

CHRONIC KIDNEY DISEASE AND MORTALITY FROM COVID-19: A LITERATURE REVIEW

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Abstract: An outbreak of COVID-19 occurred in Wuhan, Hubei Province, China in December 2019 and was declared a global pandemic by the World Health Organization. COVID-19 is highly contagious through person-to-person transmission and can cause critical illness and until the death. There have been over 250 million confirmed cases and over 5 million deaths as of November 15, 2021. Recent clinical evidence has revealed that COVID-19 patients with Acute Kidney Injury have had fatal outcomes. This implies the lives of patients with pre-existing Chronic Kidney Disease. The aim of the present study will be to assess the influence of pre-existing CKD on the risks of all-cause mortality, hospitalization and critical condition among patients with COVID-19 infection. An integrative literature review will be carried out in PubMed, Embase and Cochrane Library databases. The following will be used as inclusion criteria for the selection of articles: articles published within the time frame (2020-2021) and in the English language. It is expected to note that Chronic Kidney Disease may be associated with an increased risk of severe COVID-19 infection. Finally, it is expected that the presence of CKD must be considered an important factor in future risk stratification models for COVID-19.

Keywords: Chronic Kidney Disease, COVID-19, hospitalization, mortality.

INTRODUCTION

An outbreak of coronavirus disease 2019 (COVID-19) occurred in Wuhan, Hubei Province, China, in December 2019, and was declared a global pandemic by the World Health Organization (WHO) (HUANG et al. 2020). COVID-19 is highly contagious by person-to-person transmission and can cause critical illness and even death (CHAN et al.2020). There have been more than 250 million confirmed cases and more than

5 million deaths as of 15 November 2021 (WHO, 2021). Although underlying diseases have been considered a major risk factor for clinical outcomes such as Severe Acute Respiratory Syndrome (SARS), sepsis, shock and all-cause mortality (WANG et al. 2020; YANG et al. 2020). However, the relationship between the specific underlying disease, eg renal dysfunction, and these COVID-19 patient outcomes remains unclear.

The main clinical features of severe COVID-19 infection are lung destruction and respiratory failure, but some studies have shown that COVID-19 infection also involves other organs, including kidney and liver (CHENG et al. 2020; CHEN et al. 2020). Recent clinical evidence has revealed that COVID-19 patients with Acute Kidney Injury (AKI) had fatal outcomes (CHENG et al. 2020; LIM et al. 2020; CHU et al. 2005). This implies that patients with pre-existing Chronic Kidney Disease (CKD) who have functional defects in their innate and adaptive immune cells may be at increased risk of COVID-19 infection and death (BETJES et al. 2013; SUN et al, 2020). Physicians must pay more attention to the medical management and prevention of COVID-19 infection in the population.

Although several investigations have reported CKD in patients with COVID-19 infection, the data collected were generally restricted to a single hospital or country (FLYTHE et al. 2021; KANG et al. 2020). Therefore, we will perform an integrative literature review to assess the influence of pre-existing CKD on all-cause mortality, hospitalization, and critical illness risks among patients with COVID-19 infection.

GOAL

GENERAL GOAL

The present study aimed to assess the influence of pre-existing CKD on mortality

risks in patients with COVID-19 infection.

SPECIFIC OBJECTIVES

- To assess the influence of pre-existing CKD on mortality risks from COVID-19 hospitalization.
- Assess the influence of pre-existing CKD on all-cause mortality risks from critical conditions among patients with COVID-19 infection.
- Assess whether pre-existing CKD and AKI complication are involved in the COVID-19 pandemic.

MATERIAL AND METHODS

An integrative literature review was carried out as it is considered a unique tool in the field of health, as it allows the synthesis of available evidence on a given topic and directs clinical practice based on scientific knowledge. The guiding question of the research is: “what is the potential association between CKD and the severity of COVID-19 infection?”. A bibliographic search was carried out in the PubMed, Embase and Cochrane Library databases, using the following descriptors: “COVID-19” OR “coronavirus disease 2019” AND “Renal” OR “Kidney” with the Boolean operators “and/or”. The following will be used as inclusion criteria for the selection of articles: articles published within the time frame (2020-2021) and in the English language. Articles that did not fit the research topic and duplicate articles were excluded. All research articles on patients through randomized controlled trials, prospective or retrospective observational, case-control, cross-sectional, and case series studies that analyzed the outcomes of COVID-19 infection in patients with preexisting CKD are included. Studies with patients under 18 years of age, receiving transplantation or on maintenance dialysis, animal studies and those without abstract or

full text for additional data extraction were excluded. The following article types were excluded: articles other than the original research (e.g. review articles, letters to the editor, editorials or comments) and articles in other languages.

As the novel Coronavirus Disease 2019 (COVID-19) outbreak expands, identifying predictors for severe infection is essential to enable risk stratification, optimize the reallocation of hospital resources, and guide health recommendations and interventions. Chronic kidney disease (CKD) is associated with an increased risk of nosocomial and outpatient pneumonia (CHOU et al. 2014). In addition, the mortality rate related to pneumonia in CKD patients appears to be 14–16 times higher than in the general population (SARNAK et al. 2001). In this article, we aim to explore the potential association between CKD and the severity of COVID-19 infection.

RESULTS

Non-steroidal anti-inflammatory drugs have three different main actions, the anti-inflammatory, analgesic and antipyretic 4, where their use inhibits the arachidonic acid cascade, affecting the formation of prostaglandins, which act as vasodilators and increase renal perfusion, which may so the use of the drug causes vasoconstriction, spinal cord ischemia and acute kidney injury, in addition to inhibiting the transport of sodium and chloride in the loop of Henle and collecting ducts, resulting in natriuresis, diuresis and sometimes edema formation 5.

HOSPITALIZATION

Analysis of hospitalization was performed in seven studies. Among 62,490 patients with COVID-19, a total of 25,906 patients were hospitalized during the study period: 2,520 patients in the CKD group and 23,386 patients

in the non-CKD group. The heterogeneity test showed high heterogeneity among these studies ($I^2 = 78\%$), and a random effects model was used. Pooled analyzes of all included studies and multivariate-adjusted studies showed a significantly higher risk of hospitalization in patients with CKD than in those without CKD (OR 4.29, 95% CI 2.93–6.28, $p < 0.001$; OR 2.59, 95% CI 1.92–3.51, $p < 0.001$; respectively).

DISCUSSION

To the best of our knowledge, this is one of the few studies to assess the outcomes of COVID-19 infection in patients with CKD in the early period of the pandemic. After integration of data from included studies with multivariable adjustment for individuals with COVID-19 infection revealed that patients with CKD were at risk significantly higher all-cause mortality and hospitalization compared with those without CKD. Patients with CKD suffering from COVID-19 infection also had a higher risk of progressing to a serious condition than those without CKD in the pooled analysis of included studies and subgroup analyzes of multivariate-adjusted studies, although no results reached statistical significance.

Patients with CKD, at higher risk of severe disease due to a higher incidence rate of infections and cardiovascular diseases than in the general population, have been considered immunocompromised due to functional defects of the innate and adaptive immune system, leading to frequent infectious complications. Changes in the immune system of patients with CKD mainly include phagocytic dysfunction of B and T cells and increased reaction of pro-inflammatory cytokines and inflammatory monocytes; these may progress gradually as kidney function declines. Some investigations have shown that this chronic systemic

inflammation contributes to increased morbidity and mortality in patients with CKD. In our study, patients with CKD also had a higher risk of mortality, hospitalization and critical condition. Therefore, clinicians must pay more medical attention to this population in COVID-19 infection and may consider earlier hospitalization to help prevent disease deterioration and spread.

Renal involvement has been reported in patients with COVID-19 infection, supported by the findings of coronavirus PCR products in blood and urine samples. The etiology of renal involvement in patients with COVID-19 may be associated with direct cytopathic effects via the angiotensin-converting enzyme 2 (ACE2)-dependent pathway, with increased expression of ACE2 in patients with CKD, as a cellular entry receptor of coronavirus and indirect effect of cytokines or mediators related to viral infection in kidney tissues. It is noteworthy that predisposed CKD is recognized as a risk factor for the development of AKI, which is associated with an increased risk of progressive CKD, end-stage renal disease (ESRD) and mortality. Thus, early detection of kidney injury in COVID-19 infection must be done in patients with CKD, thus allowing timely appropriate medical strategies to prevent progression to poor outcomes.

Due to the lack of vaccine or approved specific therapies against COVID-19 in the early pandemic period of COVID-19 infection, the principle of management of COVID-19 infection in patients with CKD was supportive care, similar to the general population. In addition to being quarantined on initial COVID-19 infection, maintenance of stable hemodynamic status, adequate supply of oxygenation, close monitoring of changes in renal function, and drug prevention of renal toxicity must be performed in patients infected with

COVID-19. with CKD. More large clinical trials are needed to clarify the effect and safety of drugs against COVID-19, such as vaccines and antiviral or anti-inflammatory agents, particularly in patients with CKD due to their insufficient ability to excrete drugs.

Although our study analyzed clinical outcomes with a large sample of patients, there are still some limitations. First, the total sample size of patients with CKD was relatively small in some included studies, and this may reduce the significance of the results. Second, the causes of pre-existing CKD and the serum creatinine level were not clearly stated in the included studies. Therefore, our study did not explore the potential difference in outcomes between various etiologies or stages of CKD. Third, the exact information of other coexisting diseases besides CKD, such as diabetes mellitus, hypertension, cardiovascular disease, and detailed characteristics, such as age or sex, in the included studies were insufficient. To examine the impact of confounding potential, we performed subgroup analyzes of studies with or without multivariate adjustment, comprising age, sex, diabetes mellitus, hypertension, cardiovascular disease, etc. We observed small differences in pooled estimates between adjusted and unadjusted studies. More large-scale, higher-quality studies are needed to further confirm the influence of COVID-19 on outcomes in patients with CKD in the future.

COVID-19 infection will be diagnosed as a positive result in a reverse transcriptase-polymerase chain reaction (RT-PCR) assay (WANG et al. 2020). The primary endpoint will be all-cause mortality related to COVID-19 infection. Secondary outcomes will be risks of any hospitalization and critical conditions, including respiratory failure, endotracheal tube intubation, major adverse cardiovascular events, sepsis, septic

shock, and any ICU admission (ZAYED et al. 2020; SINGER et al. 2016).

FINAL CONSIDERATIONS

In summary, patients with CKD had a significantly higher risk of all-cause mortality and hospitalization compared to those without CKD. Physicians must pay more medical attention to this population in COVID-19 infection and apply timely appropriate medical strategies to prevent progression to poor outcomes.

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