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Effect of coronavirus disease in patients with kidney disease in India

Shashi Prabha Singh[1], Preeti Sharma[1], Durgesh Singh[2], Pradeep kumar[*1], Rakesh Sharma[3], Rachana Sharma[4]

[1]Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad- 201009, Uttar Pradesh, India
[2]Department of Anatomy, Government Medical College, Saharanpur-247232, Uttar Pradesh, India
[3]Department of Biochemistry, Government Medical College, Saharanpur-247232, Uttar Pradesh, India
[4]Department of Biochemistry, TSM Medical College, Lucknow-226008, Uttar Pradesh, India

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Abstract

Coronavirus disease 19 is a global pandemic which infects over millions of people worldwide in a limited time and changes the lifestyle, clinical spectrum lies from asymptomatic infection to pneumonitis with cardiorespiratory failure and finally death. Higher mortality occurs in senior and who are suffering from co-morbidities like chronic kidney disease, (HTN) hypertension, (DM TYPE II) diabetes mellitus or (CVD) cardiovascular diseases. However, rather than normal individuals, patients with chronic kidney disease (CKD) are under higher risk for infections. The chronic systemic inflammatory state is a significant cause for morbidity and mortality in CKD patients. The objective of this review is to discuss the pathogenesis of COVID-19 in CKD, changes observed in the immune system of CKD patients, COVID-19 infections risk in CKD and therapeutic approach of COVID-19 in CKD patients. From the standpoint of frequent renal co-morbidities in covid19 patients, renal complications were explored in covid19 patients received at level 2 tertiary care Santosh Hospital, Ghaziabad, U.P. Delhi-NCR India during March to August 2020 as per the protocol of Nephrology Society of India. Relevant clinical trials were reviewed in support. Meta-analysis and clinical trials are covered in this review study. Duplicate studies are not taken into account. Whereas in intensive care, CKD occurs more frequent than DM type II and CVD. So,COVID-19 pathogenesis in CKD patients, risk of COVID-19, immunologic changes and therapy COVID-19 in CKD can add support in the effective management of COVID-19.

*Corresponding Author

Name: Pradeep kumar
Phone: 9313177768
Email: kanurajsharma2007@gmail.com

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INTRODUCTION

As now we came to known that novel (SARS-CoV-2) severe acute respiratory syndrome coronavirus 2 is responsible for contagious coronavirus disease 19 (COVID-19) (Sun *et al.*, 2020). These global pandemic infect over 8.5 million people worldwide and over 924951 deaths till mid-September 2020 (World Health Organization, 2020a). It spreads from a person to another via cough droplets or direct contact. The incubation period of the disease is one to 14 days. As large number of population is affected by this SARS virus, and the clini-

cal symptoms of the disease range from minor manifestations like diarrhoea to major manifestations like, septicemia, cardiopulmonary arrest, bilateral pneumonitis, acute respiratory distress syndrome (ARDS) and ultimately death due to loss of immunity and inflammation (Ruan *et al.*, 2020). An outburst of SARS-CoV-2 is mainly seen in senior and people who are already suffering from chronic diseases. COVID-19 mostly occur in those kidney disease patients whose kidney is transplanted or those who are immunosuppressed and undergone hemodialysis. It is assumed that behind high incidence and prevalence of mortality in CKD patients is systemic inflammation (Kurts *et al.*, 2013). In this review article focus on COVID-19 pathogenesis in CKD patients and the association between CKD, immune dysfunction and COVID-19 along with therapy of COVID-19 in CKD.

Pathogenesis of Covid-19 in CKD

Coronavirus disease incubation period is of 1–14 days during which the virus is transmitted, and the subject suffering is generally asymptomatic (Lu *et al.*, 2020). COVID 19 is transmitted through close contact from a person to another, and infection occurs mainly through coughing or sneezing (Rubens *et al.*, 2020). COVID-19 virus enters the lungs through a surface receptor ACE2 (angiotensin-converting enzyme 2). It starts infection this shows that there is a strong association between COVID-19 and CKD and finally with RAS (renin-angiotensin system) (Gurwitz, 2020). In the RAS pathway, two enzymes, ACE2 and ACE (angiotensin-converting enzyme) play vital roles in pathogenesis. In the RAS pathway angiotensinogen is converted to angiotensin I (AngI) and angiotensin II (AngII) catalyse by renin (secreted in the kidney by the juxtaglomerular cells) and ACE respectively and while the same time ACE2 convert AngII to angiotensin-(1-7) (Ang[1-7]). AngII acts via two receptors: angiotensin II receptor type 1 (AT1R) and angiotensin II receptor type 2 and Ang [1-7] act via MAS receptor. Both angiotensins (AngII and Ang 1-7) exert opposite actions vasoconstrictive and vasodilatory, respectively. AngI regulates ACE and ACE2 formation, and AngII respectively depicted in Figure 1. In lung ACE2: ACE ratio is 1:20, and in kidneys ACE2: ACE ratio is 1:1. Attention should be paid toward drugs that increase ACE2/Ang-(1-7)/Mas or decrease ACE/Ang II/AT1R pathway to treat COVID-19 and understanding the role of ACE2 in the disease (Tan *et al.*, 2018).

In healthy individuals, interferon (IFN) type, I play a major role against infection. Coronavirus may reduce the IFN type I and lead to overproduction of pro-inflammatory cytokines due to which viral load increase limitless, and also thought to play a major role in pathogenesis, as proven by therapeutic trials of both antiviral drugs and neutralising anti-interleukin-6 (IL-6) antibody. Defence against COVID-19 infection is mainly to prevent oxidative stress and inflammation, but if not appropriately regulated effect may be harmful (Dounousi *et al.*, 2006). Lymphocyte, Natural killer (NK) cells, B and plasma cells play a role in defence mechanism by neutralising SARS-CoV-2 and protect tissue from injury. Depletion of Lymphocyte, NK, B and plasma cells is thought to impair antiviral defence. (Giamarellos-Bourboulis *et al.*, 2020)

In COVID-19, there is the involvement of complement, and so the use of both strategies the anti-complement C5 and the complement C3 inhibitor, antibody eculizumab and the Amyndas -101 should be triggered respectively (Risitano *et al.*, 2020).

CKD, Immune Dysfunction and Covid-19

Presently, few data are available on CKD and COVID-19. CKD causes persistent systemic inflammation and finally lead to immunosuppression (Figure 2). CKD cause alteration in an immune system characterised by phagocytic B and T cell disturbance and also increased pro-inflammatory cytokines and finally progress towards renal disease (Vaziri, 2012).

In CKD, a neutrophil function is decreased, and finally, an immune disturbance occurs (Martin-Sanchez *et al.*, 2018). Likewise, in advance stage of CKD B lymphocytes increase the rate of apoptosis that may contribute to B lymphopenia, and T cells are activated in an early state. Activated T cells lead to immune dysfunction, apoptosis and finally, infection (Meier *et al.*, 2002).

Persistent inflammation progress CKD and cardiovascular disease (Cohen and Hörl, 2012). There are multiple causative factors of chronic inflammation in CKD, like oxidative stress, infections and haemo dialyses related factors (Haag-Weber and Hörl, 1996). Thus, there is an association in DNA/RNA of microorganism with oxidative stress, serum C-reactive protein, cytokines and dialyses (World Health Organization, 2020b). Currently, it is not clear to what extent the coronavirus damages renal cells or whether the cytokine storm syndrome is the cause of kidney injury (Cheng *et al.*, 2020). Knowledge on the involvement of kidney and stages of injury in COVID-19 will be helpful in theranostics of COVID patients.

CDC COVID-19 Response Team analyses 7162 COVID-19 positive cases and found that CKD was

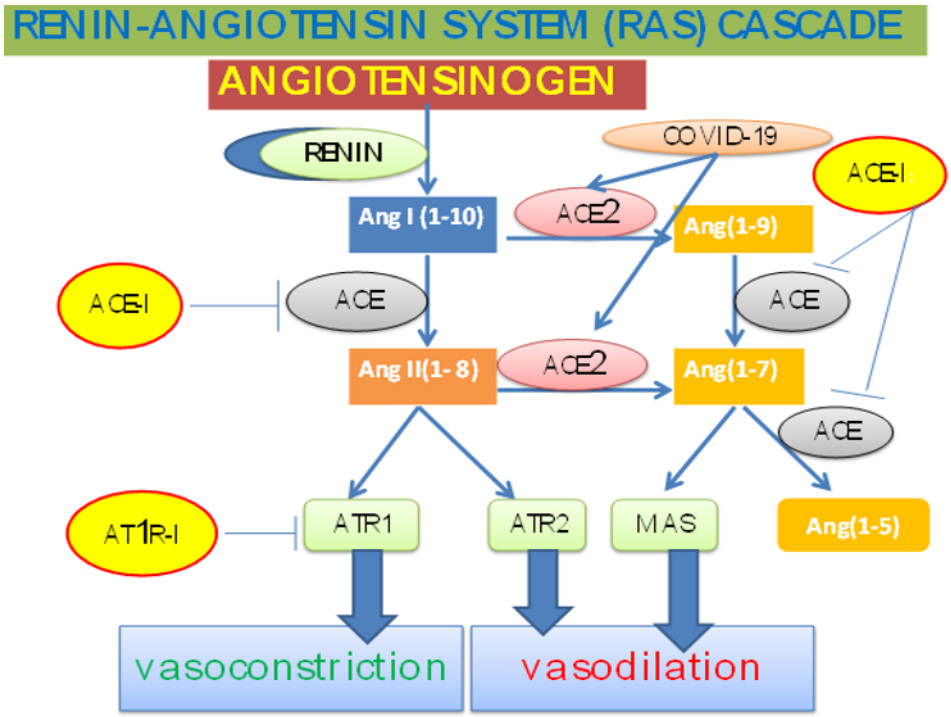

Figure 1: RAS: renin-angiotensin system cascade, ACE&ACE2: angiotensin-convertingenzyme&2, ACE2, Ang I & Ang II: angiotensin I& II, ATR1&ATR2: angiotensin receptor 1& 2, MAS: proto-oncogene

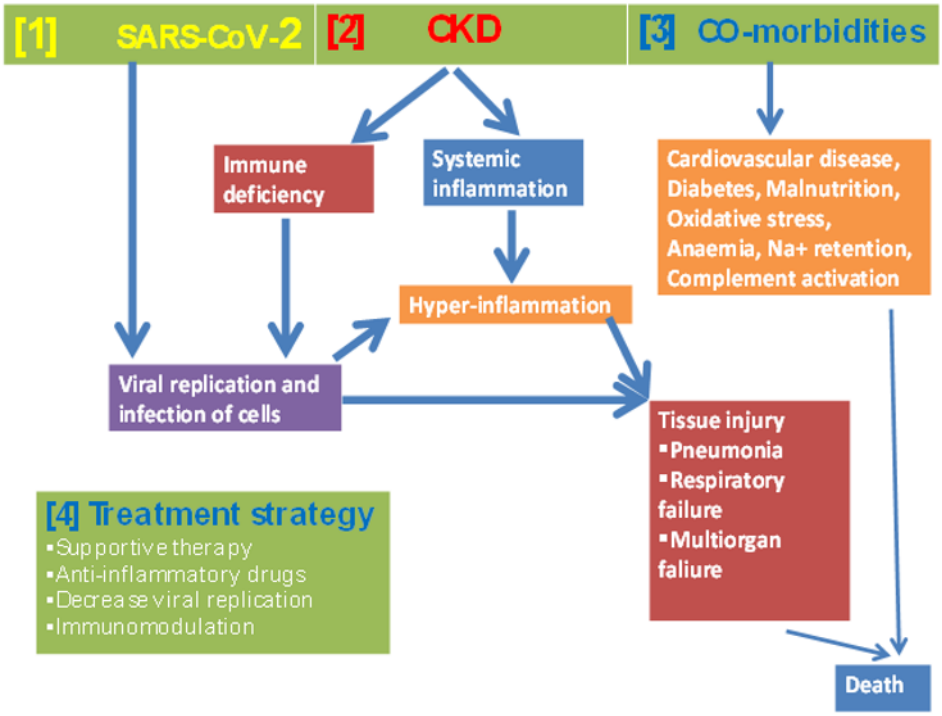

Figure 2: Interaction between CKD and COVID19. [1] [2] Immune deficiency and systemic inflammation are the primary manifestations of CKD [3] Relation between CKDco-morbidities [4] therapy

9-fold more frequent in hospitalised and 12-fold more frequent in those with ICU admission COVID-19 patients than non admitted patients. The prevalence ratio in ICU patients ranged from 2- to 6.7-fold (Chow *et al.*, 2020).

Henry BM and Lippi G. in their meta-analysis on CKD and COVID-19 after analysing 1389 COVID-19 patients from four studies found that COVID-19 disease occurs more often in CKD patients [odds ratio 3.03 (95% CI 1.09–8.47), $I2\frac{1}{4}$ 0.0%, Cochran's Q, $P\frac{1}{4}$ 0.84], among which severe disease was found in 273 (19.7%) (Henry and Lippi, 2020). Cheng et al. also shows in their studies that there is the relation between CKD and COVID -19 they found among 710 hospitalised patients with COVID-19, 44% had proteinuria and 26.7% had hematuria on admission (Cheng *et al.*, 2020).

In CKD Treatment of Covid-19

At present, no effective treatment is available for COVID-19. Treatment of COVID-19 with CKD may be general, supportive and other measures include complications treatment and treatment of secondary infection and if require replacement of kidney.

General management

All COVID-19 patients need an N95 mask and PEP kit to cover the whole body to prevent the transfer of infections to other healthy individuals and quarantined. Early admission of severely ill patients to ICU (intensive care unit) and. PICU in tertiary hospitals along with Supportive care such as bed rest, nutritional and fluid support, and maintenance of blood pressure and oxygenation.

Therapy for the virus

There is not any particular therapy for the virus of COVID-19 at present. Chloroquine phosphate show some amount of resistant against COVID-19. COVID 19 can be treatment Successful with remdesivir (World Health Organization, 2020b).

Others treatments

High-volume haemofiltration remove inflammatory cytokines (IL-6). Continuous renal replacement therapy can be used in the treatment of SARS and improved the Organ Failure within seven days in patients with sepsis. Therefore, CRRT may play a role in CKD patients with COVID-19 and sepsis or multiorgan failure syndrome (Chu *et al.*, 2005).

COVID convalescent plasma

COVID convalescent plasma therapy (CCP) is effective to reduce viral load and to prevent further tissue damage in COVID patients before the development of inflammatory life-threatening organ failure.

Passive immunity monoclonal antibody therapies

Clinical trials are going onto monoclonal antibody therapies on behalf of actual data to fight against specific SARS-CoV-2 (Park *et al.*, 2019).

CONCLUSION

CKD patients are more likely infected with COVID-19 virus. Whereas in intensive care, CKD occurs more frequent than DM type II and CVD. So,COVID-19 pathogenesis in CKD patients, risk of COVID-19, immunologic changes and therapy COVID-19 in CKD can add support in the effective management of COVID-19.

Authors' Contributions

Dr Pradeep Kumar, Dr Preeti Sharma and Shashi Prabha Singh play a task in conceptualisation, acquisition and analysis of the information besides in drafting and submission of the manuscript, Dr Durgesh Singh Dr Rakesh Sharma, and Dr Rachana Sharma participated in the coordination, conception and designing of the manuscript.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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Ethical Approval

The Institutional Ethics Committee approved the study.

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