational study. 542 patients with real time-PCR and rapid antigen test confirmed COVID 19 infection admitted in KIMS intensive care unit, Hubballi were taken for study. Patients with chronic kidney disease were excluded from the study. Clinical examination and laboratory investigations including renal function test, liver function test, complete blood count, chest x-ray, d-dimer, ferritin, LDH, CRP was done for all the patients.

Duration: 1 year (2020 August -2021 July)

Results: Out of 542 patients, 166 patients developed acute kidney injury accounting for 30.62 %. 145 patients died (87.47) who had acute kidney injury. And 27 patients were discharged (12.6%) who recovered from acute kidney injury.

Results: Among the patients who did not developed AKI(376) . 300(79.81) died and 76(20.2) got discharged. The p value was 0.034 which was significant for increase in mortality among patients who developed AKI. The incidence of mortality among COVID patient admitted to KIMS ICU was 82.1%.

Conclusion: The mortality was significantly higher in COVID patients developing AKI. So we can predict the outcome in COVID infected patients who develops acute kidney injury. AKI is one of manifestation in COVID patients due to tropism of corona virus to ace receptors present in kidney.

Keywords: COVID, acute kidney injury, ace2 protein, rt-pcr

Introduction

Severe acute respiratory syndrome coronavirus 2 (sars-cov-2) was first described in December 2019 and is responsible for coronavirus disease 2019 (covid-19) and the current global pandemic. The pulmonary manifestations of covid-19 are most prominent, but acute kidney injury (AKI) is also now recognized as a common complication of the disease, and is often evident at hospital admission requiring intensive care management[1].

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The clinical spectrum resulting from infection with the responsible virus, severe acute respiratory syndrome coronavirus 2 (SARS-cov-2), is broad, ranging from an asymptomatic response or development of a mild upper respiratory tract infection to critical illness. Initial reports of hospitalized patients in Wuhan described a high proportion of individuals with atypical pneumonia requiring critical care admission with features of acute respiratory distress syndrome (ARDS)[1,2]. The primary pulmonary pathology seemed to show not only diffuse alveolar damage but also evidence of direct viral cytopathy, implying a direct causative role of virus-induced damage in the development of ARDS rather than it resulting from a generalized inflammatory response[3].

The main binding site for sars-cov-2, like sars-cov, is the ace2 protein, which is expressed in the kidney much more than the lungs([2].Ace2 is expressed on the brush border apical membrane of the proximal tubule, where it colonizes with angiotensin-converting enzyme (ace), and is also present at lower levels in podocytes. An important report on autopsy findings from deceased patients with COVID-19 again demonstrated prominent acute proximal tubular injury, but also peritubular erythrocyte aggregation and glomerular fibrin thrombi with ischemic collapse[4]. It is conceivable that the virus could enter the kidney by invading podocytes first, and thus gain access to the tubular fluid and subsequently bind to ace2 in the proximal tubule. In primary human airway epithelia, ace2 is expressed apically, and sars-cov-2 infection predominantly occurs on the apical surface, but infection can occur on the basolateral surface at low efficiency[4].

Systemic haemodynamic instability very likely contributes to tubular injury. Despite descriptions of COVID-19 as a cytokine storm syndrome, levels of circulating cytokines are often lower in patients with COVID-19 than in patients with acute respiratory distress syndrome with causes other than COVID-19. Tissue inflammation and local immune cell infiltration have been repeatedly observed and might have a critical role in kidney injury, as might endothelial injury and microvascular thrombi. Findings of high viral load in patients who have died with AKI suggest a contribution of viral invasion in the kidneys, although the issue of renal tropism remains controversial. An impaired type I interferon response has also been reported in patients with severe COVID-19. In light of these observations, the potential pathophysiological mechanisms of COVID-19-associated AKI may provide insights into therapeutic strategies[1].

Mortality among hospitalized patients with COVID-19-associated AKI (COVID-19 AKI) is higher than for those without kidney involvement. As with all instances of AKI in the context of multi-organ failure requiring ICU admission, mortality among patients admitted to the ICU with COVID-19 AKI requiring KRT is especially high[5].

Pathophysiology

Direct pathogenic mechanisms

1. Histopathological data are limited, but a wide range of pathological findings have been described in patients with covid-19, in keeping with the idea that multiple causes of AKI exist, including those commonly found in critically ill patients.
2. Sars-cov-2 might display viral tropism and directly affect the kidney.
3. Endothelial dysfunction, coagulopathy and complement activation are likely important mechanisms for AKI in a subset of patients with covid-19.
4. The role of systemic inflammation and immune dysfunction in the development of covid-19 AKI is still uncertain.

Indirect pathogenic mechanisms

1. Systemic effects of covid-19 and critical care interventions may contribute to AKI.
2. Organ crosstalk is likely an important mechanism for in AKI with covid-19.

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3. Baseline patient characteristics contribute to AKI, acting as modifiers of direct pathogenic mechanisms. [4]

Factors that may contribute to COVID-19 associated acute kidney injury

1. Acute Tubular Injury

- Vascular injuries
- Endothelitis
- Microthrombi
- Thrombotic microangiopathy
- Glomerular injury
- Collapsing glomerulosclerosis
- Glomerulonephritis regional inflammation
- Direct viral infection
- Renal compartment syndrome
- Tissue hypoxia hypoperfusion leading to hypoxaemica, hypertension
- Hypovolemia and heart failure
- Nephrotoxic induced injuries due to drugs
- Rhadomyolysis

2. Interstitial Injuries

- Acute interstitial nephritis
- Interstitial edema

Macrothrombi and microthrombi have been constantly observed in kidneys of patient who have died of COVID-19 or have involved only a small proportion of renal capillaries.

Methodology

Study design

This was a prospective observational study conducted in Karnataka institute of medical sciences, Hubballi.

All patients aged above 18 years admitted to KIMS ICU with COVID infection by rtpcr or rapid antigen test ware considered for study.

A study population of 542 patients were included for the study.

The patient selected for ICU care was based on

1. Patient requiring mechanical ventilation support
2. Hemodynamically unstable patient
3. Patient on high demand of oxygen (NRBM >10 L o2)

Patients with prior known CKD were excluded from the study.

Definition and measurements

AKI was defined according to KDIGO (kidney disease improving global outcome)

As follows-

Stage 1: as in increase in s.creatinine level by 0.3mg/dl within 4 hours or 1.5 to 1.9 times increased in or level from baseline within 7 days.

Stage 2: as 2 to 2.9 times increase in s.creatinine or level within 7 days.

Stage 3: as 3 or more times increase in s.creatininelevel within 7 days or initiation of dialysis

The covid testing was done by means of rt-pcr and rapid antigen test.

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A total of 542 patient was studied including their demographic profile ,prior history of kidney disease and associated documentation requiring serum creatinine or usg abdomen was collected.
The vitals of patient was taken in to account to study level of hypoxemia with regard to AKI several inflammatory markers like serum CRP, S.Ferritin , LDH and d-dimer and troponin I were studied.
The outcome was studied based on mortality of patients developing AKI and mortality without AKI in covid.

Inclusion criteria
1. Age > 18
2. COVID patient requiring ICU care

Exclusion criteria
1. Age < 18 years old
2. Known cases of chronic kidney disease

Statistical analysis
Data was entered in microsoft^{tm} excel and analysed using r software[(16)]. Categorical variables were summarised as frequency and percentage, continuous variables were summarised as mean(sd), median(iqr). Categorical variables were analysed using chi square test. Relation between two continuous variables were analysed using pearson' s correlation. P value < 0.05 was considered as statistically significant.

Result
In the study of total 542 patients majority of them were males accounting for 72% (390 patients) and females were 28% (152 patients). The age of the patients ranged from 23 to 90 years with mean age of 59.23 years majority of patients belonged to age group between 50-70 years.
Among 542 patients 166 patients developed acute kidney injury accounting for 30.62 %. Among the patients who developed AKI, 145 patients died (87.47) and 27 patients were discharged (12.6%).
Among the patient who did not developed AKI(376) . 300(79.81) died and 76(20.2) got discharged.
The p value was **0.034** which was significant for increase in mortality among patients who developed AKI.
The incidence of mortality among covid patient admitted to KIMS ICU was 82.1%.

Variable		**Discharge(%)**	**Death (%)**	**Total (%)**	**P value**
Gender	Male	68 (17.4)	322 (82.6)	390 (100)	0.654
	Female	29 (19.1)	123 (80.9)	152 (100)	
	Total	97 (17.9)	445 (82.1)	542 (100)	
Ferritin	Normal	43 (22.3)	150 (77.7)	193 (100)	**0.048 (Sig)**
	Abnormal	54 (15.5)	295 (84.5)	349 (100)	
	Total	97 (17.9)	445 (82.1)	542 (100)	
CRP	Normal	14 (30.4)	32 (69.6)	46 (100)	**0.02 (Sig.)**
	Abnormal	83 (16.7)	413 (83.3)	496 (100)	
	Total	97 (17.9)	445 (82.1)	542 (100)	
D. Dimer	Normal	26 (19.5)	107 (80.5)	133 (100)	0.567
	Abnormal	71 (17.4)	338 (82.6)	409 (100)	

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	Total	97 (17.9)	445 (82.1)	542 (100)	
LDH	Normal	56 (20)	224 (80)	280 (100)	0.187
	Abnormal	41 (15.6)	221 (84.4)	262 (100)	
	Total	97 (17.9)	445 (82.1)	542 (100)	
AKI	NO	76 (20.2)	300 (79.8)	376 (100)	**0.034 (Sig.)**
	YES	21 (12.6)	145 (87.4)	166 (100)	
	Total	97 (17.9)	445 (82.1)	542 (100)	

Table 1- Outcome of COVID19 Patients

Discussion

Out of 542 covid-19 positive patients studied in this study, 166 patients developed acute kidney injury accounting for 30.62 %.this significant association in patients with no previous kidney disease suggests viral mediated kidney injury[2].

In the present study out of 542 patient studied, majority of them were male 390 (72%) and 152 patient were female (28%). In 2020 jia h ngetal[6] in their study, outcome among patient hospitalized with covid 19 and acute kidney injury, 58% were male who did not develop AKI and 58.4 were male who developed AKI.

In 2021 hakkiarikan et al[7] study, 60.9% of patients were male .

In the present study, mean age of patient was 59.23 .In 2021 hakki et al[7] in their study mean age of patients was 69 years. In the present study, incidence of AKI was30.2% .In jia h ng et al[6] study, incidence of AKI was 38.4%.in hakki et al[7] study incidence of AKI was 43.4%

In the present study mortality of patient with AKI was 87.4 which was consistent with hakkietal[7] study which had mortality of 74.8%, and in jiang et al(5) study, 79.3% patient died who had AKI admitted to ICU.

CRP, d-dimer and serum ferritin are inflammatory markers and are significantly elevated in severe covid-19 disease[8]. Which also predict poor outcomes in covid infected patients.

Conclusion

Covid-19 affects kidney by multiple mechanisms leading to deranged kidney function test. Patients with increased risk of severe disease and mortality have severely deranged renal function profile. The incidence of AKI in covid is common and it is more in patient admitted to ICU. The mortality was significantly higher in patients developing AKI which was statistically proved. So we can predict the worst prognosis for covid patients developing AKI. Renal function test being a routine test can help in prognostication of covid-19 disease and provide scope for improving management. However, still more studies are needed to study implications of kidney injury in prognosis of the disease.

Limitations

This study has several limitations. This is a single centre based retrospective observational study lacking detailed history and epidemiological characteristics. Medication history of patients were not known. Hence role of drugs in kidney injury could not be studied.

References

1. Legrand M, Bell S, Forni L, Joannidis M, Koyner JL, Liu K, Cantaluppi V. Pathophysiology of COVID-19-associated acute kidney injury. Nature Reviews Nephrology. 2021 Nov;17(11):751-64.
2. Serfozo P, Wysocki J, Gulua G, Schulze A, Ye M, Liu P, Jin J, Bader M, Myöhänen T, García-Horsman JA, Batlle D. Ang II (angiotensin II) conversion to angiotensin-(1-7) in the circulation is POP (prolyloligopeptidase)-dependent and ACE2 (angiotensin-converting enzyme 2)-independent. Hypertension. 2020 Jan;75(1):173-82.

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3. Nadim MK, Forni LG, Mehta RL, Connor MJ, Liu KD, Ostermann M, Rimmelé T, Zarbock A, Bell S, Bihorac A, Cantaluppi V. COVID-19-associated acute kidney injury: consensus report of the 25th Acute Disease Quality Initiative (ADQI) Workgroup. Nature reviews nephrology. 2020 Dec;16(12):747-64.
4. Jia HP, Look DC, Shi L, Hickey M, Pewe L, Netland J, Farzan M, Wohlford-Lenane C, Perlman S, McCray Jr PB. ACE2 receptor expression and severe acute respiratory syndrome coronavirus infection depend on differentiation of human airway epithelia. Journal of virology. 2005 Dec 15;79(23):14614-21.
5. Batlle D, Soler MJ, Sparks MA, Hiremath S, South AM, Welling PA, Swaminathan S. Acute kidney injury in COVID-19: emerging evidence of a distinct pathophysiology. Journal of the American Society of Nephrology. 2020 Jul 1;31(7):1380-3.
6. Hirsch JS, Ng JH, Ross DW, Sharma P, Shah HH, Barnett RL, Hazzan AD, Fishbane S, Jhaveri KD, Abate M, Andrade HP. Acute kidney injury in patients hospitalized with COVID-19. Kidney international. 2020 Jul 1;98(1):209-18.
7. Arikan H, Ozturk S, Tokgoz B, Dursun B, Seyahi N, Trabulus S, Islam M, Ayar Y, Gorgulu N, Karadag S, Gok M. Characteristics and outcomes of acute kidney injury in hospitalized COVID-19 patients: A multicenter study by the Turkish society of nephrology. PloS one. 2021 Aug 10;16(8):e0256023.
8. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus– infected pneumonia in Wuhan, China. Jama. 2020 Mar 17;323(11):1061-9.