ISSN: 1607-8322, e-ISSN: 2220-5799 Anaesthesia, Pain & Intensive Care
Vol 25(4); August 2021 DOI: 10.35975/apic.v25i4.1567

ORIGINAL RESEARCH INTENSIVE CARE

Acute kidney injury in COVID–19: A single–center experience in Nigeria

Olayinka Rasheed Ibrahim [1], Taofeek Oloyede [2], Hakeem Gbadamosi [2], Yusuf Musa [2], Rasaki Aliu [3], Surajudeen Oyeleke Bello [4], Michael Abel Alao [5], Bello Mohammed Suleiman [1], Olanrewaju Timothy Adedoyin [6]

Author affiliations:

1. Department of Pediatrics, Federal Medical Centre, Katsina, Nigeria.
2. Department of Internal Medicine, Federal Medical Centre, Katsina, Nigeria.
3. Federal Teaching Hospital, Gombe, Nigeria.
4. Department of Pediatrics, Dalhatu Araf Specialist Hospital, Lafia, Nigeria.
5. Department of Pediatrics, University College Hospital, Ibadan, Nigeria.
6. Department of Pediatrics, University of Ilorin, Ilorin, Nigeria

Correspondence: Olayinka Rasheed Ibrahim, {ORCID:0000–0002–2621–6593}; E–mail: ibroplus@gmail.com; Phone: 234 08066188403

Abstract

Background & objective: Despite available data from developed countries, suggesting a high incidence of acute kidney injury (AKI) in coronavirus disease 2019 (COVID–19), there is scarce data from African countries, including Nigeria. We conducted this study to determine and document the incidence, the associated factors and the outcome (in–hospital mortality) of AKI among COVID–19 patients managed in a center in Nigeria.

Methodology: It was a retrospective review of confirmed COVID–19 cases managed at a center in Nigeria. AKI was defined using 2012 Kidney Disease: Improving Global Outcomes (KDIGO) creatinine criteria. We extracted relevant data from the electronic records of the COVID–19 patients admitted to our hospital and analyzed. Fischer's exact tests were used to test factors associated with AKI for discrete variables, Mann–Whitney U test was used for skewed continuous data, and T–test for continuous normal distribution variables.

Results: This study involved 41 of the 56 confirmed COVID–19 cases. The mean age was 45 ± 17.94 y. A majority of the patients were males (33; 80.5%). AKI occurred in 6 (14.6%) of the patients. Of the 6 AKI; 4 (66.7%) and 2 (33.3%) were in stages 1 and 3 respectively. One patient (16.7%) had had hemodialysis. Of the 6 with AKI, 3 died with a mortality rate of 50.0%. Factors associated with AKI included age above 45 years, body weakness, severe and critical COVID, urea > 10 mmol/l, and serum creatinine > 1.5 mg/dl. Only severe and critical disease was predictive of AKI (adjusted odds ratio 1.777, 95% CI 1.028, 3.074).

Conclusion: The results of our study show that AKI is common in severe and critical COVID–19 and is associated with a poor outcome.

Key words: Acute kidney injury; AKI; COVID–19; Mortality

Abbreviations: AKI – Acute kidney injury; KDIGO – Kidney Disease: Improving Global Outcomes 2012; eGFR – estimated glomerular filtration rate; MDRD – Modification of Diet in Renal Disease

Ethical Review Committee Approval: MOH/ADM/SUB/1152/1/374

Citation: Ibrahim OR, Taofeek Oloyede T , Gbadamosi H , Musa Y , Aliu R , Bello SO , Alao MA , Suleiman MS , Adedoyin OT. Acute kidney injury in COVID–19: A single–center experience in Nigeria. Anaesth. pain intensive care 2021;25(4):470–477. **DOI:** 10.35975/apic.v25i4.1567

1. Introduction

The coronavirus disease 2019 (COVID–19), declared a pandemic in March 2020 by the World Health Organization (WHO), remains a major challenge facing global health with no end in sight.[1] As of 26th June 202, the Wikipedia report showed over 180 million cases with over 3.91 million deaths.[2] African countries accounted for about 4% of the global burden of the disease and the situation report in Nigeria showed over 60,000 reported cases with over a thousand deaths.[3,4]

Most of the COVID–19 cases present as a non–severe disease with a predominance of respiratory illnesses.[5] However, about 15 to 20% of cases present with severe to critical disease, with multi–organ dysfunction, the kidney being one of the prime target organs.[6,7] The kidney dysfunction could be because of many factors including viral trophism and replications with damage to the tubules and podocytes; cytokines storm with exaggeration of pro–inflammatory makers that damage the kidney; hemodynamic changes with renal ischemia and pre–renal injury; and effects of interventions including mechanical ventilation and nephrotoxic medications.[8–10]

The manifestation of kidney involvement ranges from proteinuria to acute kidney injury (AKI) with a preponderance of collapsing glomerulosclerosis on renal histology, especially among the African–American patients.[10,11] The incidence of AKI varies globally with a lower incidence being reported among Chinese and a higher incidence among European and American cohorts.[12] The reported incidence of AKI in China ranged from 0% to 29% depending on the cohorts.[7,13,14] In the United States, an incidence of AKI was 46% among the hospitalized COVID–19 cohort, with a much higher incidence of 76% in critically ill patients in the same study.[15] In Europe, the pooled incidence of AKI was 28% (95% CI 19.8–39.5). Despite available data suggesting a high frequency of renal involvement in COVID–19 in developed countries, there is scarce data from Africa. Hence, we aimed to document the incidence, factors associated with and the outcome (in–hospital mortality) of AKI among COVID–19 cases managed at a designated treatment center in Nigeria.

2. Methodology

2.1. Study design and setting

We conducted a retrospective review of confirmed COVID–19 patients managed from April 15, 2020 to June 30, 2020, at a designated treatment center in a tertiary–care health facility in Northwestern Nigeria. This fifteen–bed isolation and treatment unit is equipped with essential facilities including multi–parameter monitors, two dedicated mechanical ventilators, and a hemodialysis machine to support the care of severe and critical COVID–19 patients.

2.2. Study participants

The COVID–19 infection was confirmed through a real–time polymerase chain reaction (PCR) test carried out on the nasopharyngeal and oro–pharyngeal samples at the National reference laboratory. The patients aged 18 y and above were included. We excluded children and adolescents less than 18 y, patients with no serum urea and creatinine testing during hospitalization, and those with underlying or a history suggestive of chronic kidney disease. We classified the patients as asymptomatic, mild, moderate, severe, and critical COVID–19 following China classification of the index of severity.[16] The classification of COVID–19 at the outcomes (discharge or death) was the final disease classification. The patient management included the administration of lopinavir/ritonavir, azithromycin, vitamin C and zinc for all the patients. Besides, severe and critical cases received intravenous methylprednisolone. A third–generation cephalosporin was added to those with suspected concomitant bacterial sepsis. Patients with hypertension and/or diabetes mellitus medications as appropriate. Those with hypoxemia (oxygen saturation < 92%) had oxygen therapy. One patient with stage 3 AKI had four sessions of hemodialysis.

We discharged patients based on the national guidelines, which included a negative repeat test for COVID–19, or ten days after initial positive results with stable vital signs in the preceding three days. The subjects also had baseline full blood count, liver function tests, chest X–ray, serum electrolytes and blood culture, where indicated.

2.3. Definition and classification of AKI

Acute kidney injury was defined based on 2012

Table 1: The clinical characteristics of patients with AKI and without AKI. Data given as n (%) or Mean ± SD.

Variables		Total n= 41	No AKI n=35	AKI n=6	P value
Age (Mean ± SD) (y)		45.56 ±17.94	42.2 ± 16.11	65.17 ± 16.47	0.003*
Gender	Male	33 (80.5%)	29 (82.9)	4 (66.7)	0.578
Presenting complaints	Fever	18 (33.9)	13 (37.1)	5 (83.3)	0.070
	Cough	13 (31.7)	12 (34.3)	1 (16.7)	0.645
	Breathlessness	9 (22.0)	8 (22.9)	1 (16.7)	1.000
	Reduced appetite	7 (17.1)	5 (14.3)	2 (33.3)	0.268
	Anosmia	6 (14.6)	5 (14.3)	1 (16.7)	1.000
	Vomiting	3 (7.3)	2 (5.7)	1 (16.7)	0.386
	Diarrhea	5 (12.5)	4 (11.4)	1 (16.7)	0.567
	Body weakness	6 (14.6)	3 (8.6)	3 (50.0)	0.031
Normal and abnormal vital signs	LOC	3 (7.3)	0 (0.0)	3 (50.0)	0.002
	Tachypnea	24 (58.5)	20 (57.1)	4 (66.7)	1.000
	Tachycardia	8 (19.5)	8 (22.9)	0 (0.0)	0.322
	Abnormal chest findings	10 (24.4)	8 (22.9)	2 (33.3)	0.622
	Hypoxemia	14 (34.1)	10 (28.6)	4 (66.7)	0.157
	SBP [mmHg]	130.61 ± 15.10	129.69 ± 15.20	136.00 14.59	0.350*
	DBP [mmHg]	81.27 ± 11.0	80.51 ± 11.076	85.67 10.23	0.294*
Systemic disease	Diabetes mellitus	2 (4.9)	2 (5.7)	0 (0.0)	1.000
	Hypertension	10 (24.4)	9 (25.70	1 (16.7)	1.000
Duration of symptoms [median (IQR)] days		2 (0–6)	1 (0–6.5)	3.5 (2–5)	0.315≠
Duration of hospitalization [median (IQR)] days		11 (9–16)	11 (9–16)	11.5 (9–20)	0.782≠
Outcome	Severe***	12 (29.3)	7 (20.0)	5 (83.3)	0.005
	Mortality	5 (12.2)	2 (5.7)	3 (50.0)	0.017

*SD – Standard deviation; *Independent T–test; ≠ Man– Whitney U test; SBP – systolic blood pressure; DBP – diastolic blood pressure; ***index of severity at the final diagnosis, LOC – loss of consciousness*

Kidney Disease: Improving Global Outcomes (KDIGO) serum creatinine criteria. 17 In brief, AKI was defined as a rise of 26.5 µmol/l (0.3 mg/dl) or more in the serum creatinine from baseline within 48 h of admission or an increase of 50% or more in serum creatinine within 7 days on admission.

Stage 1 was defined as a rise of 1.5–1.9 times from baseline value of serum creatinine or ≥ 0.3 mg/dl.17
Stage 2 was defined as a rise of 2.0–2.9 times from the baseline serum creatinine.

Stage 3 was defined as a rise of 3 times or more in the baseline serum creatinine or increase in the serum creatinine ≥ 4.0 mg/dl or the initiation of kidney replacement therapy.[17]

Premorbid baseline was not available in the subjects; hence we followed the KDIGO recommendation to estimate the baseline using Modification of Diet in Renal Disease (MDRD) formula referencing baseline estimated glomerular filtration rate (eGFR) of 75 ml/min per 1.73m^2 as baseline.[17]

Table 2: characteristics of patients with COVID–19 AKI

Variables	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age (y)	53	76	70	90	56	46
Gender	Male	Male	Male	Female	Male	Female
Duration of symptoms (days)	3	2	5	4	14	0
Key findings on Exam (at presentation)	Bilateral crepitation	Unconscious	Unconscious, bilateral crepitation	Unconscious	Bilateral crepitation	nil
Comorbidity	Nil	Hypertensive				
Creatinine (mg/dL)	140	1371	137	377	500	116
Stage of KDIGO	1	1	1	3	3	1
RRT	No	No	No	No	Yes	No
Severity of index of COVID–19	Severe	Severe	Severe	Severe	Critical	Asymptom atic
Duration of hospitalization	2	9	24	11	11	1
Outcome	Death	Discharged	Discharged	Death	Death	Discharged

RRT= renal replacement therapy; KDIGO = Kidney Disease Improving Global Outcomes

Table 3: Laboratory findings in patients AKI and without AKI.

Variables		Total (n= 41)	No AKI (n=35)	AKI (n=6)	P value
Blood chemistry	Sodium [mmol/l]	135 ± 6.55	134.94 ± 4.28	140.83 ± 13.56	0.338
	Potassium [mmol/l]	3.89 ± 0.92	3.85 ± 0.94	4.08 ± 0.86	0.574
	Chloride [mmol/l]	102.73 ± 8.24	101.40 ± 3.32	110.50 ± 19.60	0.307
	Bicarbonate [mmol/l]	20.56 ± 5.64	20.54 ± 5.79	20.67 ± 5.164	0.959
	Urea [mmol/l]	5.10 ± 3.47	4.13 ± 1.60	10.80 ± 5.75	0.036
	Creatinine [mg/dl]	1.20 ± 0.91	0.95 ± 0.22	2.65 ± 1.84	<0.001
WBC [%]	< 3.5	1	1	0	0.354
	3.5–10	34	30	4	
	> 10	6	4	2	
Lymphocytes [%]	< 20	6	5	1	0.979
	20–40	13	11	2	
	> 40	22	19	3	
Neutrophils [%]	< 40	12	11	1	0.691
	40–60	21	17	4	
	> 60	8	7	1	
Monocytes [%]	< 10	25	19	6	0.065
	≥ 10	16	16	0	
Platelets [X 109/l]	<100	6	5	1	1.000
	100–300	35	30	5	
Hematocrits [%]	< 30	3	1	2	0.051
	≥ 30	38	34	4	

WBC = White blood count. Data expressed as % or Mean ± SD

The primary outcome measure was the incidence of AKI. The secondary outcomes were factors associated with AKI and in–hospital mortality.

2.5. Data collection and statistical analysis

We retrieved data from electronic health records and double–checked it for correctness. The data extracted included age, sex, presenting complaints, examination findings at presentation, the severity of COVID–19, and laboratory findings. The continuous data (age) that was normally distributed and were summarized as Mean ± SD, while the skewed data (duration of the symptoms and hospitalization) were reported as median with interquartile range (IQR). We summarized categorical variables as percentage and frequency tables. Fischer's exact tests were used to test factors associated with AKI for discrete variables, Mann–Whitney U test was used for skewed continuous data, and T–test for continuous normal distribution variables. Factors that were significant in bivariate analysis were subjected to multivariate analysis using binary logistic regression to identify those that were predictive of AKI. The multivariate analysis was reported as an adjusted odds ratio (aOR) with a 95% confidence interval. The level of statistically significant was set at a $p < 0.05$.

3. Results

This study involved 41 out of 56 COVID–19 cases managed during the study period. The mean age was 45.0 ± 17.94 years (range–18 to 90 years). Most (33; 80.5%) were males. More of the study population (22; 53.7%) were 45 years and below. The most common symptoms among the patients were fever (18, 33.9%) and cough (13, 31.7%). The median (interquartile range [IQR]) of symptoms before presentation was 2 (0–6) days. At presentation, 24 (58.5%) had tachypnea, while 14 (34.1%) had hypoxemia. The median (IQR) duration of hospitalization was 11 (9–16) days. Based on the spectrum of the COVID–19, 17, (41.5%) were asymptomatic, 8 (19.5%) were mild, 4 (9.8%) were moderate, 11 (26.8%) were severe disease while a case was critical. Overall mortality was 5 (12.2%) in all the cases (Table 1).

Out of the 41 confirmed cases of COVID–19, 14.6% (6/41) had acute kidney injury based on KDIGO criteria and 35 (85.4%) had no AKI. Out of the six cases with AKI, four (66.7%) were KDIGO stage 1 and the remaining two (33.3%) cases were KDIGO stage 3. Of the two cases with KDIGO stage 3, one patient (16.7%) had four sessions of hemodialysis. Out of the six cases with acute kidney injury, three died with a case fatality rate of 50.0%, which was significantly higher compared with patients without AKI (2, 5.7%) as shown in Tables 1 and 2.

Although the serum values of sodium, potassium, chloride, and bicarbonate were higher among patients with AKI, they were not statistically significant (Table 2). Both the blood urea and nitrogen and serum creatinine were significantly higher among patients with AKI as shown in Table 3.

Factors associated with AKI included age above 45 y, presence of body weakness, history of loss of consciousness, and severe and critical cases, blood urea nitrogen above 10 mmol/L, and elevated serum creatinine above 1.5 mg/dl (Table 4). After controlling for confounders, the only factor predictive of acute kidney injury in the COVID–19 patients was a severe disease (adjusted odds ratio 1.777, 95% CI 1.028, 3.074).

4. Discussion

Acute kidney injury initially thought to be uncommon in COVID–19 is now a recognized manifestation associated with an increased risk of a poor outcome. Our study shows an incidence of 14.6%, which is higher than most reports from China.[13,14] In contrast, the observed incidence of AKI in this cohort study is lower compared with the findings from Europe and the USA cohorts.[12,15] Though not as high as the findings from Europe and the USA, this study shows that African cohorts of COVID–19 may also be prone to kidney related complications and hence the need for a high index of suspicion. Whereas a high incidence of AKI was observed among African Americans with COVID–19, probably due to the high incidence of APOL1 genetic mutation, this was not supported by the relatively lower incidence of AKI observed in the present study.[11] This suggests that factors other than APOL1 gene mutation may play an important role in COVID–19 with AKI among blacks.

Table 4: Multivariate analysis of factors associated with AKI

Variables	Categories	OR	95% CI	aOR	95% CI
Age (y)	≤ 45	1.462	1.077, 1.984	1.629	0.952, 2.788
	> 45 ref				
Body weakness	Yes	5.833	1.519, 22.406	1.732	0.891, 3.367
	No ref				
LOC	Yes	0.079	0.027, 0.234	0.726	0.263, 2.001
	No ref				
Classifications	Severe	1,675	1.058, 2.653	1.777	1.028, 3.074
	Non–severe ref				
Urea (mmol/l)	> 10	12.667	4.276, 37.524	1.841	0.545, 6.224
	≤10 ref				
Creatinine (mg/dl)	≤ 1.5	36	5.212, 248.656	1.740	0.661, 4.578
	> 1.5 ref				

OR – Odds ratio; CI – Confidence interval, aOR – adjusted odds ratio; LOC – loss of consciousness. Ref – reference

Most of our patients with AKI were in the early stages, which is consistent with observations from studies outside Africa.[18] The rate of kidney replacement therapy among our cohort also falls within global reports among patients with COVID–19 with AKI. In Europe, the USA and China, about 5–20% of patients with AKI required dialysis at any point in time.[7,18,19] The requirement for dialysis in COVID–19 is not unexpected, considering the progressive nature of AKI and suggests the need for prompt and early diagnosis, especially in resource constraints settings like ours to improve the clinical outcomes.

This study also shows factors associated with AKI to include older age groups (greater than 45 y), loss of consciousness, body weakness, severe and critical COVID–19, and elevated urea and creatinine. In the USA, factors associated with AKI included; male gender, hemodynamic instability, presence of underline comorbidities (hypertension, diabetes, coronary heart disease), higher body mass index, and black race [15,19,20]. In China, factors associated with AKI included being male gender, severely sick cases, baseline eGFR < 60, elevated BUN, and creatinine.[14,21] The inability to identify any underlying chronic disease (diabetes mellitus, hypertension) with AKI in this study may be because of the relatively small sample size and predominance of the younger age group of this cohort study.

The only factor predictive of AKI in COVID–19 was severe and critical disease. This finding is consistent with the observation that severe and critical COVID–19 have a higher rate of AKI with a poor outcome.[22] This is not unexpected as such diseases are likely to have an intense inflammatory response (cytokine storm), hemodynamic changes, high viral loads, and interventions (use of nephrotoxic medications, mechanical ventilation) that may put the kidney at a higher risk of injury.[23] All the factors may have contributed to extensive kidney damage often seen in the severe COVID–19. These findings call for the need to prioritize the evaluation of kidney functions in patients with severe and critical COVID–19 for early detection and prompt management of kidney disease.

Although our cohorts showed more of the early stages of AKI, the mortality rate (50.0%) was very high among COVID–19 with AKI. This is similar to the findings in New York, where the mortality among COVID–19 with AKI was 50.0%. [15] The mortality rate observed in this cohort is also comparable to 52% in a systematic and meta–analysis by Robbins–Juarez *et al.*[18] In contrast, it was slightly lower compared with 57.1% found in a cohort in Beijing, China.[21] The relatively high mortality among the patients with COVID–19 may be due to the limited capacity to support advanced renal care required in resource constraint settings like ours.

5. Limitations

Our study has several limitations. The sample size is very small as compared to many of the similar studies from other countries; it was a retrospective study with incomplete data for some of the patients. Besides, this is a single center data, so our findings may not represent the whole of the country.

6. Conclusion

Our study shows that in this Nigerian cohort, acute kidney injury is common and associated with a poorer outcome. Factors associated with acute kidney injury include age greater than 45 y, generalized body weakness, loss of consciousness, severe and critical illness, and elevated blood urea nitrogen and serum creatinine above 1.5 mg/dl. The presence of severe disease is highly predictive of impending acute kidney injury.

7. Competing interests

The authors declare no competing interest.

8. Authors' contributions

ORI, HG, TO, YM, MOA, RS, SOB and GH conceptualized the work, literature review, drafted and revised the manuscript.

HG, ORI, MOA, YM and BSM extracted and analyzed the data and revised the manuscript.

BSO, GH, BSM and OTA drafted and critically appraised the manuscript. All the authors read and approved the final draft for publication

9. References

1. World Health Organization. WHO Director–General's opening remarks at the media briefing on COVID–19 – 11 March 2020. WHO Dir. Gen. speeches 2020. Available from: https://www.who.int/dg/speeches/detail/who–director–general–s–opening–remarks–at–the–media–briefing–on–covid–19–11–march–2020
2. Wikipedia. Template: COVID–19 pandemic data. Available on: https://en.wikipedia.org/wiki/Template:COVID–19_pandemic_data
3. Africa CDC. Outbreak Brief 38: Coronavirus Disease 2019 (COVID–19) Pandemic. 2020. Available from: https://africacdc.org/download/outbreak–brief–38–coronavirus–disease–2019–covid–19–pandemic/
4. Nigeria Centre for Disease Control (NCDC). COVID–19 Situation Report: Situation Report 232. 2020.
5. Fu L, Wang B, Yuan T, Chen X, Ao Y, Fitzpatrick T, et al. Clinical characteristics of coronavirus disease 2019 (COVID–19) in China: A systematic review and meta–analysis. J Infect. 2020;80(6):656–65. [PubMed] DOI: 10.1016/j.jinf.2020.03.041
6. Guan WJ, Ni ZY, Hu Y, Liang W, Ou CQ, He JX, et al. Clinical characteristics of coronavirus cisease 2019 in China. N Engl J Med. 2020;382(18):1708–20. [PubMed] DOI: 10.1056/NEJMoa2002032
7. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS–CoV–2 pneumonia in Wuhan, China: a single–centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475–81. [PubMed] DOI: 10.1016/S2213-2600(20)30079-5
8. Khouchlaa A, Bouyahya A. COVID–19 nephropathy: probable mechanisms of kidney failure. J Nephropathol. 2020;9(4):e35–e35. DOI: 10.34172/jnp.2020.35
9. Benedetti C, Waldman M, Zaza G, Riella L V, Cravedi P. COVID–19 and the kidneys: an update. Front Med. 2020;7(Jul):1–13. [PubMed] DOI: 10.3389/fmed.2020.00423
10. Vijayan A, Humphreys BD. SARS–CoV–2 in the kidney: bystander or culprit? Nat Rev Nephrol. 2020;1–2. [PubMed] DOI: 10.1038/s41581-020-00354-7
11. Mubarak M, Tolouian R, Pezeshgi A. Collapsing glomerulopathy following COVID–19 infection; possible relationship with APOL1 kidney risk alleles in African–Americans. Immunopathol Persa. 2020;6(2):e18–e18. DOI: 10.34172/ipp.2020.18
12. Fu EL, Janse RJ, Jong Y De, Endt VHW Van Der, Milders J, Willik EM Van Der, et al. Acute kidney injury and kidney replacement therapy in COVID–19: a systematic review and meta–analysis. Clin Kidney J. 2020;13(4):550–63. [PubMed] DOI: 10.1093/ckj/sfaa160
13. Wang L, Li X, Chen H, Yan S, Li D, Li Y, et al. Coronavirus disease 19 Infection does not result in acute kidney injury: An analysis of 116 Hospitalized patients from Wuhan, China. Am J Nephrol. 2020;51:343–8. [PubMed] DOI: 10.1159/000507471
14. Wang J, Wang Z, Zhu Y, Li H, Yuan X, Wang X, et al. Identify the risk factors of COVID–19–related acute kidney injury: A single–center, retrospective cohort study. Front Med. 2020;7(Jul):1–10. [PubMed] DOI: 10.3389/fmed.2020.00436
15. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S, et al. AKI in Hospitalized Patients with COVID–19. J Am Soc Nephrol. 2020;31:1–10. [PubMed] DOI: 10.1681/ASN.2020050615
16. Chinese General Office of National Health Commission. Diagnosis and Treatment Protocols for Patients with Novel Coronavirus Pneumonia (Trial Version 5, Revised) [Internet]. 2020. Available from: http://www.kankyokansen.org/uploads/uploads/files/jsipc/protocol_V5.pdf
17. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SL, et al. Kidney disease: Improving global outcomes (KDIGO) acute kidney injury work group. KDIGO clinical practice guideline for acute kidney injury. Kidney Int. Suppl 2012;2(1):1–138. [Free Full Text]

18. Robbins–juarez SY, Qian L, King KL, Stevens JS, Husain SA, Radhakrishnan J, et al. Outcomes for patients with COVID–19 and acute kidney injury: A systematic review and meta–analysis. Kidney Int Reports. 2020;5(8):1149–60. [PubMed] DOI: 10.1016/j.ekir.2020.06.013

19. Zahid U, Ramachandran P, Spitalewitz S, Alasadi L, Chakraborti A, Azhar M, et al. Acute kidney injury in COVID–19 patients: An inner city hospital experience and policy implications. Am J Nephrol. 2020;11212:786–96. [PubMed] DOI: 10.1159/000511160

20. Fisher M, Neugarten J, Bellin E, Yunes M, Stahl L, Johns TS, et al. AKI in hospitalized patients with and without COVID–19: A comparison study. J Am Soc Nephrol. 2020;31(9):2145–57. [PubMed] DOI: 10.1681/ASN.2020040509

21. Cui X, Yu X, Wu X, Huang L, Tian Y, Huang X, et al. Acute kidney injury in patients with the coronavirus disease 2019: A multicenter study. Kidney Blood Press Res. 2020;45(4):612–22. [PubMed] DOI: 10.1159/000509517

22. Ali H, Daoud A, Mohamed MM, Salim SA, Yessayan L, Baharani J, et al. Survival rate in acute kidney injury superimposed COVID–19 patients: a systematic review and meta– analysis. Ren Fail. 2020;42(1):393–7. [PubMed] DOI: 10.1080/0886022X.2020.1756323

23. Singh S. Acute kidney injury associated with COVID–19: understanding its underlying mechanism. Appl Sci Technol Ann. 2020;1(1):173–5. DOI: 10.3126/asta.v1i1.30302