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PROBIOTICS DELAY THE DECREASE OF KIDNEY FUNCTION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT

Chronic kidney disease (CKD) is defined as kidney impairment or reduced estimated glomerular filtration rate (eGFR). The prevalence grows over time. A progressive decrease in kidney function eventually necessitates renal replacement therapy (dialysis or transplantation). Appropriate treatment determines the clinical outcome. One of them is the dietary approach. This review aims to gather evidence of the potential of probiotics to delay CKD damage progression. This scoping review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist. The review gathers publications from four databases and synthesizes them as evidence. Were 357 publications found, three of which matched the inclusion criteria and were evaluated. The article's synthesis results reveal that probiotics suppress intestinal dysbiosis. These beneficial complicated processes make significant contributions. Thereby, the worsening of renal disease is prevented. Based on the findings, it was concluded that the probiotic positively affected the clinical outcomes of chronic kidney disease.

Keywords: chronic kidney disease; inflammation; probiotic

INTRODUCTION

Chronic kidney disease (CKD) is kidney damage lasting at least three months. CKD results in functional renal problems and a lower glomerular filtration rate (GFR) (less than 60 mL/minute/1.73 m^2) (Webster et al., 2017). It is a clinical anomaly or kidney senility disease that reveals a disproportionate arrangement of chemicals in the urine or blood and the presence or absence of blockages based on imaging data (Karinda et al., 2019) CKD affected about 10% of the world's population and was the sixteenth top cause of mortality in 2017 (NKF, 2023) ; (Roth et al., 2018). According to RISKESDAS statistics (2018), the prevalence of CKD is 3.8 ‰ in Indonesia. CKD can lead to various consequences if not treated effectively. Cardiovascular and metabolic diseases are among the CKD consequences (Karinda et al., 2019).

Proper care is required to avoid future complications from CKD. Pharmacological and non-pharmacological treatment is used. CKD treatment is separated into two stages: conventional and renal replacement therapy. Traditional chronic kidney disease treatment comprises slowing the progression of chronic kidney disease, normalizing the patient's health, and treating reversible problems. Intermittent dialysis or kidney transplants are the most effective treatment for end-stage renal failure or CKD (Price & Wilson, 2015) One of the non-pharmacological approaches is a dietary approach (Naber & Purohit, 2021). The dietary process uses a Low Protein Diet (Ria et al., 2022) and other nutritional supports such as probiotics (McFarlane et al., 2023). It is necessary to supplement this diet with probiotics and/or antioxidants to aid in its management (Qi et al., 2020)

A lot of recent research links changes in the digestive environment to the health of other organs, including the kidneys. Research has shown evidence that probiotics have dietary treatment potential, but the present information is insufficient to investigate these pathways connected to dysbiosis and inflammation. As a result, this scoping review aims to map and synthesize data on the potential of probiotics to slow the course of CKD damage.

METHOD

This study uses the Preferred Reporting Items for Systematic Review reporting protocol and the Meta-Analysis for Scoping Review (PRISMA-ScR) extension. This study used English to determine eligibility criteria by selecting journals or full-text articles published in the last five years (2019 – 2023). For research methods in the journal concerned using Randomized Control Trials (RCT). Research subjects in humans. Regarding chronic kidney disease and probiotics associated with CKD biomarkers related to dysbiosis and inflammation. A reference search was conducted on 28 May 2023 using the electronic databases Science Direct, PubMed, Google Scholar, and Scopus to find relevant articles. The search strategy uses keywords ("Chronic Kidney Disease OR CKD OR Renal Disease" AND "Probiotic OR Dysbiosis OR Inflammation").

RESULTS AND DISCUSSION

Finding

The scoping review contained three papers in all. The first search produced 357 records from four databases. Following removing nine duplicate article records, 345 unique records were evaluated for eligibility by title and abstract. Two hundred sixty-one were removed because they did not satisfy the review's defined topic and goal. In addition, 84 articles were retrieved. However, if Article 65 is not full text, it should be removed. The remaining 19 articles fulfilled the criteria. 16 is excluded for a reason. The main reasons for exclusion were that the study was not an RCT, that the participants were from the wrong demographic (not human), that animal/in vitro models were used, that the publication was a review, that it was not relevant to CKD, and that it was inaccessible. The full texts of the following three articles were then included.

Study Characteristic

In total, 204 people took part in the three studies. A description of the findings is presented in Table 1. One article researched the evaluation of the benefits of probiotics on malnutrition status and quality of life of CKD patients with peritoneal dialysis in terms of changes in gut microbiota, development of CKD stages, increased cardiovascular risk, uremic toxicity, and inflammation. One study explored the effect of probiotics in CKD stage 3 patients on the incidence of dysbiosis with markers from several laboratory results, and other articles researched the impact of giving a low protein diet with probiotic supplementation in CKD patients on reducing uremic toxins, microbiota, and proatherogenic toxins.Participants in the three articles ranged from 18 to 80 years old. The treatment sessions lasted seven days to 26 weeks and were carried out daily. The studies were carried out in China and Italy.

Study Selection

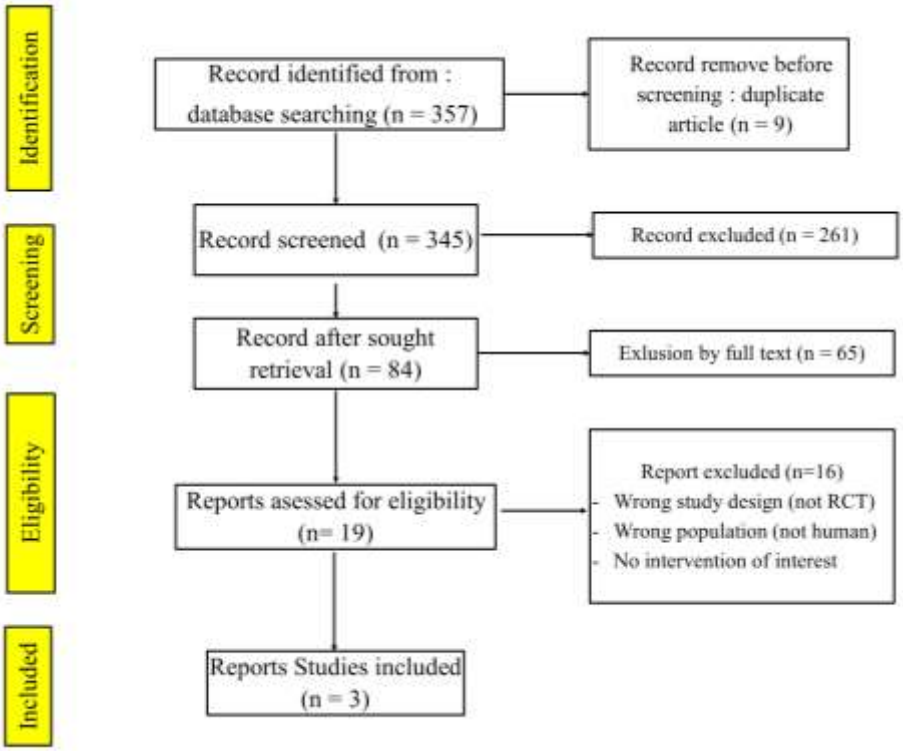

Figure 1. Preferred reporting item for PRISMA-ScR flow diagram

Table 1.
Study Characteristic

Author	Title	Subject	Result
(Pan et al., 2021)	Effects of Probiotics on Malnutrition and Health-Related Quality of Life in Patients Undergoing Peritoneal Dialysis: A Randomized Controlled Trial.	18 and 75 years who are undergoing PD at the outpatient clinic.	After two months of treatment, the levels of high-sensitivity C-reactive protein and interleukin-6 in patients taking probiotics were reduced.
(De Mauri et al., 2022).	Probiotics-Supplemented Low-Protein Diet for Microbiota Modulation in Patients with Advanced Chronic Kidney Disease (ProLowCKD): Results from a Placebo-Controlled Randomized Trial.	Patients aged 18 to 80 years, affected by CKD, with eGFR less than 25 mL/min/1.73 m^2, and who were not on dialysis.	Subjects in the probiotics group showed a trend in reducing microbiota toxins.
(Simeoni et al., 2019).	An open-label, randomized, placebo-controlled study on the effectiveness of a novel probiotics administration protocol (ProbiotiCKD) in patients with mild renal insufficiency (stage 3a of CKD).	Patients with stable CKD stage 3a, referring to the Nephrology Unit at the University Hospital of Catanzaro (Italy), age > 18 years, (eGFR) ranging 60–45 ml/min/1.73 m2.	Only in the probiotics group were mean fecal Lactobacillales and Bifidobacteria concentrations raised following treatment. The probiotic treatment technique demonstrated its efficacy in treating CKD-related intestinal dysbiosis.

Synthesis Findings

This review was conducted with the aim of mapping and synthesizing evidence of the potential of probiotics to delay CKD damage progression. We found three articles it explains that. In this review, we share the findings of a synthesis of numerous publications we discovered. Findings should be interpreted in light of the evaluated literature's strengths and limitations. Two articles explore the impact of probiotics on inflammation. The result is that inflammation markers such as C-reactive protein (CRP) (De Mauri et al., 2022; Pan et al., 2021) and interleukin 6 (IL-6) values of the probiotic group were lower than those of the control group after two months of treatment (Pan et al., 2021). Like previous research, consuming yogurt as probiotics can reduce levels of inflammation in CKD patients. One of the reasons for persistent inflammation in CKD is dysbiosis. This situation can be seen in early-stage CKD and can cause the host to become increasingly pro-inflammatory. In CKD patients, dysbiosis resulted in the prevalence of bacterial families with urease-, indole-, and p-cresol-forming enzymes. Uraemic toxins that arise accumulate in bodily fluids and lead to inflammation. Probiotics can alter the composition of the gut microbiota, produce a more favorable environment, and, in theory, reduce inflammation (Wagner et al., 2022).

Because considerable increases in Actinobacteria and Proteobacteria characterize the uremic microbiota and decreases in the genera Bacteriaceae and Lactobacillaceae, it is not unexpected that intervention efforts for restoring saccharolytic colonic flora focus on Lactobacillus and Bifidobacteria. The most often used probiotics have a negative, positive, or neutral relationship between probiotic supplementation and uremic toxins. Anti-inflammatory probiotic bacterial strain. Consequently, inflammation is reduced (De Mauri et al., 2022). Another article explored the intervention of a low protein diet (LPD) and a new formulation of probiotics on dysbiosis of gut microbiota-related uremic toxic and progressive CKD. The result is probiotics group showed a trend in reducing microbiota toxins (De Mauri et al., 2022). CKD conditions make changes to dysbiosis (Cao et al., 2022). Gut dysbiosis is an imbalanced intestinal microbial community with quantitative and qualitative changes in gut microbiota composition and metabolic activity (Simeoni et al., 2019).

Modifying gut dysbiosis with probiotics, prebiotics, and synbiotics can potentially decrease the progression of kidney disease (Cao et al., 2022). Probiotics may partially heal gut dysbiosis by modulating the gut microbiota (Choy et al., 2023). Additionally, the probiotic is enhanced intestinal dysbiosis and minimizes the development of gut-derived uremic toxins. In most probiotic-consuming patients, there was a significant change in gut microbiota composition and intestinal bacterial metabolism. In addition, Bifidobacteria have been demonstrated to create short-chain fatty acids, specifically butyrate, via a cross-feeding process that promotes the growth of other bacterial species, such as Lactobacillales. Butyrate promotes the generation of antimicrobial peptides (AMP) and the expression and activity of intestinal alkaline phosphatase (IAP), which plays a crucial role in maintaining intestinal homeostasis (Simeoni et al., 2019). Finally, our research discovered evidence that probiotics can help with inflammation and dysbiosis in CKD patients.

Strength and Limitation

The current review is unusual in that it examines probiotics and CKD. Even though we methodically sought evidence, this review has limitations. First, the article does not cover the natural process in detail. Second, the article only includes reviews of RCTs, despite this being one of our review's strengths; there is little data that can be synthesized on the topic. Strengths of this

review, this study followed a search strategy of relevant data, resulting in a potent synthesis of evidence.

CONCLUSION

Our findings conclude that probiotic intervention positively impacts improving and delaying further damage to kidney function due to CKD. These mechanisms are related to the modulation of dysbiosis and reducing inflammation. Future directions need further proof of the role of probiotics in repairing kidney function from massive damage.

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