

Chronic Kidney Disease and Mortality Risk: A Systematic Review

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ABSTRACT

Bilateral tubal ligation (BTL) is a widely practiced permanent CKD is considered a worldwide health worry because it greatly increases the risk of dying from heart disease. Recent studies published in Scopus journals were studied to determine which clinical, biochemical and sociodemographic markers affect mortality in people with chronic kidney disease. Nurses consider 15 high-risk factors from reviews of current studies, including patients who undergo dialysis and those who do not, young and old, from many parts of the world. Many of the main factors such as lower Fetuin-A, higher TyG-BMI, increased uric acid levels, extreme protein intake, depression, low blood sugar and being female were found to predict more deaths from all causes and cardiovascular diseases. Almost the same measuring results were found to be continuous (46.7%) or categorical (53.3%). Both the Kidney Failure Risk Equation (KFRE) and the Estimated Pulse Wave Velocity (ePWV) tools seemed to improve the way cardiovascular disease risk is ranked. What we know from these outcomes points to multiple factors linked to the risk of death from CKD and the importance of giving patients appropriate care.

Keywords: Tubal ligation, postoperative changes, patient awareness, side effects, surgical approach, informed consent, gynecologic surgery.

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1. INTRODUCTION

More than 10% of adults worldwide have chronic kidney disease (CKD) which also greatly contributes to the number of early deaths. If renal function declines, those with CKD are at a higher risk of developing heart diseases, infections, problems with their blood or sugar levels and ultimately kidney failure that may need dialysis or a transplant [1, 2]. Death in those with chronic kidney disease (CKD) is influenced by factors other than low glomerular filtration rate (GFR) such as different kinds of health-related, chemical, situation and social factors [3, 4].

In recent times, different studies have aimed to find out what is linked to higher mortality in CKD patients to detect illnesses early on, design proper treatment methods and offer support that targets individuals at higher risk [5, 6]. Blood pressure and proteinuria are examples of standard predictors and new indicators include gut microbiota changes, signs of inflammation, mental health problems and differences in financial resources [7, 8]. Studying how different elements link to impact survival both helps clinical decisions and chances of patient recovery [9, 10]. Figure 1 provides a summary of the important factors that contribute to the risk of dying with CKD and how they interact.

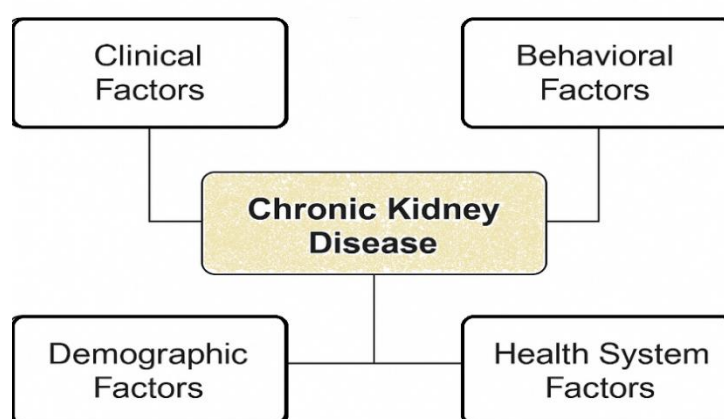


Figure 1. Framework for Identifying Mortality Risks Associated with Chronic Kidney Disease

A Figure outlining different and interacting domains that play a role in the mortality risk of chronic kidney disease such as biological, behavioral, psychological and systemic ones.

Because the field is complex, this systematic review reviews articles that examine death-related indicators in patients with CKD. The subsequent section provides a detailed summary of these studies and focuses on the important variables, people studied and the outcomes of their deaths.

2. LITERATURE REVIEW

Around the world, chronic kidney disease (CKD) is becoming more common because it develops slowly and is associated with poor health and higher death rates. More studies were published in the last five years on the risks of CKD-related mortality, especially driven by current health crises like COVID-19 and a rising number of non-communicable illnesses like obesity and heart disease.

The research study used Google Scholar and ScienceDirect to find studies published between 2020 and 2024 using the search term "chronic kidney disease" AND "mortality". The upward trend is evident from looking at Figure 1 which depicts the growth in published studies, reaching a number that is nearly triple the number recovered in 2021. Because CKD leads to risks outside of renal failure, especially when it hastens death from heart, metabolic and infectious diseases, it demands careful attention.

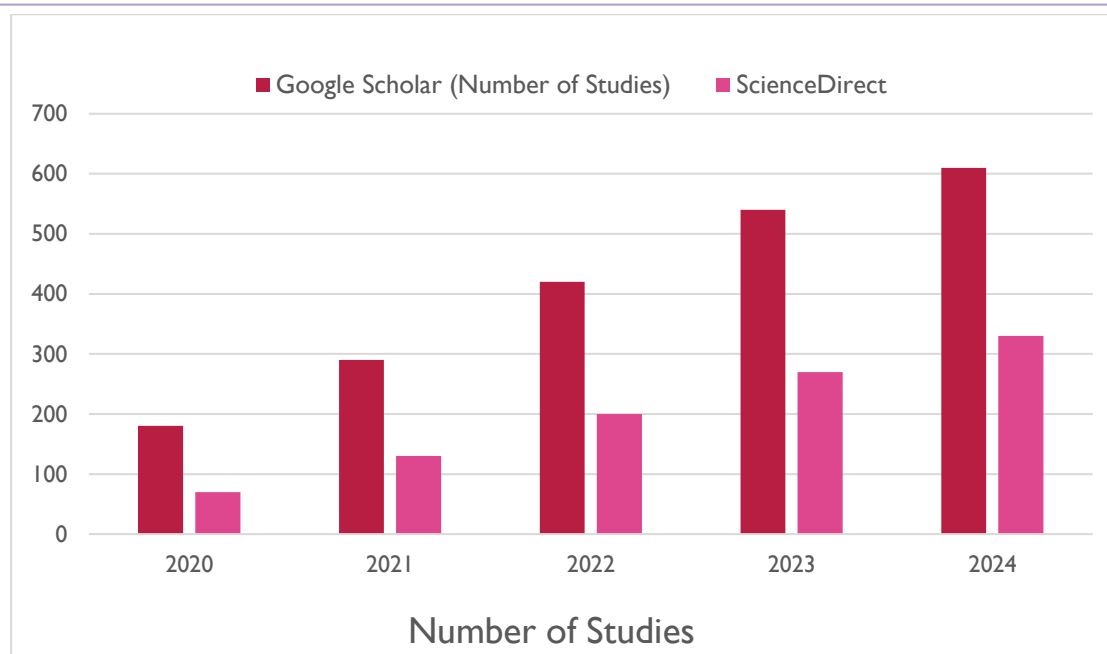


Fig. 2: Annual Number of Publications in Google Scholar and ScienceDirect (2020–2024)

Lots of research has pointed out that the risk of dying due to COVID-19 is higher for CKD patients. The study by Gibertoni et al. (2021) concluded that having CKD without starting dialysis greatly raised a person's risk of death because of troubled immunity and fewer chances for adequate care [1]. Also, Puicón-Suárez et al. (2022) showed that CKD was strongly connected to higher risk of dying from COVID-19, especially in older patients and those with diabetes and other metabolic diseases [2].

Being diagnosed with CKD means the leading cause of death for these patients is heart disease. Matsushita et al. (2022) explain that poorer kidney function greatly increases the risk of dying from heart disease because of high blood pressure, troubles in the vessels and the buildup of calcium on the walls [3]. Izzo and his team (2024) explained that mineral bone disorder (MBD) in CKD is a risk factor for vascular calcification which leads to a higher risk of dying from heart disease [4].

Obesity is now known to play a key role in causing and advancing CKD.

Nawaz et al. (2023) found that obesity can cause CKD which might result in more inflammation and insulin resistance; these factors contribute to a higher risk of early death. With advanced CKD, kids often lose weight and get weaker which adds to the difficulties of metabolism control [5].

Wilkinson et al. (2021) proved that having sarcopenia independently raises the risk of both dying from any cause and developing ESRD, in patients with early CKD stages [6]. Studies by Chatzipetrou et al. (2022) recognize sarcopenia as a prevalent condition in CKD patients, mostly affecting older individuals, who often experience frailty, need to be hospitalized and die sooner [7].

Pelletier et al. (2022) investigated the effect of kidney disease in patients receiving allogeneic stem cell transplants, showing that poor kidney health decreased survival and free-of-relapse outcomes, thus demonstrating the importance of tailoring care to such patients [8].

There are still noticeable holes in literature, even as it continues to expand. Many studies examine risks individually instead of as a group which makes it hard to compare or total studies across groups of people. There are not many studies that look at depression, the ability to access care or sticking to medicine regimens, even though they are important in determining CKD outcomes. Many mortality studies concentrate on severe CKD, but neglect the easily overlooked risks found in less advanced CKD. Many of these studies look at people only at a given time, so it is hard to tell what causes the diseases or how they develop over time. As a result, this systematic review focuses on compiling detailed, indicator-based information about the risks of death in CKD patients using the Following- :

- Classifying indicators into continuous (biomarkers, anthropometric measures) and categorical (comorbidities, sex, depression) groups.
- Evaluating how drugs' effects on various mortality outcomes (including heart disease, kidney disease and

infections) vary.

- Suggesting new areas of research and clinical attention based on current findings.

Through this structured approach, the review enhances understanding of the multi-factorial nature of mortality in CKD, paving the way for more personalized risk stratification tools and targeted interventions.

3. CKD AND CARDIOVASCULAR MORTALITY

Chronic Kidney Disease (CKD) contributes to an increased risk of cardiovascular death through various physiological factors. A major reason for this is that CKD patients experience constant inflammation and oxidative stress which damages the blood vessels and supports atherosclerosis [5, 7, 29]. Specific changes in mineral metabolism such as high blood phosphate and secondary hyperparathyroidism, also help lead to vascular calcification and stiff arteries, important causes of cardiovascular mortality.[19,14]

The condition of hypertension which can result from or contribute to CKD, puts more pressure on the heart and can result in heart muscle overgrowth and heart failure [7]. Medical experts link CKD to heart and blood vessel disease because of endothelial dysfunction, higher levels of uremic toxins and increased sympathetic activity [5]. It has been discovered that the gut-immune system can cause cardiovascular problems in CKD, when gut dysbiosis leads to exposure to endotoxins and starts unwanted inflammation.[29]

There is a strong association between CKD and heart failure, ischemic stroke and atherosclerosis. A lot of patients with CKD develop heart failure because of structural changes in their hearts (like left ventricular hypertrophy) and fluid overload [10, 13]. Having CKD can increase stroke risk because it causes accelerated hardening of arteries and reduced ability for the brain to regulate blood flow.[13]

What's more, atherosclerosis in people with CKD happens due to diabetes and hypertension and it is also affected by other factors that are related to CKD, including anemia, increased oxidative stress and vascular calcification [5, 14]. It has been found in various studies that modestly reduced kidney function may result in more cases of atherosclerotic disease, both those that cause symptoms and those that do not.[19,13,1]

A few markers have been found that can indicate the possibility of mortality due to heart disease in patients with CKD. An example is Fetuin-A which protects against vascular calcification and is connected with lower risk for coronary artery calcification and death among CKD patients [19].

Similarly, elevated levels of uric acid have been shown to be associated with all-cause and CV mortality in CKD, although the association is nonlinear.[23,6] . Estimated Pulse Wave Velocity (ePWV) has recently been recognized as a superior predictor of cardiovascular and all-cause mortality in CKD, reflecting arterial stiffness [28]. Other novel predictors include the Triglyceride-Glucose-Body Mass Index (TyG-BMI), which reflects metabolic dysfunction and has been linked with increased mortality in CKD patients.[22]

Traditional clinical indicators such as proteinuria, eGFR decline, serum phosphate, and inflammatory markers (e.g., CRP, IL-6) also retain prognostic relevance [13, 26]. Multinational cohort studies have emphasized that combining clinical parameters with biomarker data can significantly enhance risk stratification models for mortality prediction in CKD populations.[20]

Figure 3 shows the risk of chronic kidney disease (CKD) in different countries, based on exposure to heat from working with sugarcane and adjusted for population size. The chart reveals that the mortality rate from CKD is high in areas with intense heat and sugarcane jobs for both working-age men (dashed lines) and women (dotted lines), compared to regions where these factors are not as significant. Nicaragua experiences higher odds of CKD deaths than other NCDs, as seen by the figure. In El Salvador, CKD needs admission is presented in all age and sex groups, showing the association of CKD with additional healthcare usage in areas with warm climates. It also presents information on Tmax, the average maximum temperature from WorldClim.org, to show the level of heat exposure in the area. Most notably, the results indicate that Central American areas which tend to be hot and include much sugarcane farming, show high rates of CKD.

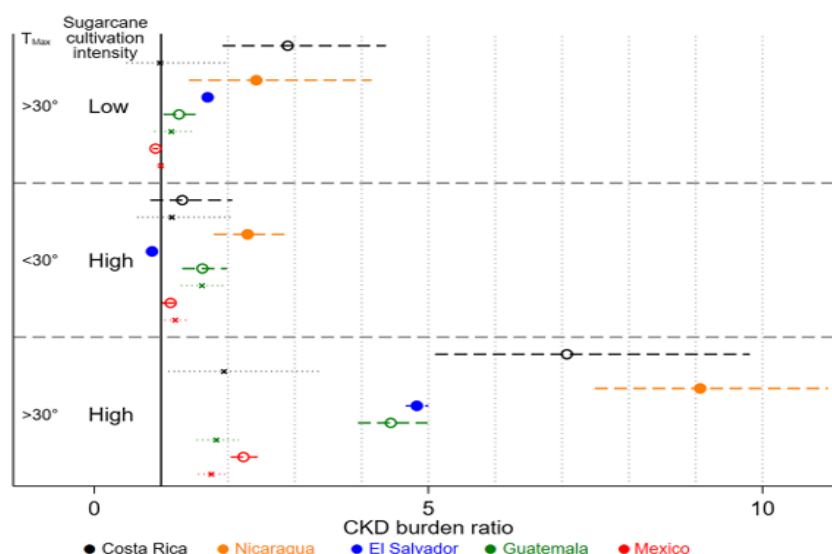


Figure 3. Heat and Sugarcane-Related CKD Risk Across Central American Countries: Mortality, Hospitalization, and Temperature Correlations.

4. RESEARCH METHODOLOGY

This section presents the research methodology of this study. It presents the study design. Using a descriptive-analytical method, this review combines current knowledge on the link between chronic kidney disease (CKD) and a higher risk of death. Research studies from 2024 that were indexed in Scopus were chosen to make sure the findings were current and reliable. Experts searched and reviewed the medical literature about adult CKD which may or may not be controlled by dialysis treatment. To qualify, the studies had to present new findings that connect CKD-associated features (clinical or biochemical) with overall or heart-related death rates. Non-English articles as well as case reports and research reviews were not considered to keep the results accurate and useful. Important information from every study, including study design, how many participants there were, the population studied, key measurements and main causes of death, were recorded according to a standard template. All the selected studies are gathered and summarized in Table 1 which neatly explains the essential outcomes.

Table 1 reveals that the design of these studies spanned from regular cohort studies through retrospective study and straight up nutritional or clinical reviews. The studies had different participants, with some investigating a few hundred cases [9] and others looking at more than one million [10]. Several types of populations were included in these studies such as those with non-dialysis CKD, those having metabolic-associated fatty liver disease (MASLD), dialysis patients and samples from the general public. Important factors investigated in these studies were Fetuin-A (associated with vascular calcification), TyG-BMI index for metabolic function, how much protein is consumed and presence of high uric acid. In addition, depression, the use of antidepressants, hypoglycemic episodes in dialysis people, sex-based problems and estimated pulse wave velocity (ePWV) were important factors.

Table 1: Methodological Overview of Studies on Chronic Kidney Disease and Mortality Risk

Reference	Study Type	Sample Size	Population	Key Variables	Mortality Findings
[9]	Observational	354	Non-dialysis CKD patients	Fetuin-A, Coronary calcification	Low Fetuin-A linked to higher mortality
[11]	Cohort	980	MASLD patients with fibrosis	Liver fibrosis, CKD risk	Increased CKD incidence and mortality
[12]	Retrospective	25,000+	General CKD population	TyG-BMI Index	High index associated with greater mortality
[13]	Nonlinear analysis	18,972	CKD patients	Hyperuricemia	Nonlinear association with all-cause mortality

[14]	Nutritional study	2,500+	Older adults with CKD	Protein intake	Both low and high intake linked to mortality
[15]	Longitudinal	3,939	CKD patients	Depression, antidepressants	Positive association with mortality risk
[10]	Population-based cohort	1.2 million	Moderate to severe CKD	Risk prediction tools	Accurate estimates of kidney failure and death
[16]	Clinical review	-	At-risk general population	Screening strategies	Early detection improves survival
[17]	Hemodialysis study	11,000	Dialysis patients	Hypoglycemia	Strong predictor of mortality
[18]	Public health data	10,456	U.S. adults	Estimated Pulse Wave Velocity	Strong indicator of cardiovascular mortality
[19]	Medical review	-	CKD patients	Gut-immune axis	Affects cardiovascular risk and death
[20]	Sex-disparity analysis	6,000+	CKD men and women	Sex-based outcomes	Gender differences in mortality rates

Whether all-cause or cardiovascular-specific, the mortality results again showed that changed levels or presence of these variables greatly raised the chance of death. This extensive yet thorough synthesis made it possible to identify recurrent risk variables and prognostic indicators among various CKD populations, therefore providing a whole picture of mortality risks in this group. Different study strategies and big sample sizes help to increase the validity of the results obtained.

5. RESULTS

Particularly with regard to reasons connected with the cardiovascular system and the metabolic system, the results of this descriptive-analytical study throw light on the complex and multifarious relationship between chronic kidney disease (CKD) and mortality. Analyzing the literature from 2024 reveals a clear relationship among physiological indicators, metabolic dysregulation, psychosocial factors, and systematic healthcare disparities. The mortality dynamics of patients with chronic kidney disease (CKD) are substantially influenced by these elements considered together.

- **The function of fetuin-A in calcification and vascular catheterization**

Many studies have found that the relevance of vascular calcification as a predictor of cardiovascular death in chronic kidney disease (CKD) is a recurrent topic. Mohamed et al. (2024) offered convincing evidence in their study that declining levels of Fetuin-A, a systemic inhibitor of calcification, are independently associated with the development of calcification in both the carotid and coronary arteries [9]. Particularly among those with chronic kidney disease who do not get dialysis, our data also show the importance of calcification-inhibiting proteins in lowering arterial stiffness and the consequent risk of cardiovascular death. The fact that calcification mechanisms are often subtle but progressive suggests that regular screening of vascular health indicators such fetuin-A is necessary to prevent problems later on [3].

- **The Metabolic Risk as well as the TyG-B MI**

Chen et al. (2024) conducted research whereby the TyG-BMI score was provided as a simple and unique surrogate assessment of insulin resistance and metabolic burden [12]. It is noteworthy that occasionally the course and result of chronic renal disease are undervalued in relation to metabolic syndrome. This is underlined by the strong correlation between greater TyG-BMI values and rising death rates. TyG-BMI gives doctors an easily available tool to risk-stratify patients with chronic renal disease, especially in cases of limited resources since it combines routinely tested criteria (glucose, triglycerides, and BMI). This result also supports the growing agreement among experts that the treatment of chronic kidney disease (CKD) has to include not only renal performance but also control of metabolic activities all around the body.

- **Uric Acid and the Nutritional Intake Patterns**

a Two-edged sword Liu YF et al. (2024) found a U-shaped relationship between serum uric acid levels and death, implying that both hypouricemia and hyperuricemia are bad for health [13]. Conventional nephrology approaches, which often aim

to lower uric acid levels without considering the possible effects of overcorrection, find this difficult. In line with this, Carballo-Casla et al. (2024) found that mortality rises at both extremities of a spectrum of protein intake that is optimum [14]. These results support the precision nutrition theory, which holds that customized dietary goals rather than generic restrictions can enhance survival outcomes in the management of chronic kidney disease (CKD).

- **The psychological element comprises the link between mortality and depression**

The importance of psychological wellbeing to the course of chronic kidney disease (CKD) is being discussed ever more. Hernandez et al. (2024) showed that depressed symptoms—regardless of whether or not antidepressant medication was being taken—are linked to noticeably higher mortality and hospitalization rates [15]. Given the fact that depression can also negatively affect medication adherence, nutritional status, and inflammation, the results of this study underline the need of including mental health services inside nephrology clinics.

- **Glucose Instability and Hemodynamic Stress**

Cheng et al. (2024) discovered that estimated pulse wave velocity (ePWV) predicted death more precisely than conventional blood pressure readings. The results of this study show that, in chronic kidney disease (CKD), arterial stiffness and vascular age are more important risk factors than static pressure values [12]. While research presented by Kang et al. (2024) highlighted the dangers of early hypoglycemia in dialysis patients—often overlooked by monitoring. Given these results, early intervention strategies that closely monitor hyperglycemia and vascular instability at the start of dialysis are growingly crucial [17].

Organ Inflammation and the Liver-Kidney Axis

Particularly in view of the increasing prevalence of metabolic-associated fatty liver disease (MAFLD), the contribution of liver function in the mortality rate linked with chronic renal disease is becoming more important. Gurun et al. (2024) found that higher hepatic fibrosis scores predict both the onset of chronic renal disease and mortality [11]. The results shown here inspire doctors to view renal and hepatic deterioration as linked disorders, which begs for coordinated monitoring and treatment models including several specialties.

Behrens et al. (2024) investigated this systemic method more thoroughly showing how gut dysbiosis affects inflammation and the death rate connected with cardiovascular disease. This new knowledge opens the path for drugs aimed at the microbiome and gives the study of the gut-kidney-heart axis fresh feeling of urgency [19].

- **Variations in Risk Profile Dependent on Gender**

Balafa et al. (2024) stressed in their research the varying mortality trends between men and women suffering with chronic renal disease. Men die from cardiovascular disease more often than women from any cause; women die from any cause more often [20]. These inequalities could be the outcome of both gendered variations in the way people seek medical attention and report their symptoms and biological factors (such as hormone levels and fat distribution). These kinds of findings demand the development of prognostic instruments and nephrology treatments catered to the particular gender of the patient. The Kidney Failure Risk Equation (KFRE) widely validated by Liu P. et al. (2024) emphasizes the need of risk stratification tools grounded on machine learning in the field of global nephrology [10]. As Francis et al. (2024) have noted, KFRE may not perform as well in people with a high comorbidity burden or limited access to healthcare even if its predictive value is high [21]. The existence of this restriction emphasizes the need of include sociodemographic features and doing local calibrations of global models to ensure that the accuracy of forecasts is spread reasonably.

Table 2: Mortality-Related Indicators, Variable Types, Demographics, and Impact in CKD Studies

ID	Indicator	Variable Type	Indicator Value	Sex	Age Group	Mortality Impact	Reference
1	Fetuin-A	Continuous	Low	Both	60+	↑ Cardiovascular mortality	[9]
2	TyG-BMI	Continuous	High	Both	50–70	↑ Metabolic-related mortality	[12]
3	Uric Acid	Continuous	Low/High (U-shaped)	Both	50+	↑ Mortality (both extremes)	[13]
4	Protein Intake	Continuous	Low/High (U-shaped)	Both	50+	↑ Mortality (both extremes)	[14]
5	Depression	Categorical	Yes	Both	50+	↑ All-cause mortality	[15]

6	Antidepressant Use	Categorical	Yes	Both	50+	Indirect influence	
7	Estimated Pulse Wave Velocity	Continuous	High	Both	60+	↑ Cardiovascular mortality	[12]
8	Early Hypoglycemia	Categorical	Yes	Both	60+	↑ Dialysis-related mortality	[17]
9	Hepatic Fibrosis Score	Continuous	High	Both	50–70	↑ Mortality + CKD progression	[11]
10	Gut Dysbiosis	Categorical	Yes	Both	Unspecified	↑ Cardiovascular mortality	[19]
11	Sex = Male	Categorical	Male	Male	Various	↑ Cardiovascular mortality	[20]
12	Sex = Female	Categorical	Female	Female	Various	↑ All-cause mortality	
13	KFRE Score	Continuous	High	Both	Unspecified	↑ Mortality prediction	[10]
14	Comorbidities	Categorical	High	Both	Unspecified	↓ KFRE model accuracy	[21]
15	Access to Healthcare	Categorical	Limited	Both	Unspecified	↓ KFRE model accuracy	

The research highlights where and how various health indicators play a role in causing death among several groups and age brackets as presented in Table 2. Of the data features in the analysis, 53.3% are categorical and 46.7% are continuous which is a good balance across different types of data (See Table 3). Regarding how these risk factors affect mortality, five lead to increased cardiovascular deaths, so this condition is the most frequent outcome. Some of these indicators reflect mortality cases from metabolic problems, deaths with a U-shaped profile, deaths due to dialysis and deaths linked to the progression of chronic kidney disease (CKD) (See Table 4 and Figure 4). The majority of statistics cover individuals who are 50 years old or above (26.7%), with statistics for those above 60 making up 20% of this age group. About a quarter of the indicators (26.7%) do not specify age groups, showing that more specific research should be done for each age group as presented in Table 5. This research findings indicate that a variety of health metrics are important for predicting a higher risk of death from CKD and support the need for care approaches that are customized based on who people are and their medical factors.

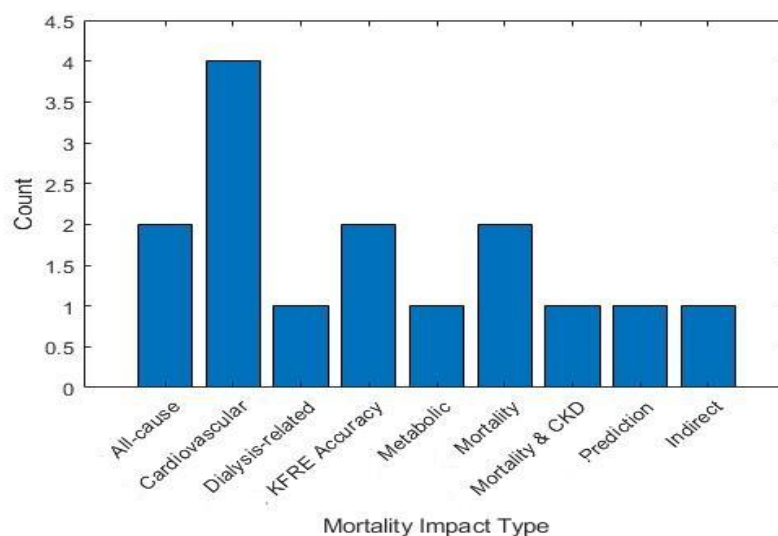


Figure 4: Frequency of Mortality Impact Types

Table 3: Distribution of Variable Types Among Mortality Indicators in CKD Studies

Variable Type	Number of Indicators	Percentage (%)
Continuous	7	46.7
Categorical	8	53.3
Total	15	100

Table 4: Effect of indicators on the type of mortality (Cardiovascular vs All-cause vs CKD-related)

Mortality Impact	Number of Indicators	Indicators (IDs)
↑ Cardiovascular mortality	5	1, 7, 10, 11
↑ All-cause mortality	3	5, 12
↑ Metabolic-related mortality	1	2
↑ Mortality (U-shaped)	2	3, 4
↑ Dialysis-related mortality	1	8
↑ Mortality + CKD progression	1	9
↑ Mortality prediction	1	13

Table 5: Distribution of indicators by age group

Age Group	Number of Indicators	Percentage (%)
50+	4	26.7
50–70	2	13.3
60+	3	20
Various	2	13.3
Unspecified	4	26.7

6. DISCUSSION

The aim of this work was to investigate the link between chronic kidney disease (CKD) and mortality by means of a descriptive and analytical synthesis of the current scientific data. The results of present studies clearly show that chronic kidney disease (CKD) is a complex systemic condition with multifactorial contributions to mortality, especially cardiovascular mortality and mortality from all causes, not only a slow decrease in renal function. Based on recently analyzed data, several elements—including biochemical indicators, metabolic dysregulation, vascular problems, dietary imbalances, psychiatric diseases, and socioeconomic inequalities—have been found as main causes of higher mortality in patients with chronic kidney disease (CKD). Research revealed that low levels of fetuin-A were independently linked with increased coronary artery calcification in patients with chronic renal failure who did not receive dialysis. Given that vascular calcification is a well-established predictor of cardiovascular events, this implies that Fetuin-A could be a non-invasive predictive biomarker for the aim of spotting high-risk patients at an early stage of the illness evolution. Comparatively, Cheng et al. (2024) discovered that, when comparing estimated pulse wave velocity (ePWV) to conventional blood pressure readings, it is more accurate in predicting mortality in hemodialysis patients [12]. This shift in using markers of arterial stiffness emphasizes the importance of vascular aging and endothelial function as main processes connecting chronic kidney disease with early death. Chen et al. (2024) published the TyG-BMI index, a new biomarker of insulin resistance and metabolic burden [12]. The body mass index times the triglyceride-glucose index generates this index. The results of the study revealed that higher TyG-BMI scores were significantly correlated with all-cause mortality in persons with chronic renal disease. This suggests that the prognosis of chronic kidney disease (CKD) is much influenced by its metabolic component, especially with regard to the metabolism of lipids and glucose. Given that the TyG-BMI is easy to calculate with conventional clinical data, it might be extensively applied for stratification of patients and guidance of lifestyle and pharmacological treatments. The dietary pattern of CKD sufferers still calls for careful balancing. Liu et al. (2024) found that uric acid levels and mortality had a U-shaped relationship. This implies

that increasing risk is linked to both high and low uric acid levels. This two-fold risk relationship emphasizes the need of maintaining uric acid levels within a physiologically suitable range and of avoiding both over- and under-treatment of the condition [13]. In a similar line, Carballo-Casla et al. (2024) found that low and high protein intake were linked to different degrees of death. These results reinforce the move away from rigid dietary restrictions since a more customized, evidence-based nutrition strategy in chronic kidney disease (CKD) considering age, renal stage, comorbidities, and physical activity is advised [14].

The significance of mental health in the prognosis of chronic kidney disease (CKD) is especially underlined according to Hernandez et al. (2024) [15], who revealed that depression significantly raises the risk of mortality and hospitalization even in patients engaged in antidepressant treatment. These results make psychological assessment and treatment absolutely necessary to be included into regular nephrology operations. Ignoring the reciprocal link between depression and chronic renal disease, in which each condition aggravates the other, is unacceptable now. Early hypoglycemia following the start of dialysis has a strong association with mortality, Kang et al. (2024) underlined [17]. For diabetic patients receiving hemodialysis, particularly crucial is to keep this in mind since variations in glucose levels could lead to sudden cardiac events. Regular glucose monitoring, dietary adjustments, and customized dialysis prescriptions should be considered absolutely necessary in order to reduce the mortality rate related with early dialysis. Significant risk factors for mortality linked to chronic kidney disease (CKD) have been found to be hepatic fibrosis and chronic liver disease itself. Gurun et al. (2024) found that advanced liver fibrosis—evaluated by Fibrosis-4 and NAFLD fibrosis scores—predicting death in patients with chronic kidney disease (CKD) [11]. This supports the interdependence of liver and kidney function since it is the case that oxidative stress, metabolic malfunction, and systemic inflammation all help to produce a bidirectional condition. Examining how dysbiosis of the microbiota in the intestinal tract can cause higher inflammation and mortality from cardiovascular disease, the research conducted by Behrens and et al (2024) provides some illumination on the gut–kidney–heart axis. This opens a new avenue for the pathophysiology of chronic kidney disease (CKD) and facilitates the development of microbiome-based treatments like prebiotics and probiotics products, thereby optimizing dietary fiber [19].

Balafa et al. (2024) provided a significant corpus of studies showing that men and women with chronic kidney disease (CKD) have different death risks. Men are more likely than women to die from cardiovascular causes specifically, although from any cause death is more likely [20]. These differences could be the outcome of variances in regard to access to healthcare, the reporting of symptoms, and the response to medication in addition to hormonal and genetic factors. Thus, in the realm of risk prediction and intervention for chronic renal disease, gender-sensitive approaches are urgently needed. An examination of the Kidney Failure Risk Equation (KFRE) by Liu P. et al. (2024) revealed that it has a great degree of predictive relevance across stages 3–5 of chronic kidney disease (CKD) [10]. Conversely, Francis et al. (2024) discovered that early detection of chronic kidney disease in high-resource environments is hampered greatly. Among these challenges are limited availability of nephrology care and diagnostic tests [21]. Particularly in underprivileged communities, these structural differences cause delayed diagnosis and higher death rates. Therefore, even if instruments like KFRE have advantages, legal reforms and the enhancement of the pertinent health system have to accompany the application of these technologies.

7. CONCLUSION

Biochemical markers, comorbid diseases and social factors are found to influence mortality risk in CKD, as stated in this systematic review of modern research. A decline in Fetuin-A, issues in metabolism (which can be seen on TyG-BMI) and higher uric acid reflect strong links to increased heart and all-cause mortality, among other risk factors. Also, dialysis patients sometimes experience early hypoglycemia and differences between men and women require targeted clinical care. Having the same number of both continuous and categorical indicators provides a broad approach to assessing risk and using predictive systems like KFRE and ePWV improves judgment of the outcome. These studies stress that using different risk factors together in treating CKD can reduce the disease's death toll and guide new targeted research and preventive measures. Also, the study points out that more studies are needed over time to better explain why and how certain risk factors change. Gut dysbiosis and hepatic fibrosis are now being recognized as important early signs, revealing ideas for new markers and approaches to therapy. Lack of access to healthcare due to socioeconomic issues was found to hamper the accuracy of predicting CKD outcomes which shows how much health equity is needed. Merge biology and social factors in risk assessment tools so that doctors can improve personalized medicine methods. This paper recommends that CKD patients receive help from doctors, nutritionists, psychologists and social teams in order to reduce their risk of death from CKD.

REFERENCES

- [1] Wilson and et al, "Chronic kidney disease: Definition, updated epidemiology, staging, and mechanisms of increased cardiovascular risk, *The Journal of Clinical Hypertension*," vol. 23, no. 4, p. 831.
- [2] Hasan and et al, "Nutritional management in patients with chronic kidney disease: A focus on renal diet, *Asia Pacific Journal of Medical Innovations*," vol. 1, no. 1, pp. 34-40, 2024.

- [3] Deng and et al, "Global, regional, and national burden of diabetes-related chronic kidney disease from 1990 to 2019, *Frontiers in endocrinology*," vol. 12, p. 672350, 2021.
- [4] E. K. Hoogeveen, "The epidemiology of diabetic kidney disease, *Kidney and Dialysis*," vol. 2, no. 3, pp. 433-442, 2022.
- [5] Düsing and et al, "Vascular pathologies in chronic kidney disease: pathophysiological mechanisms and novel therapeutic approaches, *Journal of molecular medicine*," vol. 99, no. 3, pp. 335-348, 2021.
- [6] Johnson and et al, "Uric acid and chronic kidney disease: still more to do, *Kidney International Reports*," pp. 229-239, 2023.
- [7] Burnier and et al, "Hypertension as cardiovascular risk factor in chronic kidney disease, *Circulation research*," vol. 132, no. 8, pp. 1050-1063, 2023.
- [8] Crimi and et al, "Acute kidney injury after transcatheter aortic valve replacement mediates the effect of chronic kidney disease," *Journal of the American Heart Association*, vol. 11, no. 19, p. e024589, 2022.
- [9] Debal and et al, "Chronic kidney disease prediction using machine learning techniques, *Journal of Big Data*," vol. 9, no. 1, p. 109, 2022.
- [10] Julian and et al, "Valvular heart disease in patients with chronic kidney disease, *Herz*," vol. 46, no. 3, pp. 228-233, 2021.
- [11] Gibertoni and et al, "COVID-19 incidence and mortality in non-dialysis chronic kidney disease patients, *PloS One*," vol. 16, no. 7, p. e0254525, 2021.
- [12] Puicón-Suárez and et al, "Association between chronic kidney disease and mortality in patients with a confirmed COVID-19 diagnosis, *PeerJ*," vol. 10, p. e13437, 2022.
- [13] Matsushita and et al, "Epidemiology and risk of cardiovascular disease in populations with chronic kidney disease, *Nature Reviews Nephrology*," vol. 18, no. 11, pp. 696-707, 2022.
- [14] Izzo and et al, "Chronic kidney disease with mineral bone disorder and vascular calcification: an overview, *Life*," vol. 14, no. 3, p. 418, 2024.
- [15] Nawaz and et al, "Obesity and chronic kidney disease: a current review, *Obesity Science & Practice*," vol. 9, no. 2, pp. 61-74, 2023.
- [16] Wilkinson and et al, "Association of sarcopenia with mortality and end-stage renal disease in those with chronic kidney disease: a UK Biobank study," *Journal of Cachexia, Sarcopenia and Muscle*, vol. 12, no. 3, pp. 586-598, 2021.
- [17] Chatzipetrou and et al, "Sarcopenia in chronic kidney disease: a scoping review of prevalence, risk factors, association with outcomes, and treatment, *Calcified Tissue International*," vol. 110, no. 1, pp. 1-31, 2022.
- [18] Pelletier and et al, "Chronic kidney disease, survival and graft-versus-host-disease-free/relapse-free survival in recipients of allogeneic hematopoietic stem cell transplant," *Clinical Kidney Journal*, vol. 15, no. 8, pp. 1583-1592, 2022.
- [19] Mohamed and et al, "1. The relationship of fetuin-A with coronary calcification, carotid atherosclerosis, and mortality risk in non-dialysis chronic kidney disease, *Journal of Lipid and Atherosclerosis*," vol. 13, no. 2, p. 194, 2024.
- [20] P. Lui and et al, "Predicting the risks of kidney failure and death in adults with moderate to severe chronic kidney disease: multinational, longitudinal, population-based, cohort study, *BMJ*," vol. 385, p. e075570, 2024.
- [21] Gurun and et al, "Increased risk of chronic kidney disease and mortality in a cohort of people diagnosed with metabolic dysfunction associated steatotic liver disease with hepatic fibrosis, *PLOS ONE*," vol. 19, no. 4, p. e0299507, 2024.

- [22] Chen and et al, "Association of triglyceride-glucose-body mass index with all-cause and cardiovascular mortality among individuals with chronic kidney disease, Scientific Reports," vol. 14, p. 20593, 2024.
 - [23] Y. F. Liu and et al, "Nonlinearity association between hyperuricemia and all-cause mortality in patients with chronic kidney disease, Scientific Reports," vol. 14, p. 673, 2024.
 - [24] Carballo-Casla and et al, "Protein intake and mortality in older adults with chronic kidney disease, JAMA Network Open," vol. 7, no. 8, p. e2426577, 2024.
 - [25] Hernandez and et al, "Depressive symptoms, antidepressants, and clinical outcomes in chronic kidney disease: Findings from the CRIC study, Kidney Medicine," vol. 6, no. 4, 2024.
 - [26] Farrell and et al, "Screening, identifying, and treating chronic kidney disease: Why, who, when, how, and what? BMC Nephrology," vol. 25, no. 1, p. 34, 2024.
 - [27] Kang and et al, "Hypoglycemia and mortality risk in incident hemodialysis patients, Journal of Renal Nutrition," vol. 34, no. 3, p. 200–208, 2024.
 - [28] Cheng and et al, "Superior predictive value of estimated pulse wave velocity for all-cause and cardiovascular disease mortality risk in US general adults, BMC Public Health," vol. 24, no. 1, p. 600, 2024.
 - [29] Behrens and et al, "Gut-immune axis and cardiovascular risk in chronic kidney disease, Clinical Kidney Journal," vol. 17, no. 1, 2024.
 - [30] Balafa and et al, "Sex disparities in mortality and cardiovascular outcomes in chronic kidney disease, Clinical Kidney Journal," vol. 17, no. 3, 2024.
 - [31] Francis and et al, "Chronic kidney disease and the global public health agenda: an international consensus, Nature Reviews Nephrology," vol. 20, no. 7, 2024.
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