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The Correlation of Chronic Kidney Disease and Diabetes Mellitus: A Literature Review

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ABSTRACT

Chronic Kidney Disease (CKD) is defined as a persistent abnormality in the kidney structure or function present for more than three months with bad implications for health. Chronic kidney disease might be linked to various diseases, such as diabetes mellitus, hypertension, and other kidney diseases. On the other hand, another metabolic disease, diabetes mellitus, may cause chronic kidney disease through its various complications, mainly microangiopathy. These two conditions may coexist and cause complicated conditions. Therefore, effective management and treatment of both chronic kidney disease and diabetes mellitus are very important to tackle further obstacles.

Keywords: chronic kidney disease; end-stage renal disease; CKD; ESRD; diabetic kidney disease; diabetes mellitus.

INTRODUCTION

Chronic kidney disease is defined as a persistent abnormality in kidney structure or function (eg, glomerular filtration rate (GFR) <60 mL/min/1.73 m2 or albuminuria ≥30 mg per 24 hours) for more than 3 months. Chronic kidney disease, also defined as the presence of irreversible structural or functional kidney damage, increases the risk of poor outcomes due to its association with multiple complications, including altered mineral metabolism, anemia, metabolic acidosis, and increased cardiovascular events. Chronic kidney disease has been identified as a major global public health issue. Worldwide, CKD prevalence is estimated to be 13.4% (11.7-15.1%). Numerous illnesses, including diabetes mellitus, hypertension, and other renal diseases, may be associated with chronic kidney disease. However, diabetes mellitus, another metabolic condition, can lead to chronic kidney disease through its many consequences, primarily microangiopathy. Complicated situations may result from the coexistence of these two factors. In order to overcome additional challenges, it is crucial to effectively manage and treat both diabetes mellitus and chronic kidney disease.

REVIEW CONTENT

Chronic Kidney Disease

- *Definition*

Chronic kidney disease (CKD) arises from many heterogeneous disease pathways that alter the function and structure of the kidney irreversibly, over months or years. Chronic kidney disease is also defined as decreased kidney function, regardless of the underlying cause, present for more than 3 months, accompanied by significant clinical indicators such as a glomerular filtration rate (GFR) of less than 60 mL/min per 1.73 m2 or markers of kidney damage like albuminuria with a rate of AER ≥30 mg/24 hours and ACR ≥3 mg/mmol, or even both. Haematuria, electrolyte abnormalities caused by a compromised tubular system, urine sedimentation anomalies, histological and anatomical abnormalities, and kidney transplantation history could all be additional markers of CKD.

- *Epidemiology*

Chronic kidney disease has emerged as one of the leading causes of mortality worldwide, and it is one of a small number of non-communicable diseases that have shown an increase in associated deaths over the past 2 decades. Over 800 million people worldwide, or 10% of the population, are affected by CKD. Global Burden of Disease (GBD) Chronic Kidney Disease Collaboration reported that since 1990 until 2017, the prevalence of CKD has increased by 29.3%. Furthermore, the mortality rate of CKD from 1990 to 2017 was 41.5%; as a result, it made up 4.6% of the total mortality worldwide in 2017, proceeding it up from the 17th place it held in 1990 to the 12th position in 2017. CKD typically has a larger toll on vulnerable and underprivileged populations.

In many regions, persons with lower socioeconomic status have a higher prevalence of CKD, limited access to treatment, and poorer outcomes.

• *Risk Factors*

Chronic kidney disease is usually linked to non-communicable diseases, such as diabetes and high blood pressure rate, as both of them are the two most prevalent causes of the disease. However, in low- and middle-income nations, there are other additional potential etiologies, such as infectious diseases and environmental toxins, but many remain unidentified. There are several etiologies that contribute to CKD: Diabetes Mellitus (DM), hypertension, polycystic kidney disease, glomerulonephritis, etc.

• *Pathophysiology*

Chronic kidney disease occurs as a consequence of two mechanisms: an initial trigger and a perpetuating mechanism. The initial trigger of CKD could come from a preexisting kidney disease or abnormality; it may arise during the development process or through injury throughout one's lifetime. Furthermore, it may be initiated by problems caused by inflammation, an impaired immune system, or even toxins. The damaged kidney leads to adaptation by hyperfiltration and hypertrophy of the nephrons. Both hyperfiltration and hypertrophy are caused by various pathways, including hormones, growth factors, and cytokines. As a result of the nephrons' hyperfiltration and hypertrophy, there will be an increase in arterial filling pressure, changes in the glomeruli structures, and eventually, the kidney's ability to filter as it should decline.

The overactivation of the renin-angiotensin system (RAS) also contributes significantly to the development of CKD. The juxtaglomerular apparatus first secretes renin, which subsequently cleaves angiotensinogen to produce angiotensin I. Angiotensin I is converted into angiotensin II, an active byproduct of RAS, by the angiotensin-converting enzyme (ACE). Angiotensin II will be mediated by the AT1a receptor in the kidney, resulting in its being produced independently by the kidney. Circulating angiotensin II can also be actively internalized into proximal tubular cells by AT1a receptor-dependent mechanisms. As a result, the level of angiotensin II will be much higher in the kidney than in other locations, and the physiological action of angiotensin II, such as afferent and efferent vasoconstriction, renal tubular salt reabsorption, and tubuloglomerular feedback control mechanisms, will be shown.

• *Screening, Diagnosis, and Management*

Chronic kidney disease is one of the leading causes of death worldwide, yet 5% of people with early CKD are unaware of their disease. Therefore, early and effective screening, diagnosis, and management are crucial to avoid various negative consequences caused by the progression of CKD, including cardiovascular disease, end-stage renal disease (ESRD), and mortality. The National Kidney Foundation has developed a kidney profile test that includes measuring both serum creatinine for estimating GFR and urine ACR. Numerous clinical guidelines recommend screening and a risk-based approach in individuals older than 60 years old or those with a history of diabetes mellitus or hypertension. Screening should also be considered in those with clinical risk factors, including autoimmune disease, obesity, kidney stones, recurrent urinary tract infections, reduced kidney mass, exposure to certain medications such as NSAIDs or lithium, and prior episodes of acute kidney injury, among others.

The diagnosis of CKD should be determined when the patient has one or more criteria of the following: (1) GFR less than 60 mL/min/1.73 m2; (2) albuminuria (ie, urine albumin ≥30 mg per 24 hours or urine albumin-to-creatinine ratio [ACR] ≥30 mg/g); (3) abnormalities in urine sediment, histology, or imaging suggestive of kidney damage; (4) renal tubular disorders; or (5) history of kidney transplantation (KDIGO, 2012). Once the diagnosis of CKD is clear, the next step is to determine the stage of the disease, which is based on the GFR and albuminuria category.

The management of CKD should include blood pressure control, proteinuria reduction, prevention of AKI and cardiovascular disease, as well as lifestyle interventions such as reducing sodium intake to <2 g per day, achieving a healthy body mass index of 20 to 25 kg/m2, smoking cessation, exercising for 30 minutes five times per week, and good diabetes control with a target hemoglobin A1c level of 7%. This recommended key management is critical in order to prevent disease progression. The management of CKD should be adjusted to each patient's risk factors and conditions.

• *Classification*

Chronic kidney disease can be classified by the CGA classification or staging. The CGA classification stands for cause, GFR category, and albuminuria category (Andrassy, 2013). The cause of CKD is identified by considering the presence of systemic disease that follows and by observing the pathologic-anatomic findings. Systemic diseases could affect the kidney and cause glomerular, tubulointerstitial, vascular, cystic, and congenital damage, which eventually leads to CKD. Additionally, CKD is divided into 3 stages based on albuminuria and 5 stages depending on GFR. The combined understanding of the staging based on GFR and albuminuria category can predict the prognosis and outcomes of CKD (KDIGO, 2012). In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD. The numbers shown in the albuminuria table represent the equivalent prediction of the ACR (albumin-creatinine ratio).

• *Complications*

The clinical manifestations of chronic kidney disease are different in each patient with different ages, etiology, stages, and comorbidities. Chronic kidney disease affects more than just kidney structure and function; it also affects the endocrine balance.

Examples of complications caused by CKD are metabolic acidosis, hyperkalemia, anemia, and mineral and bone impairment.

Correlation of Chronic Kidney Disease and Diabetes Mellitus

- *Direct Correlation*

Diabetes mellitus, both type 1 and type 2 is one of the most common causes of chronic kidney disease, especially in the Western world. Though quite different, with type 1 being caused by an autoimmune disease attacking beta cells in the pancreatic islets of Langerhans which produces insulin, and type 2 caused by a combination of insulin resistance and insufficient insulin response, both type 1 and type 2 share many similarities. One of the similarities includes microvascular and macrovascular complications, which although having different pathophysiology between the 2 phenotypes of diabetes, may cause CKD.

In type 1 diabetes, the primary pathway to CKD is through microvascular diseases, this condition is commonly referred to as 'diabetic kidney disease' or 'diabetic nephropathy'. The cascade starts with hyperglycemia alongside other overlapping pathways such as changes in haemodynamics, metabolism, and inflammatory. These pathways may cause hyperfiltration and an increase in intraglomerular pressure. Hyperfiltration can clinically be seen as an increased glomerular filtration rate (GFR). The constant high GFR will eventually cause nephrons to break and decrease in numbers. Hypertension and albuminuria will subsequently occur as the condition of the kidney worsens and the kidney disease develops. Type 2 diabetes patients are usually of an older age group, in which other diseases may have already caused CKD. It was concluded that in type 2 diabetes, CKD is likely a more compounded issue, as it might have been caused by a combination of other chronic disease.

- *Indirect Correlation*

Diabetes mellitus is the root of many chronic diseases and is a risk factor in many others, as it has many complications. One of the more common and early chronic complications of diabetes is microangiopathy, which can cause conditions such as hypertension, narrowing of blood vessels, coronary artery disease, and other heart diseases. Diabetes can also cause the human body to be more susceptible to infections including infections to the kidneys.

Chronic kidney disease and hypertension are two conditions with multifaceted relations, with both hypertension being the primary cause of CKD, and hypertension found in patients after being diagnosed with CKD. The connecting pathways between the two conditions include sodium dysregulation, increased sympathetic nervous system, and changes in the RAAS (renin-angiotensin-aldosteron-system).

Heart failure (HF) and chronic kidney disease (CKD) are closely linked through shared risk factors such as hypertension and diabetes, as well as intertwined pathophysiological mechanisms. HF exacerbates CKD by reducing renal blood flow and causing ischaemic injury, while CKD accelerates HF progression through fluid overload, anaemia, uraemia, and neurohormonal dysregulation. This bidirectional relationship creates a vicious cycle, with each condition worsening the other.

CONCLUSION

Chronic Kidney Disease or CKD is a non-communicable disease defined as a persistent and irreversible abnormality in kidney structure or function for more than 3 months. Over the past two decades, it has shown an increase in associated deaths and therefore emerged as a leading cause of mortality worldwide. The diagnosis of CKD is made through both clinical and laboratory examination. The two most prevalent causes of CKD are diabetes and hypertension, and naturally many guidelines recommend screening and risk-based approach for individuals over the age of 60 and/or those with a history of diabetes mellitus and/or hypertension. Diabetes may cause CKD through its various complications, mainly microangiopathy, furthermore, diabetes is a risk factor in many diseases and conditions that can lead to CKD, such as heart failure, hypertension, and other heart diseases.

COMPLIANCE WITH ETHICAL STANDARDS

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