World kidney day in COVID-19 years; a narrative review

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ABSTRACT

Introduction: The COVID-19 pandemic posed an unprecedented challenge to healthcare systems. COVID's high mortality rates, lack of intensive care unit (ICU) beds, multiple restrictions, and the vaccination process have affected almost all health policies and aspects of individual life. The high mortality rate of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection in patients with chronic diseases, especially CKD, and concerns about the increasing prevalence of non-communicable diseases during the pandemic have drawn much attention to the association between CKD and COVID-19. One of the most critical efforts to combat CKD is the world kidney day (WKD) campaign. World kidney day is the international society of nephrology (ISN) and the international federation of kidney foundations (IFKF) joint initiative to increase public awareness about the importance of kidneys and related diseases, especially CKD. World kidney day 2023, kidney health for all - Preparing for the unexpected, supporting the vulnerable, aims to raise awareness about the importance of kidneys and CKD. Moreover, this campaign encourages screening, and preventive behaviors, in patients at risk for CKD. Based on limited evidence, the COVID-19 pandemic has increased the risk of CKD risk factors such as obesity, diabetes, hypertension, and higher intake of fat and high-salt foods. On the other hand, reducing patients' access to health care has reduced screening in high-risk patients and reduced primary care for CKD patients.

Results:

Learning outcome:

The goal of this paper is to provide an overview of the opportunities, challenges, and solutions to deal with the effects of the COVID-19 pandemic on nephrology healthcare workers. Also:

1 Explain the 2023 world kidney day (WKD) campaign goals and the effect of the COVID-19 pandemic on each one

2. Discuss barriers to quality nephrology patient care in the COVID-19 pandemic and strategies to overcome these barriers.

3. Describe how Nephrology health care workers can improve the quality of care to patients with CKD in this era.

Keywords: COVID-19, World Kidney Day, Awareness, Chronic kidney disease

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روز جهانی کلیه در سالهای COVID-19 ؛ یک مقاله مروری روایی

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چکیده

همه گیری COVID-19 چالش بی سابقه ای را برای سیستم های مراقبت های بهداشتی ایجاد کرد. نرخ بالای مرگ و میر ناشی از کووید، کمبود تختهای بخش مراقبتهای ویژه (ICU)، محدودیتهای متعدد و فرآیند واکسیناسیون تقریباً بر تمام سیاستهای بهداشتی و جنبههای زندگی فردی تأثیر گذاشته است. نرخ بالای مرگ و میر ناشی از عفونت سندرم حاد تنفسی ویروس کرونا ۲ (SARS-COV-2) در بیماران مبتلا به بیماری های مزمن، به ویژه CKD، و نگرانی در مورد افزایش شیوع بیماری های غیر واگیر در طول همه گیری، توجه زیادی را به ارتباط بین CKD و COVID-19 ایجاد نموده است. یکی از حیاتی ترین تلاش ها برای مبارزه با بیماری مزمن کلیه، کمپین روز جهانی کلیه (WKD) است. روز جهانی کلیه، ابتکار مشترک انجمن بین المللی نفرولوژی (ISN) و فدراسیون بین المللی بنیادهای کلیه (IFKF) برای افزایش آگاهی عمومی در مورد اهمیت کلیه ها و بیماری های مرتبط با آن، به ویژه CKD است. روز جهانی کلیه ۲۰۲۳، سلامت کلیه برای همه - آمادگی برای موارد غیرمنتظره، حمایت از افراد آسیب پذیر، با هدف افزایش آگاهی در مورد اهمیت کلیه ها و بیماری مزمن کلیه است. علاوه بر این، این کمپین غربالگری و رفتارهای پیشگیرانه را در بیماران در معرض خطر CKD تشویق می کند. بر اساس شواهد محدود، همهگیری COVID-19 ، خطر ابتلا به عوامل خطر CKD مانند چاقی، دیابت، فشار خون بالا و مصرف بیشتر غذاهای چرب و پر نمک را افزایش داده است. از سوی دیگر، کاهش دسترسی بیماران به مراقبت های بهداشتی باعث کاهش غربالگری در بیماران پرخطر و کاهش مراقبت های اولیه برای بیماران CKD شده است.

کلید واژهها: COVID-19، روز جهانی کلیه، آگاهی، بیماری مزمن کلیه

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Introduction

World kidney day (WKD) is a global campaign that raises awareness about kidney conditions, especially chronic kidney disease (CKD). This condition is a significant health issue globally. Chronic kidney disease prevalence is estimated to be 13.4% (95% CI, 11.7%-15.1%) worldwide, with Europeans having a higher prevalence of CKD than people on other continents. Chronic kidney disease imposes a significant burden on all communities and is estimated to be increased in the next few decades. WKD aims to decrease CKD prevalence, incidence, and eventually its burden. The COVID-19 pandemic affected these efforts notably [1].

Infection with SARS-CoV-2 leads to COVID-19. Since 2019 millions of people have been infected and died due to COVID-19. COVID-19 has various clinical and paraclinical characteristics. In other words, COVID-19 affects the respiratory system and activates the immune system, leading to multi-system involvement, especially renal failure. The novel 2019 SARS-CoV-2 enters the host cell by binding the viral surface spike glycoprotein (S-protein) to the cellular angiotensin-converting enzyme 2 (ACE2) receptor. Angiotensin-converting enzyme 2 is present in many cell tissues, especially renal tissues. Kidney injury is relatively prevalent in COVID-19 patients and is linked with poor prognosis and higher morbidity and mortality rates. As COVID-19 plays a crucial role in the current surge in the number of CKD cases and has affected health systems notably, all efforts to reduce the incidence, morbidity, and morbidity of CKD have been influenced by COVID-19.

In 2023, the theme of the WKD campaign was kidney health for all. In line with this theme, the campaign defined six objectives: raising awareness, screening high-risk patients, developing preventive measures, educating clinicians, stressing the role of healthcare systems, and encouraging kidney transplantation [1]. The current study aims to review the literature regarding the Impact of COVID-19 on CKD based on the WKD campaign objectives.

Raising awareness about CKD in the COVID-19 era.

Raising public awareness is a key factor in managing communicable and non-communicable diseases. It is estimated that most CKD patients are aware of their diagnosis but do not feel the need to get screened. In addition, studies have shown that CKD is a stronger predictor of poor COVID-19 outcomes than conditions such as hypertension, diabetes, and even most immunodeficiency disorders [2]. Due to the increased incidence of CKD and a surge in the number of COVID-19 patients, increasing public awareness about the risk factors of both conditions is particularly important. As shown in Fig 1, risk factors for CKD are a network of multiple diseases, each leading to other ailments and eventually CKD. Therefore, it is possible to prevent this condition by increasing patients' awareness of CKD risk factors and screening them for underlying diseases. As our knowledge of CKD pathogenesis expands, many measures are being taken to prevent CKD. These include raising public awareness of the hazards of smoking, high sodium intake, low physical activity, and obesity. Encouraging patients at risk to get screened for diabetes mellitus type 2 (DM2), hypertension (HTN), heart disease, and metabolic syndrome is indicated [3].

Despite many efforts to raise public awareness, previous studies have revealed a relatively low awareness rate regardless of included populations. Global estimations demonstrate that only about 6% of the general population is aware of CKD and its complications, although this index is 10% in high-risk groups. There is a notable disparity in CKD awareness in different geographical settings. Despite the high end-stage renal disease (ESRD) incidence in the Taiwanese population, CKD awareness ranges from 3.5 to 9.7% (4). Other studies showed that only 8% and 10.04% of Chinese and Americans are aware of this disease, respectively [4].

More importantly, CKD awareness among high-risk patients is inconsiderable. For example, in China, only 12.1% of diabetic patients, 14.9% of HTN patients, and 26.5% of those with both DM2 and HTN are aware of CKD. Even patients with different stages of CKD are often unaware of their disease. For example, CKD awareness in Chinese patients with micro and macroalbuminuria is 8.1% and 14.5%, respectively [5]. Similarly, in 1999–2000, the national health and nutrition examination survey (NHANES) illustrated that

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8.2% of participants with stage 3 CKD self-reported a history of renal disease [5]. A systematic review conducted by Chu et al. on Adults with CKD not receiving dialysis demonstrated a shallow awareness (pooled CKD awareness, 19.2%) in these patients [6].

Before December 2019, non-communicable diseases were the leading cause of death and disability; as a result, a significant portion of public health education focused on these conditions. Conversely, the COVID-19 pandemic shifted public attention to communicable health issues, overshadowing health strategies to combat CKD risk factors, including obesity, DM2, and HTN.

On the other hand, strategies to combat the pandemic such as social and physical distancing and self-quarantining increased patients' hesitancy to participate in programs aiming to raise public awareness of CKD. Although social media have widely broadcasted COVID-related information during the pandemic, including its risk factors, they neglected routine programs to increase public awareness regarding non-communicable diseases [7].

Encouraging preventive behaviors

Various studies have clarified the relationship between lifestyle and CKD. Among them, obesity and high sodium and meat intake are the strongest predictors. For example, Mafra et al. examined the association between meat intake and the substitution of meat with CKD's risk of incident. Their data showed that the incidence of new CKD in the highest quartile of red and processed meat intake is 73% and 99% higher than in the lowest quartile, respectively [8].

The COVID-19 lockdown, like any other stressful situation, changed populations' food preferences—most notably, foods with high sugar, fat, or salt are preferred. A study by Mitchell et al. demonstrated higher emotional and stress-induced eating rates during the lockdown. Moreover, their data showed that food choices during this period might reflect desires to stock up and consume core food groups such as red meat and starchy vegetables [9]. Furthermore, studies showed that school lockdowns led to negative trends in lifestyle behaviors, as they decreased students' physical activity and significantly increased their consumption of salty potato chips, red meat, and sugary drinks.

Obesity is one of the main risk factors for CKD, and combating this condition comprises one of the main goals of CKD prevention programs globally. Despite many efforts to combat CKD, the COVID-19 pandemic has significantly impacted these programs. Due to increasing pressure on health systems at the onset of the COVID-19 pandemic, many governments and public health authorities worldwide have imposed (among other measures) home confinement and general lockdown protocols that have led to various consequences. Numerous studies have shown that quarantine and social distancing during the COVID-19 pandemic significantly increased psychological disorders, including depression, anxiety, and stress. These conditions can result in disturbed sleep cycles and shortages, leading to increased food intake and obesity risk [10].

Clemmensen et al. claimed that, aside from the significant impact of a general lockdown on COVID-19 pandemic control, these lockdowns could worsen obesity and other non-communicable diseases pandemic. Lockdowns might adversely affect metabolic health via the combined deterioration of socioeconomic conditions, psychological security, and metabolic processes. Approaches designed to decline the spread of COVID-19 have promoted obesity and associated metabolic disorders, which may eventually lead to a CKD pandemic.

Impact of COVID-19 pandemic on screening for CKD

CKD has features that propound screening tests, especially its high progression rate, long asymptomatic phase, and the high effectiveness of drug therapy in the early stage. Among the proposed screening methods, dipstick screening for proteinuria has shown the highest efficiency and lowest cost. According to studies, universal CKD screening in the general population would be time-consuming and expensive. For example, the Korean national health screening program suggests annual CKD screening only in high-risk populations, such as DM2 and HTN patients, using a Markov decision-analytic model [11].

Similar to other aspects of health care, the COVID pandemic has affected CKD screening widely. Studies have shown that during the COVID-19 pandemic, hospital admissions due to non-COVID-19-related complaints significantly decreased, potentially leading to delayed medical care. From the first days of the pandemic, studies have shown that comorbidities such as HTN, DM2, and CKD are risk factors for severe types of COVID-19. Moreover, recent studies suggest that the COVID-19 pandemic has led to a higher incidence of CKD and its risk factors, such as HTN and DM2.

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Besides, studies have shown that the COVID-19 pandemic might affect DM2. Most importantly, similar to other severe diseases, COVID-19 patients experience episodes of stress hyperglycemia which may lead to DM2 in the future. Additionally, restrictions on outdoor movements have limited sunlight exposure, leading to vitamin D deficiency [12]. Low vitamin D levels have long been regarded as a risk factor for insulin resistance, and vitamin D supplementation improves insulin sensitivity. Additionally, the Impact of drugs used in managing COVID-19 on poor glycemic control should be considered. Corticosteroids, widely used in managing COVID-19 patients, have been significantly associated with poor glycemic control and an increased risk of DM2 [13].

Likewise, studies have shown that during the COVID-19 pandemic, many DM1 children received delayed diagnoses, altering the presentation and severity of diabetic ketoacidosis (DKA). Kamrath et al. obtained and analyzed a dataset of 532 children and adolescents newly diagnosed with DM1. Their study demonstrated a significant increase in diabetic ketoacidosis and severe ketoacidosis at diabetes diagnosis [14].

This late diagnosis and DKA occurrence can lead to severe complications, including acute kidney injury, leading to CKD in the long term.

On the one hand, systemic HTN often accompanies renal diseases, especially CKD. CKD progression is accelerated by hypertension, so blood pressure control is a key factor in treating CKD. On the other hand, as discussed in diabetes studies, the association between COVID-19 and HTN is a two-way relationship. HTN increases the odds of being diagnosed with severe COVID-19, and COVID-19 leads to HTN and CKD in the long term.

The pathophysiology of these three diseases shares a similar metabolic pathway through the angiotensin-converting enzyme 2 (ACE2) receptor. ACE2 is involved in blood pressure modulation and establishing blood pressure homeostasis. Furthermore, the mechanism for SARS-CoV-2 infection necessitates the binding of the virus to the membrane-bound form of the ACE2 receptor and the internalization of the complex by the host cell. ACE2 modifies angiotensin peptide metabolism and affects the progression of CKD. Studies noted the potential over-representation of HTN among COVID-19 patients from the epidemic's beginning. For example, a study by Akpek et al. on 153 confirmed COVID-19 patients showed that COVID-19 leads to an increase in both systolic and diastolic BP and causes new-onset HTN in a considerable fraction of patients [15].

Data suggest that the COVID-19 pandemic will increase CKD incidence and its risk factors in the next few years.

Educating clinicians about the Impact of COVID-19 on CKD

The fight against CKD requires post-screening interventions by experienced medical staff, public awareness, and screening of high-risk individuals. Due to the importance of CKD management at the early stages, general practitioners (GPs) are responsible for diagnosing, referring, and administering primary treatments for these patients in most health systems. Furthermore, patients will only be referred to a nephrologist if initial treatment fails or requires further follow-ups.

CKD patients' diagnosis and management require the supervision of nephrologists, significant human resources, and budgets. The COVID-19 pandemic has led to an increase in renal complications and the workload of nephrologists. As a result, the number of nephrologists is insufficient to provide adequate kidney care, especially in the early stages of CKD.

A meta-analysis of 4873 patients suffering from CKD showed that this pandemic has significantly decreased nephrology service admission. Moreover, a significant reduction in nephrological counseling for inpatients has been reported. Hussein et al. provided similar findings—specifically, a reduction from 275 to 134 cases [16]. Studies in the United States and the United Kingdom showed that outpatients were reduced by 70–90% [16].

It has been suggested that most non-progressive CKD cases can be managed without referral to a nephrologist by GPs, and specialist referrals can be booked only for patients with a GFR less than 30 ml/min per 1.73 per m2 or if the initial treatment does not result in the intended outcome. Unfortunately, studies have shown that GPs' clinical suspicions, diagnoses, and referrals of CKD are inadequate. For example, a study found that only about 50% of internal medicine residents knew the definition of CKD, and only about one-third were aware of the staging of CKD. Besides, Stevens et al. suggested inadequate physician awareness of CKD and limited utility of administrative databases for identifying CKD patients, referring to low rates of serum creatinine testing and insensitivity of diagnostic codes for CKD, even in high-risk patients [17].

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Referral rates for CKD patients are thought-provoking. For example, Martínez-Ramírez et al. showed that 93% of patients were visited by a GP, 63% by a cardiologist, and only 31% by nephrologists. Due to the shortage of nephrologists in most health systems, limited hospital beds, and various renal complications associated with COVID-19, the training of medical staff for the diagnosis and management of CKD has become particularly important.

With the advancement of technology, various platforms have been created to increase CKD awareness among healthcare providers, including the national kidney foundation, the American society of nephrology, and Uptodate. E-learning programs for non-communicable disease prevention and treatment have been launched in many countries. For example, by 2015, more than 5000 health professionals in Mexico (including non-nephrologists) used a training platform. In the last three years, due to the COVID-19 pandemic, e-learning has been widely used as an efficient option for training healthcare providers. Alsoufi et al. surveyed 3348 medical students from 13 medical schools in Libya. Their results demonstrate that most students showed higher learning levels through online education than through face-to-face education [18].

Stressing the role of healthcare systems in CKD patients during the COVID-19 pandemic

Due to the significant impact of CKD on the health system, different countries have implemented different programs to control this disease. In 2003, Taiwan introduced a kidney health-promoting program to ban aristolochic acid-containing herbs, raise patient education, launch public awareness campaigns, develop integrated care provider teams, and fund CKD research. In recent years, the US department of health and human services has announced plans to reduce end-stage renal disease incidence by 25% by 2030. The goals of this program include different aspects such as prevention, early diagnosis, and a reduction of the incidence of risk factors such as DM and HTN.

COVID-19 has put unprecedented pressure on healthcare systems, making patients with chronic diseases, including CKD, vulnerable. Local and national healthcare systems, such as telehealth, have used various methods to overcome these conditions.

Telehealth services have been widely used in different countries in the past decade. However, increasing Internet access and social media have revolutionized these services. While people with chronic illnesses have less access to the internet than healthy adults (62% versus 81%), people with chronic illnesses are more likely to use social media to share online. Lockdowns have reduced unnecessary face-to-face visits and caused a significant increase in the use of these services. Tan J. et al. explored the potential of remote methods to provide nephrology services, especially for patients in rural areas. According to this study, remote nephrology patient management has dramatically improved the treatment outcomes of rural patients and made them similar to other patients [19].

COVID-19 vaccination in CKD

The outbreak of SARS-COV-2 has drawn much attention to developing effective vaccines against the virus. Currently, there are different WHO-approved vaccines for emergency use around the world. These vaccines use standard technology such as an inactivated virus or purified protein and new methods such as mRNA or adenovirus vectors. BBIBP-CorV (Sinopharm) and mRNA vaccines have the highest injection rates worldwide. Since the first effective vaccines against SARS-COV-2 were introduced, various studies have been conducted to determine the efficacy of different types of vaccines in the general population. Three antibodies are usually used to ensure an immune response after vaccination, including neutralizing antibodies (Abs), anti-Spike IgG, and anti-receptor binding domain (RBD). Studies have shown that the level of immunogenicity in mRNA vaccine recipients was about 95% in the general population compared to 86% in BBIBP-CorV recipients.

Some of the most critical issues related to mass-producing and increasing access to vaccines are identifying high-risk groups, determining the priority of vaccinations, and determining the number of doses required for each group. The centers for disease control and prevention (CDC) currently lists people with 21 specific medical conditions as high-risk populations, including those with DM1 and 2, CKD, and dialysis, along with kidney transplantation recipients (KTRs). Studies have shown that compared to CKD, no risk factor can put a patient at as much risk for mortality and complications from COVID-19. It is estimated that patients with ESRD or the G4-G5 stage of CKD are three to four times more likely to die from COVID-19 and its complications than the general population. Therefore, an effective and safe vaccine for CKD and KTR patients is essential.

In patients with severe renal impairment due to immunosuppressive status and uremic

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accumulation, the immunological response to antiviral vaccines such as hepatitis B and influenza is much lower than the average population. Therefore, many concerns have been raised about the performance of COVID-19 vaccines. Initially, studies by Carr et al. showed that after receiving two doses of an mRNA vaccine, a humoral or cellular immunologic response was seen in only 3–59% of KTRs. Recently, other studies have shown injecting the third dose of mRNA vaccine in KTRs. They have not developed antibodies after the second dose increases their immunity to the SARS-CoV-2 virus by 44–70% [20].

Studies on BBIBP-CorV have had relatively poor results. A survey of 100 kidney transplant patients revealed that 43.05% of patients developed at least one antibody against SARS-CoV-2 after receiving two doses of the Sinopharm vaccine. A study on CoronaVac found that 43% of KTRs became immune to the virus one month after receiving the second dose. In another study, Sadioglu et al. showed that out of 118 kidney transplant patients, only 18.8% had anti-spike and nucleocapsid antibodies. Various risk factors have been reported for this issue, including old age, immunosuppressive drugs, and little time since the transplant [21].

Overall, studies show that patients receiving kidney transplants respond much better to mRNA vaccines than BBIBP-CorV, and receiving a third and sometimes a fourth dose is necessary for many patients. It has been suggested that antibodies be tested for immunity in these patients after vaccination.

Patients with stages G4-G5 of CKD often need to undergo hemodialysis. According to the latest studies, the COVID-19 mortality rate among unimmunized hemodialysis patients is as high as 31%, which is much higher than the average population, making them one of the most at-risk groups for COVID-19. However, the study results are different; vaccination in this group has been associated with poorer outcomes. For example, Simon et al. showed that after the injection of mRNA vaccines into hemodialysis patients, the antibody level was much lower than the control group (the median was 171 U/mL for dialysis patients and 2500 U/mL for the controls) [22]. In addition, Grupper et al.'s study on the Pfizer vaccine showed that the titer of anti-spike IgG in hemodialysis patients was much lower than in the control group (the median was 2900 U/mL for dialysis patients and 7401 U/mL for the controls) [23]. In contrast, Carr et al. showed that the immunogenicity rates of mRNA and adenoviral vaccines in these patients were 71% and 97%, respectively.

Studies on the Sinopharm vaccine are limited. A study on 446 dialysis patients in the United Arab Emirates showed that after receiving the second dose of the Sinopharm vaccine, the positive anti-Spike IgG titer was seen in 50% and 78.1% of hemodialysis patients and the control group, respectively [24]. Unfortunately, none of the studies compared the efficacy of mRNA vaccines with BBIBP-CorV, and studies only noted the importance of receiving booster doses in this group.

COVID-19 and kidney transplantation

The COVID-19 pandemic has posed unprecedented challenges to ESRD patients and related health systems, including surgical access for hemodialysis, the rate of kidney donors, and advanced preventive methods for KTR.

KTRs appear to be at high risk for COVID-19 disease due to chronic immune system suppression. Nevertheless, aside from poor health outcomes, access to transplantation and dialysis services are more limited for patients with renal failure during the pandemic. Organ donation and transplants, especially at the beginning of the pandemic, have declined due to barriers to organ transport, reduced donor numbers, and reduced trauma and other emergencies. This has led to the suspension of many transplant centers. Other transplant centers had to operate various methods to prevent COVID-19 infection in patients after transplantation, including establishing medical teams to allocate ICU beds for kidney transplant patients.

On the other hand, 28.4 million surgeries have been canceled worldwide due to the risks posed by COVID-19, including hemodialysis access surgeries.

The COVID-19 pandemic has significantly impacted patients' access to dialysis services. During the pandemic, the need for dialysis increased by about 5%. However, access to these services has significantly decreased. A meta-analysis of seven studies involving 8940 participants showed that 86% of patients reported a significant reduction in receiving hemodialysis care. Barriers have been seen at various levels, including a sharp decline in the number of nurses and health workers, a 5% reduction in the number of hemodialysis centers, and an 11% reduction in dialysis sessions at these centers [25].

Obstacles to patients requiring kidney transplants are much more significant. According to studies, the chance of receiving a transplant in the

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pandemic period is 2.2 times less than in the pre-pandemic period. Besides, a significant reduction and sometimes complete suspension of kidney transplant centers and a lack of ICU beds and clinicians have been reported during this period.

In conclusion, the COVID-19 pandemic has posed an enormous threat to CKD patients because of the higher risk of mortality in CKD and the higher risk of developing CKD risk factors, such as HTN, obesity, and DM. The evidence suggests CKD patients should receive regular vaccinations and booster doses during the SARS-CoV-2 pandemic. Multiple appointments for diagnosed CKD or high-risk patients can effectively control the disease during a pandemic.

Data availability

No data have been submitted to any open-access databases. All data supporting the study are presented in the manuscript or available upon request.

Author's contribution

SM and PM were included in preparing the concept and design. MM revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript, and critically evaluated the intellectual contents. All authors have read and approved the manuscript's content and confirmed the accuracy or integrity of any part of the work.

Ethical considerations

The authors have observed ethical issues (including plagiarism, data fabrication, and double publication).

Statement of Ethics

This narrative review was conducted according to the World Medical Association Declaration of Helsinki.

Conflicts of interest

The authors declare that they have no competing interests.

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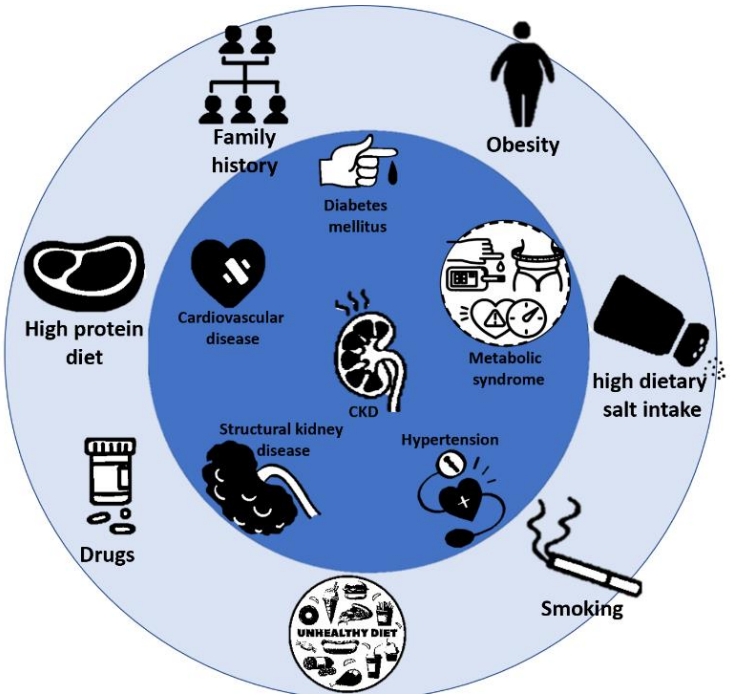
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Figure1. The main risk factors of CKD.



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