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REVIEW ARTICLE

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Adequate nutrological treatment for patients with chronic kidney disease: a systematic review

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Abstract

Introduction: In the scenario of chronic kidney disease (CKD), data from the World Health Organization show that CKD affects approximately 10% of the world population, particularly in low- and middle-income countries. In the USA alone, approximately 37 million adults are affected, given that diagnosis is late due to the lack of apparent symptoms in the early stages. Due to limited access to diagnosis and treatment, CKD has become the 12th leading cause of death in the world, making adequate nutritional therapy necessary as the main treatment. **Objective:** It was **t**o highlight the importance of adequate nutrological treatment for patients with chronic kidney disease. **Methods:** The systematic review rules of the PRISMA Platform were followed. The research was carried out from August to September 2024 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** 124 articles were found. 22 articles were evaluated and 18 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 28 studies with a high risk of bias and 22 studies that did not meet GRADE. Most studies showed homogeneity in their results, with X^2 =84.6% >50%. It was concluded that chronic kidney disease is a growing health crisis in the world, accompanying the increase in the number of patients with obesity. Diabetes and hypertension are the main causes of the development of chronic kidney disease. Lifestyle changes, adequate nutritional therapy, and lipid-lowering medications can contribute to improving the clinical outcome of patients with chronic kidney disease. Medical nutritional therapy is fundamental and vital for the treatment of chronic kidney disease, as it can delay disease progression and prevent comorbidities and mortality.

Keywords: Chronic kidney disease. Obesity. Nutrological therapy. Comorbidities. Mortality.

Introduction

In the context of chronic kidney disease (CKD), data from the World Health Organization show that CKD affects approximately 10% of the world population, particularly in low- and middle-income countries. In the United States alone, approximately 37 million adults are affected, given that diagnosis is delayed due to the lack of apparent symptoms in the early stages. Due to limited access to diagnosis and treatment, CKD has become the 12th leading cause of death worldwide. Maintenance dialysis leads to protein-energy wasting (PEW), which can be improved with different methods of nutritional support. Dietary counseling prevents and controls PEW in CKD. If dietary counseling alone does not meet the

recommended energy and protein requirements, adding oral nutritional supplements (ONSs) is necessary [1].

When these initial measures fail to achieve the recommended energy and protein requirements, nutritional support, including enteral tube feeding or parenteral nutrition (PN), should be considered a viable option to improve nutritional status. Partial PN, comprising intraperitoneal PN (IPPN) and intradialytic PN (IDPN) therapies, can be attempted as supplemental nutritional support in patients with PEW requiring peritoneal dialysis and hemodialysis, respectively. Despite the debatable efficacy of IPPN for patients undergoing peritoneal dialysis, it remains a viable means for these patients. Indications for IPPN in patients undergoing peritoneal dialysis include inadequate dietary intake of energy and protein, and barriers to oral and other forms of enteral supplementation, such as problems with adequacy, tolerance, and compliance. However, in the case of spontaneous dietary intake of energy and protein that meets the gap between IDPN provision and nutritional goals, the use of IDPN is rational. In patients with PEW and poorly functioning gastrointestinal tracts, as well as those whose enteral intake (with or without partial PN) is below recommended nutritional requirements, total PN becomes a relevant nutritional intervention [2].

In this sense, CKD is known to interfere with the body's physiological and biological mechanisms, such as electrolyte and pH balance, blood pressure regulation, excretion of toxins and waste, vitamin D metabolism, and hormonal regulation. Many patients with CKD are at risk of hyperkalemia, hyperphosphatemia, chronic metabolic acidosis, bone deterioration, blood pressure abnormalities, and edema. These risks can be minimized and disease progression can be slowed through careful monitoring of protein, phosphorus, potassium, sodium, and calcium, alleviating the symptoms experienced by patients with CKD. Current recommendations from the Kidney Disease Outcomes Quality Initiative (KDOQI) are highlighted. Dietary approaches to treating hypertension, the Mediterranean diet, and the whole-foods plant-based diet are currently being examined for their potential role in slowing the progression of CKD [3]. Given this, medical nutrition therapy is essential for patients with CKD because it can slow the progression of the disease through careful monitoring of protein, calcium, phosphorus, potassium, and sodium [4], alleviating the symptoms experienced in patients with CKD without restricting many nutrients that would put the patient at high risk of malnutrition [5].

Therefore, the present systematic review study aims to highlight the importance of adequate nutritional treatment for patients with chronic kidney disease.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 09/22/2024. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 09/22/2024.

Search Strategy and Search Sources

The literature search process was carried out from August to September 2024 and developed based on Scopus, PubMed, Science Direct, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following health science descriptors (DeCS/MeSH Terms) were used: "Chronic kidney disease. Obesity. Nutrological therapy. Comorbidities. Mortality", and using the Boolean "and" between MeSH terms and "or" between historical findings.

Study Quality and Risk of Bias

The quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. The low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument through the analysis of the Funnel Plot graph (Sample size versus Effect size), using Cohen's test (d).

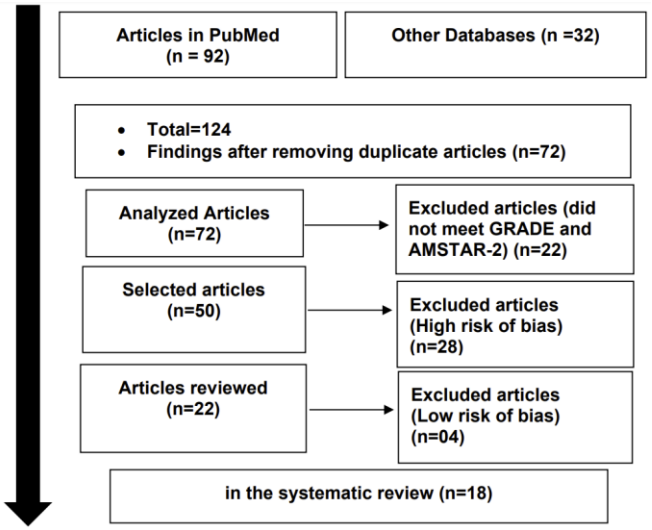
Results and Discussion

Summary of Findings

As a corollary of the literary search system, a total of 124 articles were found that were subjected to eligibility analysis and, then, 18 of the 22 final studies were selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering in the first instance the level of scientific evidence of studies in types of study such as meta-analysis, consensus, randomized clinical, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=84.6%>50%.

Considering the Cochrane tool for risk of bias, the overall assessment resulted in 28 studies with a high risk of bias and 22 studies that did not meet GRADE and AMSTAR-2.

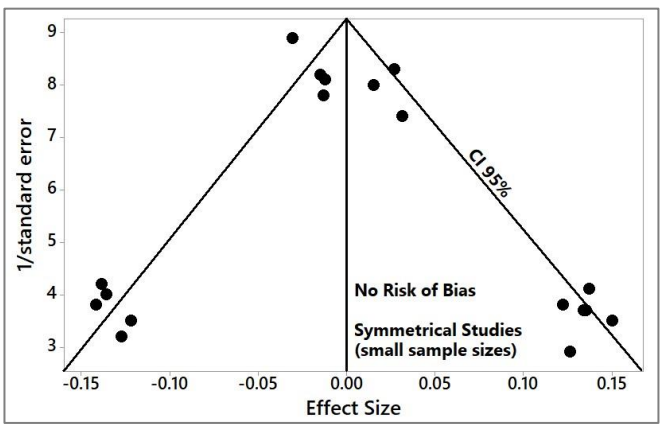
Figure 1. Flowchart showing the article selection process.



Source: Own Authorship.

Figure 2 presents the results of the risk of bias of the studies through the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). The precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, either among studies with small sample sizes (lower precision) that are shown at the base of the graph or in studies with large sample sizes that are presented at the top.

Figure 2. The symmetric funnel plot suggests no risk of bias among the small sample size studies shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=18 studies).



Source: Own Authorship.

Major Clinical Findings

Obesity and hyperlipidemia are the most prevalent independent risk factors for chronic kidney disease (CKD), as lipid accumulation in the renal parenchyma is detrimental to renal function. Non-esterified fatty acids (free fatty acids (FFA)) are especially harmful to the kidneys. Excess FFAs can damage podocytes, proximal tubular epithelial cells, and tubulointerstitial tissue through several mechanisms, in particular by increasing the production of reactive oxygen species (ROS) and lipid peroxidation, promoting mitochondrial damage and tissue inflammation, which result in glomerular and tubular injury. However, polyunsaturated fatty acids (PUFA), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), appear to help slow the progression of chronic kidney disease (CKD). Thus, lifestyle changes, adequate nutritional therapy, and lipid-lowering medications may contribute to improving the clinical outcome of patients with CKD **[6]**. Regarding potassium dysregulation, a total of 18 studies were included in the work by authors MacLaughlin et al. (2023) **[7]**. Observational studies found no association between dietary and serum potassium in populations with CKD. In two studies, increases of 40– 60 mmol in dietary/supplemental potassium increased serum potassium by 0.2–0.4 mmol/L. No studies examined dietary potassium reduction as a treatment for hyperkalemia. Healthy dietary patterns have been associated with better outcomes and may predict lower serum potassium, as dietary cofactors may support intracellular potassium shifts and increase excretion from the gut. It is recommended to limit potassium supplements, large portions of meat and milk, and include high-fiber foods: whole grains, fruits, and vegetables.

Advanced-stage CKD can lead to renal failure, which is clinically referred to as end-stage renal disease (ESRD). In such cases, patients can only sustain life through dialysis or kidney transplantation. However, the long-term accessibility of these treatments remains low. Furthermore, the efficacy of kidney transplantation is modest, representing a significant barrier to treatment in resource-limited settings and significantly impacting patient survival. To address this issue, one study strongly supports the use of dietary supplementation of the trace element zinc to prevent the development of CKD and prolong patient survival **[8]**.

Furthermore, ketogenic metabolic therapy (KMT) is indicated for the treatment of CKD. Several studies have found that various forms of KMT are safe for individuals with CKD and may lead to improved renal function. A review article discusses the rationale for the use of KMT, including plant-dominant KMT, for the treatment of CKD, clarifies common misconceptions, summarizes the

results of clinical studies, and discusses why KMT is emerging as an effective medical nutrition therapy (MNT) to consider for patients with kidney disease. KMT, including its plant-dominant versions, will become a first-line therapy for CKD **[9]**.

Protein intake recommendations for patients with CKD depend on the stage of the disease, which is determined by the decline in GFR function. Data suggest that chronic protein intake (more than 1.2 g/kg/body weight/day) leads to increased glomerular pressure and morphological changes, resulting in renal dysfunction **[10]**. High-protein diets induce glomerular hyperfiltration, hyperemia, and increased hydraulic pressure, resulting in vasodilation of the afferent arteriole. High-protein diets contribute to progressive glomerular damage, which, combined with renal deterioration of diseased kidneys, may contribute to the progression of CKD **[10]**.

The Modification of Diet in Renal Disease (MDRD) trial was the largest RCT to examine the hypothesis that dietary protein restriction delays the progression of CKD [PMID 10541304]. The study found proteinuria to be one of the two strongest predictors of the rate of CKD progression across two studies. Oba et al. collected 43 healthy (non-diseased) kidneys from living human donors to examine the effect of high-protein diets on single nephron GFR (SNGFR). This study concluded that high-protein diets can increase SNGFR and induce glomerular hyperfiltration; however, this study is unique in identifying that analysis of human SNGFR is an exemplary parameter for changes in renal hemodynamics at the single nephron level **[11]**. Low-protein diets (LPDs) have been shown to improve hyperfiltration, reduce nitrogen wasting, and alleviate renal workload by decreasing glomerular pressure **[10]**. Proteinuria decreased by 20–50% in CKD patients who adhered to a LPD **[12]**.

Although LPDs provide direct benefits to CKD patients, healthcare professionals are concerned about protein-energy malnutrition and protein-energy wasting (PEW) in CKD patients due to inadequate energy intake **[12]**. Low-protein diets and very-low-protein diets (VLPDs) (0.28–0.43 g/kg/body weight/day) can be achieved with nutritional supplementation with essential amino acids (EAAs) and keto analogs to protect against PEW. The KDOQI guidelines recommend restricting protein to slow the progression of CKD and improve quality of life (QOL) by reducing symptoms for metabolically stable patients **[1]**. The NKF defines metabolically stable as the absence of inflammatory or infectious diseases, poorly controlled diabetes, wasting diseases, antibiotics or immunosuppressive medications, significant short-term body weight loss, and no hospitalizations within two weeks **[13-16]**. Furthermore, low levels of active VD in patients with CKD are associated with increased bone resorption and reduced bone mineral density **[17]**.

Studies report a progressive decline in VD of more than 80% in patients with CKD 1-5, dialysis, and transplantation **[18]**. Vitamin D metabolism is disrupted by the inability of the second hydroxylation step of 25-hydroxyvitamin D, which converts it to the active form 1,25-dihydroxyvitamin D, which occurs in the kidneys. Inhibition of 1,25-dihydroxyvitamin D induces hypocalcemia, which stimulates the parathyroid gland to release parathyroid hormone at persistent circulating levels **[19]**. Over time, this can result in renal osteodystrophy, including secondary parathyroidism, osteitis fibrosa, osteomalacia, and dynamic bone disease **[20,21]**.

Finally, Current KDOQI guidelines for CKD nutrition state that ergocalciferol or cholecalciferol effectively treats VD deficiency/inefficiency; however, specific dosing should be individualized. This stepwise approach includes monitoring serum 25(OH)D levels serum calcium and serum phosphorus, which helps the healthcare team recommend a specific dosage tailored to the individual patient's needs **[1,22]**.

Conclusion

It was concluded that chronic kidney disease is a growing health crisis in the world, accompanying the increase in the number of patients with obesity. Diabetes and hypertension are the main causes of the development of chronic kidney disease. Lifestyle changes, adequate nutritional therapy, and lipid-lowering medications can contribute to improving the clinical outcome of patients with chronic kidney disease. Medical nutritional therapy is fundamental and vital for the treatment of chronic kidney disease, as it can delay the progression of the disease and prevent comorbidities and mortality.

CRediT

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The authors declare no conflict of interest.

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