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Original Research Article

Is AKI a menace in COVID pregnancy?

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ABSTRACT

COVID-19 is primarily thought to be a respiratory sickness, however because SARS-CoV-2 targets human cells, it can also damage the kidney. The most concerning complication in COVID-19 patients is acute kidney damage (AKI). Hypovolemia, cytokine storm, and collapsing glomerulopathy are all factors to consider. Our interest in the topic stems from an increasing number of articles that demonstrate a strong link between AKI development and greater mortality in COVID-19 patients. Although our understanding of the role of the kidneys especially in pregnancy with SARS-CoV-2 infection is constantly evolving and remains unexplored. We have studied 66 pregnant women with COVID 19 infection and AKI and we present an overview of the possible patho mechanisms of AKI in COVID-19, its clinical features, risk factors, impact on hospitalization, and management with renal replacement therapy in relation to pregnancy.

1. Introduction

COVID-19 is a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related viral disease that first appeared in Wuhan, China, in December 2019. Around 364,191,494 cases have been identified worldwide as of January 28, 2022, resulting in a global pandemic.[1] The fact that there have been so many confirmed cases is due to the virus's mode of transmission, which is due to close human-to-human contact via droplets or aerosol via coughs, sneezes, or talking. Touching infected surfaces and subsequently touching transmission routes such as the mouth, eyes, or nose can potentially cause infection.

COVID-19 mainly affects the respiratory system, manifesting as various symptoms. Fever, tiredness, and a dry cough are the most typical signs of infection. In investigations of patients, less common symptoms include sputum production, headache, hemoptysis, diarrhea, anorexia, sore throat, chest discomfort, chills, nausea, and vomiting. Patients also reported olfactory and taste problems. After an incubation period of 1–14 days (most usually around 5 days), most people showed indications of disease, and dyspnea and pneumonia developed within a median of 8 days from onset of symptoms.[2]

SARS-CoV-2 has been demonstrated to enter renal cells directly, however this is not the only patho mechanism of kidney damage. Hypovolemia, cytokine storm, and collapsing glomerulopathy are all factors to consider. Our interest in the topic stems from an increasing number of articles that demonstrate a strong link between AKI development and greater mortality in COVID-19 patients. Although our understanding of the role of the kidneys in SARS-CoV-2 infection is still evolving and needs to be further investigated, we provide an overview of the possible patho mechanisms of AKI in COVID-19, its clinical features, risk factors, impact on hospitalization, and possible management options via renal replacement therapy.

COVID-19 disease primarily affects the respiratory system, resulting in pneumonia, hypoxemia, and acute respiratory distress syndrome in more severe cases.

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Although the focus is on the pulmonary symptoms, clinicians should be mindful of the difficulties that SARS-CoV-2 infection might cause in other organs, such as the kidneys.[3]

In a study of 72,314 cases in China, 81% were classified as mild, 14% as severe cases requiring respiratory support in the form of oxygen supplementation or mechanical ventilation, and 5% were defined as critical those who had respiratory failure, had multiple organ involvement, or septic shock.[4]

The most common renal complication among COVID-19 patients admitted to the hospital is AKI.

AKI is defined as any of the following, according to KDIGO:

1. A 0.3 mg/dL (26.5 mol/L) increase in serum creatinine (SCr) within 48 hours;
2. A 1.5 times increase in SCr compared to baseline 7 days prior; or
3. A urine volume of less than 0.5 mL/kg/hour for 6.

Stage 1: rise in SCr to 1.5–1.9 times baseline or by 0.3 mg/dL;

Stage 2: increase SCr to 2.0–2.9 times baseline;

Stage 3: increase SCr to 3.0 times baseline or increase in serum creatinine to 4.0 mg/dL (353.6 mmol/L) or starting of renal replacement therapy.[3]

The maternal immune system has several difficulties during pregnancy, including building and maintaining tolerance to the fetus as well as preserving the ability to fight viruses and bacteria. As a result, immunological modifications are essential for a healthy pregnancy. In fact, as the fetus grows and develops during pregnancy, the maternal immune system adapts and changes, shifting from a pro-inflammatory state (helpful for embryo implantation and placentation) in the first trimester to an anti-inflammatory state (helpful for fetal growth) in the second trimester. It reaches a second pro-inflammatory condition in the third trimester (in preparation for the start of childbirth).[5]

A pregnant woman's immune system is well-prepared to protect against pathogenic invasion, with innate immune cells such as NK cells and monocytes responding more strongly to viral infections. Some adaptive immune responses, on the other hand, are negatively regulated during pregnancy. Furthermore, high levels of estrogen and progesterone cause the upper section of the respiratory tract to enlarge, making the pregnant lady more susceptible to respiratory viruses such as SARS-CoV-2, in addition to the restricted lung expansion during the last gestational trimester.[5]

Furthermore, AKI is significantly more common in severe and critically ill patients, and it is linked to a poor prognosis and greater mortality. As a result, knowing the underlying pathophysiology of kidney injury during COVID-19 is critical for early detection of the damage and establishment of the best therapeutic approaches and interventions.[3]

2. Epidemiology

At least one-third of the 84,230,049 cases of SARS-CoV-2 infection worldwide are asymptomatic. Approximately 80% of COVID-19 patients who develop symptoms develop mild to moderate symptoms, while 20% of cases acquire severe symptoms over the course of the disease, with 6% becoming critically ill. The overall mortality rate of COVID-19 patients is roughly 3%, but it might approach 50% in the critically ill group.[6]

An important subset comprising of pregnant women is anticipated to be a high-risk group, based on our previous experience with coronavirus epidemics in human populations. According to a recent meta-analysis, unfavorable maternal outcomes occur in 3% of pregnant women, with the risk being higher in those with comorbidities.[7]

If these respiratory illnesses are diagnosed in the last few weeks of pregnancy, especially after 28 weeks, the prognosis is worst. Asian or ethnic ethnicity, as well as a high BMI, are both high-risk factors.[8]

Around two weeks following the infection, 20% of patients in the intensive care unit (ICU) require Renal replacement therapy.[9]

3. Mechanism of Renal Cellular Infection

It is now commonly acknowledged that SARS-primary CoV-2's primary target is the lungs, specifically type II pneumocytes. Increasing research has shown that infection affects not only the lungs, but also the heart, liver, gastrointestinal tract, bone marrow, and kidneys. SARS-CoV-2 enters cells via an endogenous viral receptor called angiotensin converting enzyme 2. This results in multiorgan tropism (ACE2).[3]

SARS-CoV-2 must attach its transmembrane spike (S) glycoprotein to the cellular receptor ACE2 in order to enter the host. S is made up of two subunits, each of which has a different purpose. S1 is responsible for attachment to the host cell receptor, whereas S2 is in charge of fusing the viral membrane to the infected cell's membrane. Spike then needs proteolytic priming, which is provided by the serine protease TMPRSS2. As a result, co-expression of ACE2 and TMPRSS is a crucial factor for SARS-CoV-2 entrance into host cells. Once SARS-CoV-2 is in the infected cell's cytoplasm, its RNA is translated and virion production begins. The Endoplasmic Reticulum and Golgi double vesicles are the cell organelle where genomic replication and virion assembly take place.[3]

4. Cytokine Storm and Renal Injury

A possible cause for the development of acute renal failure is the aberrant immunological response associated with SARS-CoV-2. The cytokine storm and leukopenia are at the foundation of these abnormalities. Sepsis, which is a hemophagocytic illness, can cause a cytokine storm, nothing but a cytokine release syndrome (CRS). IL-6 is the most important cytokine involved in this disease. IL-6 is also seen in COVID-19-related ARDS complications. Intrarenal inflammation, increased vascular permeability, volume depletion, and cardiomyopathy all contribute to AKI during cytokine storm. Cardiomyopathy can produce renal vein stasis, which leads to renal hypotension and hypoperfusion, lowering the glomerular filtration rate. Endothelial destruction, pleural effusions, edema, intra-abdominal hypertension, and third-space fluid loss and resulting hypotension due to intravascular fluid loss are all part of the phenomenon called syndrome type 1.

AKI can also be caused by other organ dysfunction due to COVID-19, such as right and left ventricular failure. Right heart failure causes blood to pool in the kidneys, whereas left heart failure causes a drop in cardiac output, which leads to renal hypo perfusion. Hemodynamic instability, hypoxemia/hypercapnia, acid-base dysregulation, inflammation, and neurohormonal consequences are the five causes of AKI in ARDS.[2]

5. Materials and Methods

This is an observational study of all COVID 19 infected pregnant women with acute kidney injury and those requiring renal replacement admitted through emergency room at Gandhi hospital, a tertiary care hospital in the state of Telangana. Gandhi hospital being the nodal center in the entire state singularly accommodating all the COVID 19 infected pregnant women.

In this study we included 66 pregnant and post-natal women with AKI and COVID -19 infection, we evaluated all the demographic and obstetric data, causes of AKI, laboratory and clinical findings, requirement of ICU admission, duration of stay, need for renal replacement therapy and maternal mortality associated with the condition.

5.1. Inclusion criteria

1. Women who were found to be infected by COVID -19, confirmed by RTPCR.
2. Women who admitted either in the antenatal, postnatal or post abortal period in our center.
3. Women diagnosed with Acute kidney injury at our hospital.

5.2. Exclusion criteria

1. Women who refused or failed to provide consent.
2. Women with pre exiting renal conditions.
3. Women who left against medical advice or with incomplete medical records.

6. Aims and Objectives

Aim to study the impact of COVID 19 in AKI in pregnancy.

7. Results

Table 1: Various clinical and laboratory features related to AKI and their distribution in the study population

	No of cases	Percentage
	48	72.7%
Negative	18	27.3%
+	21	31.8%
++	15	22.7%
+++	12	18.2%
Hematuria	41	62.1%
Negative	25	37.8%
+	19	28.7%
++	15	22.7%
+++	7	10.6%
Sr. creatinine (median ±SD)	1.62±0.44	
Peak serum creatinine (median ±SD)	2.78±2.30	
BLOOD UREA (median ±SD)	30±9.6	

Table 2: Risk factors of AKI in study population

Risk factor	No of cases	Percentage
Increased maternal Age≥ 35 years	12	18.1%
Chronic Hypertension	10	15.15%
Pre-eclampsia	48	72.7%
HELLP syndrome	28	42.4%
Abruption	32	48.4%
DIC	16	24.2%
Sepsis	42	63.6%
History of treatment with ACEI or ARB	4	6%
Gestational diabetes	12	18.1%
Pre gestational Diabetes mellitus	6	9%
Liver disease	4	6%
Smoking	2	3%
Obesity	28	42.4%
Autoimmune disease	12	18.1%
History of thromboembolic events	4	6%
History of acute blood loss ≥2L	16	24.2%

Table 3: Distribution of patients across various stages of AKI

Stage	No of cases	Percentage
Stage 1	26	39.5%
Stage 2	12	18.1%
Stage 3	28	42.4%

Table 4: Various causes of AKI in study population

Pre renal		
Hypovolemia	32	48.5%
Sepsis	42	63.6%
Intrinsic renal		
Micro angiopathy (HELLP)	28	42.4%
Acute tubular necrosis	12	18.1%
Obstructive		
Renal calculi	0	0
Acute hydronephrosis	2	3%
Both Pre renal and renal	40	60%

Table 5: Hospital stay and ICU requirement in study population

	No of cases	Percentages
ICU admission	66	100%
Mechanical ventilation	41	62%
Hospital stay	12±3.5 days	
Renal replacement	46	69.9%
In hospital death	39	59%
Recovery	27	41%

8. Discussion

Although main feature of COVID 19 is pneumonia, we have focussed in our study on renal dysfunction.

Our study describes clinical features related to AKI like proteinuria, haematuria and serum creatinine values. The findings indicate that increase in serum creatinine in COVID 19 patients is found to be a negative prognostic factor. In addition, majority of patients of AKI had proteinuria and haematuria at admission and those with haematuria and proteinuria had more propensity to develop severe or critical illness. We compare our findings with other studies which have studied AKI in COVID 19. Although all these studies have not included pregnant women as their subjects, due to lack of literature on pregnant women with AKI and covid infection we have considered these studies as references. A study by Pei, G et al[10] have found proteinuria in 83% of cases to have proteinuria, 60% to have haematuria while a study by Chan L et al[11] shows 84% patients of AKI to have proteinuria, 81% to have haematuria. Another study by Li, Z et al[12] showed 60% of AKI to have proteinuria and 48% to have haematuria. All these findings are comparable to our study showing similar results.Our study shows also shows a comparison of risk factors of AKI in pregnant women with COVID 19. The most common risk factors were related to either pre-eclampsia, HELLP syndrome, placental abruption or sepsis which are the same risk factors usually found in pregnant women with AKI inferring no specific etiological features or risk factors in relation to COVID 19.[13,14] We have classified the cases of AKI into three stages and 39.5% of the cases fell into stage 1 which has a better prognosis compared to the other two stages. These findings are consistent with previous studies of AKI.[15] We have classified AKI into pre renal, intrinsically renal and post renal or obstructive causes. We have found that pre renal causes like hypovolemia and sepsis were the fore runners in causation of AKI. While intrinsic renal causes like micro angiopathy due to HELLP syndrome were also present in high numbers. It was also found that many instances had an overlap of both pre renal and renal causes leading to cumulative development of AKI. Such results are also similar to previous studies done on the subject of AKI in pregnancy.[16,17] We have studied the duration of hospital stay, requirement of renal replacement therapy, requirement of mechanical ventilation, recovery and mortality in pregnant women with AKI and COVID 10 infection. It was found that requirement of ICU admission and requirement of mechanical ventilation was also high, while the requirement of renal replacement remained marginally increased as compared to women who did not have COVID 19 infection. The overall mortality was higher and recovery rate was lower among pregnant women with AKI and COVID 19 infection.

9. Conclusion

Acute kidney injury is more common among in COVID 19 patients especially those who are critically ill and associated with greater mortality rate. Direct invasion of renal cell, cytokine storm and hypovolemia are main mechanisms related to AKI during COVID 19 infection. Among these causes, pre-eclampsia remains the most common pregnancy specific aetiology for AKI. Most critical prognostic indicators for assessing AKI was serum creatinine and presence of proteinuria and haematuria. Evidence related to COVID 19 is very minimal and further research is required to determine optimal treatment modalities. Obstetricians treating pregnant women with COVID 19 must also keep in mind the effect of COVID 19 on kidneys and be aware of the lasting effect such an infection might have on the renal function of the patient.

10. Source of Funding

None.

11. Conflict of Interest

None.

References

1. Covid19.who.int. 2022. WHO Coronavirus (COVID-19) Dashboard. [online]. Available from: https://covid19.who.int.

2. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol*. 2021;19(3):141–54.
3. Głowacka M, Lipka S, Młynarska E, Franczyk B, Rysz J. Acute Kidney Injury in COVID-19. *Int J Mol Sci*. 2021;22(15):8081.
4. Wu Z, Mcgoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323(13):1239–42.
5. Vale AJM, Fernandes ACL, Guzen FP, Pinheiro FI, DeAzevedo EP, Cobucci RN. Susceptibility to COVID-19 in Pregnancy, Labor, and Postpartum Period: Immune System, Vertical Transmission, and Breastfeeding. *Front Glob Womens Health*. 2021;17(2):602572.
6. 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.
7. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand*. 2020;99(7):823–9.
8. Zhang JP, Wang YH, Chen LN, Zhang R, Xie YF. Clinical analysis of pregnancy in second and third trimesters complicated severe acute respiratory syndrome. *Zhonghua Fu Chan Ke Za Zhi*. 2003;38(8):516–20.
9. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int*. 2020;97(5):829–38.
10. Pei G, Zhang Z, Peng J, Liu L, Zhang C, Yu C, et al. Renal Involvement and Early Prognosis in Patients with COVID-19 Pneumonia. *J Am Soc Nephrol*. 2020;31(6):1157–65.
11. 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;32(1):151–60.
12. Li Z, Wu M, Yao J, Guo J, Liao X, Song S, et al. Caution on kidney dysfunctions of covid-19 patients. 2020;doi:10.1101/2020.02.08.20021212.
13. Liu D, He W, Li Y. Epidemiology of acute kidney injury in hospitalized pregnant women in China. *BMC Nephrol*. 2019;20:67. doi:10.1186/s12882-019-1255-8.
14. Conti-Ramsden FI, Nathan HL, DeGreeff A, Hall DR, Seed PT, Chappell LC, et al. Pregnancy-Related Acute Kidney Injury in Preeclampsia: Risk Factors and Renal Outcomes. *Hypertension*. 2019;74(5):1144–51.
15. Mehta S, Chauhan K, Patel A, Patel S, Pinotti R. The prognostic importance of duration of AKI: a systematic review and meta-analysis. *BMC Nephrol*. 2018;19:91.
16. Cavin N, DeRoberts RS, Jim B. Acute Kidney Injury in Obstetric Patients. *Contrib Nephrol*. 2021;199:162–78.
17. Nwoko R, Plecas D, Garovic VD. Acute kidney injury in the pregnant patient. *Clin Nephrol*. 2012;78(6):478–86.

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