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Effect of COVID-19 in Kidney Injury: the Health Issue

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ABSTRACT

COVID-19 infectious disease triggered by SARS-CoV-2 widely spread over almost 200 countries. More than 7.5 million people are affected and approximately 1.15 lakh people died due to COVID-19 pandemic. SARS-CoV-2 is not only accountable for the disease of pneumonia but has bad effect on the body's organs including lungs, kidneys, liver and heart. Patients who are suffering from end-stage kidney disease are at greater risk with COVID-19.Kidney complications are increased due to the infection caused by SARS-CoV-2 thatmay arisecaused by direct effect of cytopathic, renal-toxic therapies or multi-organ dysfunction. In the case of COVID-19, low oxygen delivery to the kidney tissues leads to the ischemic damage of the kidney. Since kidney is one of the important organs of the body that provide essential function to the body,this review is focused on the effect of SARS-CoV-2 novel coronavirus on kidneys.

KEY WORDS: ACUTE KIDNEY INJURY (AKI), CORONAVIRUS, COVID-19 PANDEMIC, SARS-COV-2, RENAL FAILURE.

INTRODUCTION

The COVID-19 disease triggered by SARS-CoV-2 novel coronavirus instigated from Wuhan in China. In December month of 2019, many pneumonia cases reported in Wuhan city of China. Most of these patients had exposure to the sea food market, this market selling various species of live animals(Q. Li et. al. (2020)). This disease spread over other part of china as well as globally to some countries in just few days. After the proof of identity and depiction of the disease, the new coronavirus identified and named as SARS-CoV-2 as well as the infectious disease or illness instigated by this novel coronavirus known as COVID-19, it is a viral respiratory infectious disease.

Within a month, a many cases of COVID-19 exponentially increase in many nations and subsequent deaths worldwide.In the January of 2020,the International organizationWorld health organization (WHO)affirmed public wellbeingcrisisdue to COVID-19. Later on 11 March 2020, WHO was upgraded to the declaration of pandemic(C. Huang et. al. (2020)). Phylogenetically, the virus shows the similargene characteristic as shown by SARS-CoV. It is a type respiratory illness that mainly disturbs the lungs(W. Graham Carlos et. al. (2020)). The early indicationsconsist of runny nose, muscle aches as well as sore throat, and short breathing or facing the difficulty in breathing. Some other symptoms are loss of flavoras well asodor. The sign and symptoms of the coronavirus disease might beappearing in two to fourteen days just after contact. The time span between contact to the coronavirus and when indicationsseem called the incubation span. In a study it is reported that, in China, 81% of the COVID-19 patients had mild symptoms and remaining patients had severe or critical involvement.

In a recent study, it was reported that SARS-CoV-2 virus conveyed from one person to another person when a person comes in close contact with infected person. The main way of spread of this virus is respiratory droplet inhalation. The highest rate of this coronavirus has been observed in the case of clinical symptoms(W.H. Sheng et. al. (2020)). Since, COVID-19 is a respiratory disease that is why lungs are primarily affected by this disease. Depending on the severity of this disease, the other organs of the body can be also affected and organ dysfunction is possible. In most of the cases, organs are not directly affected by COVID-19 viral infection; it may affect due the body's response with

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COVID-19. The damage also occurred in Kidneys due to COVID-19. Few COVID-19 hospitalized patientsalso have acute kidney damage and sometimes hemodialysis required(W. Guan et. al. (2020).

This review article aimed to investigate the effect of SARS-CoV-2 on the kidneys as well as its development of renal failure. In the following sections, appliance of kidney injury caused by COVID-19 and effect of COVID-19 disease on dialysis and renal transplant patients will be discuss.

1. Mechanism Of Kidney Injury Due To COVID-19 Infection: In a study, it is reported that alveolar cells are found in lungs and angiotensin-converting enzyme 2 (ACE2) are found in other body's organs including kidney. Renal tubular cells expressed by both dipeptidyl peptidase-4 and ACE 2 that supports to bind MERS-CoV as well as SARS-CoV virus respectively(V. S. Raj et. al. (2005)). In addition, the urine as well as kidney tissue infection, the presence of viral RNA has been detected(J. S. M. Peiris et. al. (2003)). ACE2 receptors helpto enter the coronavirus into human body cells. The renin hormone that is released from the kidney are responsible for converting the angiotensinogen protein to angiotensin I followed by conversion of angiotensin to angiotensin II. Angiotensin II most commonly found in lungs(E. D. Sturrock et. al. (2013)). The ACE2 act as a mediator for the human respiratory tract virus NL63 and SARS-CoV. There are various isotopes of the ACE2 reduce the interaction between SARS-CoV's S protein and ACE2(Z Li et. al. (2020)). Therefore, SARS-CoV-2 outcomes in terms of sensitivity, symptoms and severity can be critical based on expression pattern as well as countenance level of humanoid ACE2 gene in various tissues(P. Zhou et. al. (2012).

In a research it is statedthat, only 6% patients of SARS-CoV was experienced acute kidney injury (AKI). It is a very uncommon feature of SARS viral disease. According to the literature, infection due to SARS-CoV and MERS-CoV, only 5% to 15% patients experienced AKI with 60% to 90% mortality rate. Recent research on COVID-19 reported only 3% to 9% incident of AKI. Lai and team found SARS viral particles using transmission electron microscopy (TEM) in the renal specimen of postmortem SARS patients suffering from the AKI. The report mentioned that the SARS-CoV never identified in any patient; therefore most probably kidney dysfunction may be related to the multi-organ failure. In the recent research, studies has been reported that infection caused by SARS-CoV-2 specifically target kidney. In another research, researchers has been investigated that antigens of SARS-CoV-2 collected in tubules of kidney and mentioned that human kidneys are directly affected by SARS-CoV-2.

2. Disease Manifestations: There are various methods adapted by medical authorities for the identification of COVID-19 disease such as antiquity of contact, clinical presentation and laboratory parameters such as detection of nucleic acid; leukopenia, serology (lgM/lgG), CT scan and enzyme-linked immunosorbent assay (ELISA). The Centre for the Disease control and prevention (CDC) recommendation for COVID-19 testing, nasopharyngeal swab sample has to be use. Gene sequencing and RT-PCR are the two approaches that are used for the detection of nucleic acid. In recent research, various biomarkers have been investigated for the diagnosis of COVID-19 such as serum amyloid A, C-reactive protein, lymphocytes, lactate dehydrogenase, platelet count and interleukin-6. Among all, lower platelet count and lymphocytes count has been observed in severe patients.

The China National Health Commission suggested some diagnostics protocol for the laboratory examination of the COVID-19 such as oropharyngeal and nasopharyngeal swab tests. In order to detect the SARS-CoV-2 novel coronavirus genome'stwo dissimilarexpanses i.e. ORF1b as well as N, early identification of the COVID-19 infection in patients has been done by suing basedon quantitative RT-PCR analyzes. Three novel RT-PCR assesses has been establishedthat targeted the RNA-dependent RNA polymerase, nucleocapsid (N) as well as spike protein (S) genetic factor of novel coronavirus SARS-CoV-2. Among the all three new RT-PCR the RdRp/Hel assay in virto, exhibit lowest detection limit. More specific and greatlydelicateassesses can help to enhance the COVID-19 analysis at laboratory level.

The SARS-CoV corona virus E gene may be correlated with one stage RT-PCR system in an attempt to enhance the test system's sensitivity, since the gene RdRp is less sensitive than the gene E of SARS-CoV. For the diagnosis of COVID-19 infection triggered by SARS-CoV-2, E-gene PCR is sufficient but in order to confirm the positive case of COVID-19 infection, RdRp protocol is recommended. In one hospital Wuhan city of China, based on RT-PCR detection system, overall 38% of positive rate of SARS-CoV-2 reported in 4890 cases. Only 54.3% of SARS-CoV-2 inveterate patients had uttered oropharyngeal swab tests and the positive rate of PCR was not very high. In the COVID-19 pandemic situation, large number of testing kits is required. In order to overcome such problem, an automated system is required that can process large number of samples in less time and can be paced up the identification of the COVID-19 infection. The detection of COVID-19 based on molecule assays shows high throughput and required relatively less time for the detection and offers reliable results.

The current laboratory based test for COVID-19 infections is consume so much time and commercial diagnostic kits are in shortage as a result the COVID-19 infection spread continuously in exponential manner. Cough, dyspnea and fever patients are usually diagnosed with the usual CT characteristics of lung, considering the unfavorable outcomes of RT-PCR. 88% showed positive chest scans for the identification of 1014 COVID-19 patients as well as 59% showed positive findings on the basis of RT-PCR. That is why it has shown similar imaging data to the results for MERS-CoV as well as SARS-CoV. This infection has been triggered by a SARS-CoV-2 in the coronaviridae family. Typical CT scan imaging included consolidative pulmonary opacities, bilateral pulmonary parenchymal and sometimes it showed the rounded shape as well asdistribution of peripheral lung. Initially, in the 21 chest CT scan imaging, 86% patients showed consolidation, 71 % patients with one

lobe and 76% patients affected by bilateral involvement. For understanding the severity of COVID-19 infection, CT scan is very useful. COVID-19 infection also evident with CT imaging of chest for those patients who showed abnormalities in asymptomatic patients. The clinical and laboratory methods in combination with CT scan imaging can help in COVID-19 detection in early stage caused pneumonia. On 12 February 2020, more than 14000 patients have been diagnosed by chest CT imaging.

3. Effect Of COVID-19 In Dialysis Patients: Treatment of COVID-19 is more challenging in those patients who are suffering from Kidney related disease and on dialysis. The immune system of the dialysis patients is very weak that makes the situation more critical if the patient is suffering from severe COVID-19 infection. In order to prevent COVID-19 epidemic, the dialysis facilities in the hospitals must be prepared. In the COVID-19 epidemic, nephrology society in Taiwanas well as the Chinese society of nephrology delivered some strategies for the dialysis amenities. In order to restrict the rick of COVID-19 in dialysis patients, some preventive measures need to be followed as shown in Table 1.

4. COVID-19 In Renal Transplant Patients: The threat of hospitalization as well as mortality caused by COVID-19 syndrome is greater in patients with renal transplants. Literature for effect of COVID-19 disease on renal transplant patients is lacking. According to the Chinese Medicinal Biotechnology Association recommendation for renal transplant patients with COVID-19, suggested that decisiveamaximumcontinuationtimetable. Due tocrisis prevention as well as control measures during COVID-19, very less renal transplant patients were infected by COVID-19 infection. Based in the clinical status of patient, severity of illness and duration of transplant, the renal transplant patients with COVID-19 should go under tailor treatment. If the patients have mild symptoms of COVID-19, the first approach should follow is reduction or suppression of antimetabolic agents. On the other hand, the patients with moderate and severe COVID-19 infection, rapamycin and anti-immunosuppressive therapy must be reduced.

Table 1. General measures for reducing the risk of COVID-19 infection in Dialysis patients

Prevention	• The patients and other persons must sanitize hands before entering into dialysis facility • In waiting rooms, the dispensers must be provided for alcoholic solutions • Patients must use facemask in order to cover nose as well as mouth properly during cough as well as sneeze. • It is must be counseled to the patients to wash hands and arms before starting dialysis
Early Recognition	• The patients who have symptoms of COVID-19 including runny nose, cough, sore throat etc. are advised to go under coronavirus screening.
Immediate referral	• In the case of adult respiratory distress syndrome or symptoms like difficulty in breathing must refer to the medical hospital
Patient placement	• The patients who have confirmed with COVID-19 infections, the hemodialysis should be done ate clean and isolated place. Minimum 6 feet distance must be preserved from indicative patients as well as others.
Personal protective equipment (PPE)	• It must be ensure that dialysis staff must wear the personal protective equipment kit including gloves, eye protecting shield, facemask and gown. • Before entering to the dialysis facility, it should be compulsory to wash hands with soap or alcoholic based solutions.

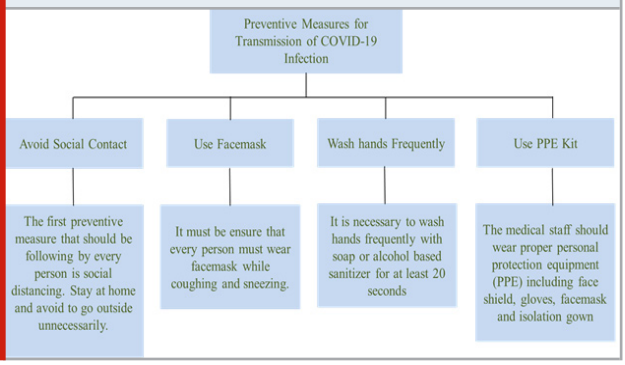
5. Prevention And Control Management Of The COVID-19 Epidemic: Government and medical authorities are trying hard in order to control as well as minimize the transmission of SARS-CoV-2 virus. In many countries, the established control management initiated universal symptom surveys from door-to-door and individuals-to-individuals for reducing the risk of community spread of novel coronavirus. The patients ofinveterate COVID-19 infection were hospitalized to the isolation regions with protective conditions and symptotic patients with mild symptomswere advised to stay at home. Many medical agencies from all across the world and World health organization (WHO) recommended some protocols for preventing novel coronavirus transmission (as shown in Figure 1).

6. Treatment of COVID-19 Infection

6.1. Antiviral Agents: There are currently no antiviral medications available in patients for treating COVID-19 infection. In an animal sample, coronavirus protease activity was investigated. Treatment of Ebola was developed with a remdesivir antiviral agent. Remdesivir indicates the wide range of antiviral action in contradiction of different RNS viruses and is the best option to RdRp. For the cure of diseasetriggered by SARS-CoV, a mouse model has been developed; in this model remdesivir shows improved

pulmonary function and decrease in the load of virus in lungs. For the treatment of MERS-CoV in rhesus macaque model, by the application of lactic remdesivir treatment before the inoculation appears, MERS-CoV virus doesn't induce the clinical disease and help to restrict the replication in respiratory tissues. For the cure of COVID-19 infection triggered by SARS-CoV-2, remdesivir was firstly used in United States. The treated patients showed the improved clinical conditions just after one day. The effectiveness and effectivenessof the remdesivir for the cure of COVID-19 needs further clinical trial in order to ensure the safety patients health.

Figure 1: Schematic representation of Preventive measures for Transmission of COVID-19



6.2. Chloroquine and Hydroxychloroquine: A medicine for the deterrence of inflammatory and antimalarial disorders, chloroquine antiviral drug, has been commonly utilized. Choloroquine prevents viral infection effectively by enhancing the endosomal pH necessary for virus. The first chloroquine test has been performed in 90 patients who have confirmed that chloroquine is efficient in reducing pneumonic exacerbation. By the medical authorities chloroquine was recommended for the cureof the COVID-19 infection triggered by the SARS-CoV-2. In order to ensure the reliability and efficacy, further clinical trials need to be done. Hydroxychloroquine is a chloroquine analog that is facing some concerns regarding drug-drug interactions. In one study, a group of researchers has been reported a physiologically based pharmacokinetic models, in this model it was found that hydroxychloroquine was more effective as compared to the chloroquine for the treatment of COVID-19. The Chinese hospitals and University of oxford launched the 21 clinical studies to ensure the efficacy of these antiviral medications for the cure of the COVID-19 infection. Chloroquine as well as Hydeoxycholoquine shows positive response in contradiction of the SARS-CoV-2 but further clinical trials needs to be done.

6.3. Antibodies: In developing COVID-19 vaccine contrary to SARS-CoV-2, antibodies play a significant part. Antibodies monitor or block the entry of the SARS-CoV-2. The SARS-CoV-2 spike proteins are accessed by antibodies. The spike protein is a major inducer to neutralize the antibodies. The SARS-CoV is a close connection to COVID-19 receptor binding domain (RBD) in particular for human CR3022 monoclonal antibody. In order to avoid and treat COVID-19 infection from the SRAS CoV2 novel coronavirus CR3022 could be a successful potential therapeutic candidate. For the treatment of Ebola Virus the antibodies MAb114 and REGN-EB3 were identified. However, their effects on COVID-19 infections are not so successful as these antibodies can only detect a single antigen epitope.

6.4. Corticosteroids: In a recent study, various clinical trials have been performed on 41 COVID-19 patients(C. Huang et. al. (2020)). Among the all patients, 21% COVID-19 patients received corticosteroids that showed the suppression of lung inflammation. The WHO restricts the use of corticosteroids against the SARS-CoV-2 novel coronavirus unless indicated for another person. In one observational study on patients who were suffering from MERS, the corticosteroids received patients need mechanical ventilators and renal transplant therapy. As per clinical indication for the use of corticosteroids against SARS-CoV-2 novel coronavirus, the treatment can be harmful because no such patients experience the benefits.

7. Treatment Of Kidney Injury With COVID-19: There is no particular medication for the curing of COVID-19 infected kidney patients. General cure is followed based on the supportive care. In order to preclude tissue hypoxia as well as worse condition under the critical infection due to SARS-CoV-2, the oxygen delivery to the patient is optimized and maintains high oxygenation parameter level. Whenpatients have fever, the proper fluid management is required. For exacerbating the condition, mechanical ventilator with high positive end expiratory pressure maneuvers gives better outcomes. In the literature, various studies done for the curing of COVID-19 with antiviral drug varies from 21% to 94%. Guan and Team stated that 35.8% patients suffering from COVID-19 had received oseltamivir therapy, for the study researchers reviewed 1099 patients. Remdesivir is actually the single antiviral drug with along RCT proofs for margarine the recovery time of patients with COVID-19.

CONCLUSION

The new coronavirus SARS-CoV-2 can damage the renal tissue. There is also no specific mechanism for affected kidney due to COVID-19 infection. It needs to be further studied. Increased kidney injury is normal in COVID-19 patients, because of lack of adequate and specific medications for the cure of COVID-19. It has diverse and complex pathophysiology of kidney involvement. In order to interfere and avoid further kidney damage, early detection of COVID-19 infection is critical. A strict protocol is required in order to minimize the danger of COVID-19 infection with renal transplants and dialysis. As soon as possible, early identification and effective management should be identified. Prevention is a vital element in the treatment of this disease. Extreme disease prevention is required to reduce the spread of the disease. Diverse effective vaccinations, potential medicines and promising therapy have been scientifically studied with the expectation that this COVID-19 pandemic condition will be successfully cured.

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