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The Impact of Specific Gut Microbiota Metabolites on Chronic Kidney Disease Progression: Novel Diagnostic Biomarkers and Therapeutic Targets

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ABSTRACT

Introduction: Chronic kidney disease is characterized by an irreversible and gradually progressive process. Recent research has highlighted the role of metabolites derived from the intestinal microbiota as important factors in the progression of this disease. Consequently, numerous studies have focused on the impact of the microbiota, its diagnostic potential, and its therapeutic applications.

Aim of the study: This study highlights the role of specific gut microbiota in chronic kidney disease and its potential applications in diagnosis and therapy.

Material and methods: An English-language literature review was conducted, analyzing studies from the PubMed database up to December 2024 regarding the correlation between specific gut microbiota and chronic kidney disease. The review was performed using the PubMed database, with 57 works used.

Conclusion: Chronic kidney disease is characterized by a slow, progressive, and irreversible decline in kidney function. Recent studies have highlighted the significant role of metabolites produced by the intestinal microbiota in the progression of this disease. Consequently, extensive research has been conducted on the impact of these metabolites for diagnostic purposes as well as their potential therapeutic applications. These metabolites can aid in both diagnosing the condition and predicting its progression. Emerging therapies that manipulate the microbiota—through approaches such as dietary changes, probiotics, modulation of bacterial metabolites, fecal microbiota transplantation, or the use of genetically modified bacteria—have shown promising results. However, further research is essential to fully develop and refine these therapeutic strategies.

Keywords: chronic kidney disease, gut microbiota, modulation of bacterial metabolites, fecal microbiota transplantation

1. INTRODUCTION

Chronic kidney disease (CKD) is a clinical syndrome secondary to the definitive change in function and/or structure of the kidney and is characterized by its irreversibility and

slow and progressive evolution. Another important aspect is that pathology represents a higher risk of complications and mortality, especially cardiovascular-related [1].

An adult patient is identified with CKD when they present, for a period equal to or greater than three months, glomerular filtration rate (GFR) lower than 60 ml/min/1.73 m2, or GFR greater than 60 ml/min/1.73 m2, but with evidence of injury of the renal structure. Some indicators of renal injury are albuminuria, changes in renal imaging, hematuria/leukocyturia, persistent hydroelectrolytic disorders, histological changes in kidney biopsy, and previous kidney transplantation. Albuminuria is defined by the presence of more than 30 mg of albumin in the 24-hour urine or more than 30 mg/g of albumin in an isolated urine sample adjusted by urinary creatinine [1].

Prevalence of CKD differs depending on geographic region, typically ranging from 10% to 20%, but it has been gradually increasing, particularly in developed countries. This trend can be partially attributed to the progressive aging of the global population. Additionally, the increased prevalence of risk factors such as diabetes mellitus (DM), hypertension, and obesity among CKD patients is noteworthy [2]. The World Health Organization (WHO) has estimated that the global annual number of deaths directly caused by CKD ranges from 5 to 10 million [3].

The main causes of CKD include diabetes, hypertension, chronic glomerulonephritis, chronic pyelonephritis, chronic use of anti-inflammatory medications, autoimmune diseases, polycystic kidney disease, Alport syndrome, congenital malformations, and prolonged acute renal disease [1]. Socioeconomic factors and lifestyle-related factors (e.g., diet, insufficient sleep, smoking, and lack of physical activity) are well-known risk factors associated with CKD progression. Intrinsic renal factors also play a critical role in influencing the deterioration of renal function, including GFR, proteinuria, glomerular, interstitial changes, and obstruction of urinary outflow (obstructive nephropathy) [2].

2. STATE OF KNOWLEDGE

2.1. Specific metabolites of gut microbiota and their importance in chronic kidney disease

Gut microbiota-derived metabolites have emerged as key players in the progression of chronic kidney disease (CKD), influencing various aspects of renal and systemic health. The

interplay between gut microbes and kidney function is complex, with several specific metabolites playing a role in disease pathogenesis. Among the most studied are uremic toxins such as indoxyl sulfate (IS) and p-cresyl sulfate (pCS), which are produced by the microbial metabolism of dietary amino acids, particularly tryptophan and tyrosine. In patients with CKD, the impaired renal clearance of these metabolites leads to their accumulation, which exacerbates inflammation, oxidative stress, and fibrosis in kidney tissues [4].

Indoxyl sulfate (IS), generated through microbial degradation of tryptophan, is known to have nephrotoxic effects. It is believed to contribute to kidney damage by promoting oxidative stress and activating pro-fibrotic signaling pathways, particularly the TGF-β pathway. These mechanisms not only worsen renal function but also increase the risk of vascular calcification, which is a significant concern in CKD patients. IS has been shown to contribute to both kidney and cardiovascular dysfunction, making it a crucial target for therapeutic interventions. Similarly, p-cresyl sulfate (pCS), produced by the metabolism of tyrosine, plays a role in the pathogenesis of CKD by inducing oxidative stress, exacerbating endothelial dysfunction, and triggering inflammatory responses. The accumulation of both IS and pCS has been associated with an increased risk of CKD progression and associated cardiovascular events, further compounding the burden of disease [4].

Another important class of metabolites in CKD progression is short-chain fatty acids (SCFAs), which are produced through the fermentation of dietary fibers by gut bacteria. SCFAs such as acetate, propionate, and butyrate have beneficial effects on gut health and systemic inflammation. They help maintain the integrity of the gut barrier, which is essential for preventing the translocation of harmful substances into the bloodstream. In CKD, however, dysbiosis—the imbalance of gut microbiota—leads to a decrease in SCFA production, contributing to gut barrier dysfunction and systemic inflammation. The reduction in SCFA levels is linked to increased intestinal permeability ("leaky gut"), which facilitates the entry of microbial metabolites and endotoxins into the systemic circulation, exacerbating renal injury and inflammation [5,6].

In addition to these metabolites, trimethylamine N-oxide (TMAO), a product of microbial metabolism of choline and carnitine found in animal-based foods, has been implicated in cardiovascular complications associated with CKD. Elevated levels of TMAO have been shown to increase the risk of atherosclerosis and thrombosis by modulating lipid metabolism and enhancing platelet aggregation, which compounds the cardiovascular burden in CKD patients [7,8].

The influence of gut microbiota on CKD is mediated through several mechanisms, including gut barrier dysfunction, systemic inflammation, and oxidative stress. Dysbiosis, a common feature in CKD patients, leads to an imbalance in the microbial community, which disrupts normal metabolic processes and promotes the production of harmful metabolites. These metabolites, in turn, contribute to kidney damage by exacerbating inflammatory pathways, increasing oxidative stress, and promoting fibrosis. As such, the gut microbiota and its metabolites represent critical factors in the pathogenesis of CKD and offer new avenues for therapeutic intervention [4].

Recent studies have highlighted the potential of dietary interventions, prebiotics, probiotics, and adsorbents such as AST-120, which can reduce the levels of uremic toxins like IS and pCS. These interventions aim to restore the balance of gut microbiota, reduce the burden of harmful metabolites, and ultimately slow the progression of CKD. Given the significant impact of gut-derived metabolites on CKD progression, understanding the precise mechanisms through which these metabolites influence renal and systemic health is essential for developing targeted therapeutic strategies that can improve patient outcomes [9].

Recent research continues to uncover the intricate relationship between gut microbiota, its metabolites, and CKD, suggesting that modulation of gut microbial communities could become a promising therapeutic strategy. By targeting specific metabolites or microbial pathways, it may be possible to mitigate the harmful effects of dysbiosis and offer more effective treatments for CKD patients [10].

2.2. Gut microbiota metabolites as new diagnostic and prognostic biomarkers

The gut microbiota plays a crucial role in maintaining host health by influencing metabolism, immune functions, and protection against pathogens. Metabolites produced by these microorganisms, such as short-chain fatty acids (SCFAs), bile acids, branched-chain amino acids (BCAAs), and tryptophan derivatives, serve as key mediators in host-microbiota interactions. Alterations in the profiles of these metabolites can reflect health or disease states, making them potential diagnostic and prognostic biomarkers for various conditions.

Short-chain fatty acids, particularly butyrate, are primary products of dietary fiber fermentation by gut bacteria. Butyrate plays a pivotal role in maintaining intestinal barrier integrity and modulating immune responses. Reduced levels of butyrate in the gut have been associated with inflammatory bowel diseases, such as Crohn's disease, as well as metabolic

disorders, including obesity and type 2 diabetes. Monitoring butyrate concentrations may thus provide valuable diagnostic and prognostic insights into these conditions.

Tryptophan derivatives, metabolized by the gut microbiota, influence signaling pathways related to the nervous and immune systems. Disruptions in tryptophan metabolism have been linked to neurodegenerative diseases, depression, and metabolic disorders. Analyzing the profile of these metabolites in bodily fluids could aid in early diagnosis and prognosis of such conditions.

Gut microbiota-derived metabolites, such as trimethylamine-N-oxide (TMAO), have also been associated with cardiovascular diseases. Elevated plasma levels of TMAO correlate with an increased risk of atherosclerosis and cardiovascular events. Assessing TMAO levels may therefore serve as a prognostic biomarker in cardiology, assisting in identifying patients at higher risk [11].

In the context of cancer, alterations in the composition of the gut microbiota and its metabolites may play a role in carcinogenesis. For instance, a decreased presence of butyrate-producing bacteria, such as *Faecalibacterium prausnitzii*, has been observed in patients with colorectal cancer. Monitoring these changes could support early detection of tumors and assessment of prognosis [12].

In summary, gut microbiota metabolites represent promising tools in the diagnosis and prognosis of various diseases. Further research into their roles and mechanisms of action may contribute to the development of new therapeutic strategies and personalized medicine [13].

2.3. Modern therapeutic approaches based on manipulation of the microbiota.

Therapeutic approaches concerning intestinal microbiome are designed to sustain a favorable metabolic balance with conventional methods focused on maintaining an optimal microbiome through a balanced diet and administering probiotics, prebiotics, and antibiotics, as well as new methods emphasizing the modulation of bacterial metabolism and novel approach of the application of genetic engineering.

2.3.1. Diet

The primary objective of dietary optimization is the prevention of dysbiosis and the decrease of toxin levels generated by the microbiota, which contributes to the slowdown of

CKD's progression. Plant-based fiber-rich and low-protein diet is recommended, as it is also known for its impact on metabolic acidosis, hypertension, cardiovascular risk and weight [14–16]. The elimination of animal proteins is aimed mainly at the reduction of urea metabolism such as indole, indoxyl sulfate and p-cresol sulfate, but another important effect is the reduction of carnitine and choline intake, which, as substrates for the metabolism of intestinal flora, are converted to trimethylamine (TMA) and TMA N-oxide (TMAO), substances with proven atherogenic effects and influence the progression of renal fibrosis and cardiovascular risk [15,16].

Study of Lobel et al. in a mouse model showed a large effect of a diet rich in sulfur amino acids in CKD course. H2S is an important mediator of the posttranslational modification of tryptophanase activity, which in turn inhibits the microbiotas activity of uremic toxin production. It was established that mice with CKD on low sulfur amino acid diet with adenine presented higher serum creatinine levels and more advanced histological changes of CKD than mice on high sulfur amino acid diet [17].

Albeit a plant-based, low-protein diet has numerous therapeutic benefits in CKD patients in many clinical trials, it is highly important to take into account that reduction of protein impact below a safe level of 0.55 to 0.6 g protein/kg per day, may induce protein energy waste (PEW) which is mortality predictor in CKD patients. Reduction in protein intake to 0.3 to 0.4 g protein/ kg per day requires supplementation of keto acids analouges composed of essential amino acids (e.g. isoleucine, leucine, phenylalanine, and valine) provided by animal proteins [18].

2.3.2. **Probiotics, prebiotics and synbiotics**

Systematic reviews and meta-analysis from the past ten years reported that probiotic, prebiotic, and synbiotic supplementation significantly reduces serum levels of uremic toxins: indoxyl sulfate and p-cresol [19–22]. Several studies carried out on partly nephrectomized animal models fed with probiotic cocktails (*Lactobacilli, Bifidobacteria, S. thermophilus*) showed reduced blood urea-nitrogen levels, decreased creatinine serum levels and then prolonged life span and improvement in quality of life [23]. Also clinical trials on patients with CKD-associated dysbiosis showed positive effects both in reducing uremic toxins and in the histopathological presentation of the disease course as the influence of *Streptococcus thermophilus, Lactobacillus acidophilus, Lactobacillus casei* and *Bifidobacterium longum*

activity [15].

The impact of prebiotics was displayed in the research of Vaziri et al., which showed the usage of high fermentable fiber in the form of amylose maize-resistant starch in diet rats with adenine-induced CKD. The result of the diet was a reduction of key markers of CKD: low creatinine clearance, interstitial fibrosis, inflammation, and tubular damage. The effect on the intestinal microbiome is due to complex carbohydrates in resistant starch which are substrates of short-chain fatty acids (SCFA) produced by the microbiome and play a crucial part in enhancing the integrity of the intestinal barrier and affects the stimulation of the local immune response. Amylose maize-resistant starch can cause the rise of the population of SCFA-forming bacteria and displacement of urease-positive bacterial species. The acidifying properties of SCFA also help reduce the production of indoxyl sulfate and P-cresol sulfate [24]. Another study about resistant starch presented that high amylose maize-resistant starch type 2 in the diet of rats exhibited interestingly less microbial diversity than rats on a low-fiber diet. However, the potentially negative decrease in diversity observed in HAMRS2-fed rats, at the same time involved an increase in the *Bacteroidetes*-to-*Firmicute*s ratio, which is a marker of the correct composition of the microbiome, and probably caused by the homogeneous structure of HAMRS2 [25].

Coadministration of probiotics and prebiotics seems as a promising tool in restoration of healthy microbiota in CKD-related dysbiosis. A clinical study presenting oral supplementation of synbiotics consisted of high–molecular weight inulin, fructo-oligosaccharides, galacto-oligosaccharides, *Lactobacillus*, *Bifidobacteria*, and *Streptococcus genera* showed reduction of serum levels of uremic toxins in CKD patients [26].

Despite numerous studies confirming the reduction of uremic toxins and the stabilization of the gut microbiota by probiotics, prebiotics, and synbiotics, further research is needed to determine the direct impact on the course and prognosis of CKD [22].

2.3.3. Modulation of bacterial metabolites

The direct action on bacterial metabolites prevents their serum levels from increasing by binding and excreting them in the gastrointestinal tract, while also enhancing the intestinal barrier, as well as through alteration of enzyme activity.

A 3-month administration of phosphate binder sevelamer (SEV) sequesters p-cresol in vitro and presents positive effects on inflammation and lipid pattern. Anti-inflammatory

properties are directly due to a reduction in the concentration of p-cresol, whose metabolite p-cresyl-glucuronate accumulates in the blood, where it has a pro-inflammatory effect on endothelial cells, monocytes, and lymphocytes. The reduction in LDL-cholesterol is due to the binding of bile acids by SEV and its excretion through the gastrointestinal tract, resulting in increased catabolism of cholesterol [20].

Another important variant of treatment is oral intestinal adsorbent AST-120. In animal models, it caused the restoration of the epithelial tight-junction proteins and the reduction of plasma endotoxin and markers of oxidative stress and inflammation due to its ability to bind low-molecular-weight compounds [27]. A Study by Ueda et al. has shown that the supplementation of AST-10 in CKD patients may delay the start of hemodialysis. The risk of dialysis initiation was increased by 3.48-fold in patients who were not administered AST-120 [28]. In adult CKD patients supplementation presented cardiovascular benefits. Despite promising reports about the advantages of AST-20 on metabolome in CKD patients, the influence on intestinal microbiota balance still remains unclear and requires further investigation [29].

A structural analogue of choline 3, 3-dimethyl-1-butanol (DMB) is trimethylamine (TMA) inhibitor that affects microbial TMA formation by reducing the activation of microbial TMA lyases. Studies on animal models have shown a decrease in plasma trimethylamine N-Oxide (TMAO) levels in mice on choline- or carnitine supplementation. Furthermore, DMB inhibited endogenous proinflammatory and atherogenic activity in mice [30].

In study by Ya-Long et al. on CKD-associated gut microbial dysbiosis performed on rat models, the treatment with fungus *Poria cocos* (PC) and its tetracyclic derivative, poricoic acid A (PAA) was proposed. PAA and PC presented a vast range of effects it mitigated microbial dysbiosis, enhanced intestinal barrier, attenuated oxidative stress, inflammation, and renal fibrosis. In addition, it lowered serum levels of microbial-derived products including glycine-conjugated compounds and polyamine metabolites [31].

The previously mentioned study by Lobel et al. shown as an example of the use of a diet rich in sulphur amino acids, is based on the post-translational modification of *E.coli* tryptophanase. Alteration of its activity by S-sulfhydration results in a reduction of indole production from tryptophan in vitro and in vivo on bacterial cultures [17].

2.3.4. Fecal microbiota transplantation (FMT)

Fecal microbiota transplantation (FMT) is still quite a novel treatment method of proven effect on *Clostridium difficile* colitis. Recent studies show promising outcomes for its use in patients with CKD-induced dysbiosis. Transplantation of the microbiome of healthy donors lead to an increase in bacterial diversity of the recipients [27]. On animal models with adenine-induced CKD significant change in alpha diversity of gut microbiota was noted in a group that underwent FMT treatment contrary to the control group. This change was also followed by a significant reduction in levels of p-cresyl sulfate and an improvement in glucose tolerance [32]. As currently no clinical trial was carried out on CKD population there is no support of FMT's influence on CKD-induced dysbiosis, however two case reports of patients with membranous nephropathy and IgA nephropathy stated FMT therapy to exert favorable effects on kidney function and albuminuria [33–35] [20-22].

FMT shows great potential as a treatment for dysbiosis induced by CKD, yet its benefits remain underexplored. It is crucial to conduct further research and clinical trials to fully understand and harness its effectiveness [29].

2.3.5. Genetically Engineered Bacteria

The use of genetic engineering showed positive effects in a study by Devlin et al. in which deletion or alteration of the activity of the *Bacteroides* gene(BT1492) encoding tryptophanase results in significant reduction of urinary indoxyl sulfate. Such action, in combination with an optimal diet supporting tryptophanase-negative *Bacteroides*, could be a breakthrough step in the control of indoxyl sulfate levels in patients with CKD [36].

2.4. Research challenges and perspectives

The correlation between gut microbiota and chronic kidney disease (CKD) is a topic that requires extensive research. Emerging evidence suggests that gut microbiota plays a role in the progression of CKD and its associated complications - cardiovascular diseases and intestinal dysfunction. The last decade has provided ample evidence of the correlation of gut microbiota with many disease models [37]. A 2020 study by Huang et al revealed changes in the gut microbiota in patients with CKD, which may suggest that new therapeutic targets for these patients may emerge shortly [38]. Enterogenic uremic toxins are produced in the

intestine, which is associated with the metabolism of the microbiota in the colon [39]. Uremic substances affect the progression of chronic kidney disease and its cardiovascular complications [40]. In the case of renal failure, CKD patients are susceptible to gastrointestinal and microbiological disorders. As a result, there is a decrease in probiotics and an increase in pathogenic bacteria, which is called gut microbiota dysbiosis [41]. This phenomenon is a potential cause responsible for chronic kidney disease and its complications. Correlations between organs allow us to distinguish the "gut-kidney-heart" axis, the mechanisms of which are still largely unknown and require further research [40]. It is currently known that kidney dysfunction leads to the accumulation of uremic toxins in the body, and they damage the intestines and heart. Intestinal dysfunction can lead to the destruction of the intestinal barrier and microbiological imbalances, which promotes the production of uremic toxins and further exacerbates systemic inflammation, which also affects kidney and cardiovascular damage [38]. These correlations show that the mutual influence of these organs can lead to a "vicious circle" and continuous progression of CKD and its complications. However, the exact mechanism remains unclear, which makes it difficult to select appropriate intervention methods. Despite an in vitro experiment conducted in 2013 by Vaziri et.al, which demonstrated intestinal barrier dysfunction by urea, its mechanisms are still unclear [42].

Uremic toxins, which mainly originate from dietary metabolites, in addition to being the result of renal failure, are also the cause of its progression by inducing various pathogenic signals [43]. Therefore, studying the mechanisms responsible for the "gut-kidney-heart" axis is crucial for developing potential therapeutic therapies aimed at modulating gut microbiota dysbiosis and reducing its pathogenic metabolites.

Currently, the following are considered as potential therapeutic strategies aimed at the gut microbiota, which aim to counteract the progression of CKD: dietary intervention, prebiotics, probiotics, Genetically Engineered Bacteria, Fecal Microbiota Transplantation, Antibiotics, Bacterial Metabolites Modulation, Conventional Drugs, Traditional Chinese Medicine and Future Therapeutic Based on Sequencing Techniques.

- **Dietary intervention** is the first-line treatment for CKD and delays, and sometimes even prevents the initiation of dialysis [16]. Many studies on diet and gut microbiota have addressed the influence of dietary fiber, protein, and phosphate [17].
- **Prebiotics** exert their beneficial effects by selectively stimulating the growth or

activity of bacteria in the colon [44]. A recent study of the oral **probiotic** Lactobacillus casei showed that it corrected gut microbial imbalance, ameliorated kidney damage, and delayed the progression of chronic kidney disease in mice, but also slowed the decline in kidney function in patients with stage 3–5 chronic kidney disease [45]. Many clinical and experimental studies in CKD have shown that taking prebiotics, probiotics, and synbiotics can reduce uremic toxins and inflammatory mediators and improve colonic epithelial permeability [46].

- **Genetically Engineered Bacteria** are associated with S-sulfhydration or mutation of E. coli TnaA - its activity is reduced, which in turn reduces the level of indoxyl sulfate in serum, and consequently less kidney damage [36].
- **Fecal microbiota transplantation (FMT)** is a new therapy that involves transferring feces from healthy donors to the gastrointestinal tract of diseased recipients [47]. Studies have shown that transplanting fecal microbiota from chronic kidney disease patients into mice can induce increased production of uremic toxins, renal fibrosis, and oxidative stress [48]. Conversely, FMT treatment in healthy mice significantly improved gut microbiota abnormalities [40].
- **Bacterial metabolite modulation** is based on: Uremic Toxin Absorbents [38], Trimethylamine Inhibitor [49], AGE Formation Inhibitors [50], and Receptors for Advanced Glycation end-product inhibitors [51].
- A 2017 study by Nazzal et. al suggests that the removal of gut microbiota with oral **antibiotics** (vancomycin) can significantly reduce plasma concentrations of gut-derived uremic substances - IS and PCS [52]. Antibiotic administration also improves renal injury by preventing the inflammatory response [53].
- **Conventional drugs** aren’t without matter for gut microbiota. Lubiprostone, a drug often used to treat constipation, when administered to rats with chronic kidney disease, reduced the level of microbiota-derived uremic toxins in plasma, probably by restoring the Lactobacillaceae family and the Prevotella genus [54]. Various studies have shown the effect of antidiabetic drugs on the gut microbiota. Metformin can increase the number of Lactobacillus and Akkermansia in mice and diabetic patients, which affects the integrity of the gut barrier [55].
- Growing evidence shows the beneficial effects of **traditional Chinese medicine** in the treatment of CKD by modulating the microbiome using, among others: Jian-Pi-Yi-Shen Decoction (JPYS), Mahuang herbal granules [56].

- **High-throughput bacterial DNA sequencing techniques**, including microbial profiling of 16S ribosomal DNA (rDNA) and shotgun metagenomics, greatly facilitate a better understanding of the composition of the human gut microbiota, which contributes to the work on understanding the pathophysiological mechanisms of its role in human diseases [57].

The current studies are only a preliminary step to understand better and further develop potential therapeutic strategies related to gut microbiota. Further clinical studies and mechanistic experiments are necessary. Unfortunately, translating metagenomic findings into key biological mechanisms remains a major challenge. However, targeting the gut microbiota is an opportunity for new therapies against CKD progression. Despite limitations, the available clinical and experimental data suggest that influencing the gut microbiota in the gut-kidney-heart axis may become a promising therapeutic strategy for patients with chronic kidney disease, especially for those who suffer from intestinal and cardiovascular complications.

3. CONCLUSIONS

Chronic kidney disease (CKD) is a progressive, irreversible condition characterized by impaired renal function, often accompanied by cardiovascular complications. The gut microbiota and its metabolites, such as indoxyl sulfate (IS), p-cresyl sulfate (pCS), short-chain fatty acids (SCFAs), and trimethylamine N-oxide (TMAO), play a significant role in CKD progression. Dysbiosis in CKD patients disrupts normal metabolic processes, leading to the accumulation of uremic toxins like IS and pCS, which exacerbate inflammation, oxidative stress, and fibrosis. Changes in profiles of these metabolites can indicate health or disease states, making them valuable diagnostic and prognostic biomarkers.

Modern therapeutic approaches targeting the gut microbiota aim to reduce CKD progression by manipulating microbial balance and metabolism. These strategies include dietary changes, probiotics, prebiotics, synbiotics, adsorbents, fecal microbiota transplantation (FMT), and genetic engineering. Dietary modification includes a plant-based, low-protein diet, which helps reduce harmful uremic toxins and alleviate cardiovascular risks associated with CKD. The use of probiotics, prebiotics, and synbiotics has shown promise in restoring a healthy gut microbiome. It reduces inflammation, and decreases the levels of uremic toxins

such as indoxyl sulfate and p-cresol sulfate. Another innovative method involves the use of adsorbents like AST-120 to bind and eliminate these toxins from the body, while compounds such as sevelamer have demonstrated anti-inflammatory effects. Fecal microbiota transplantation (FMT) is also being explored as a potential treatment, as it has been shown to improve microbial diversity and reduce toxic metabolites in animal models. Furthermore, genetic engineering techniques, such as altering bacterial genes involved in the production of uremic toxins, offer a promising new avenue for managing CKD.

Modern therapeutic methods aim to address the underlying dysbiosis and metabolic imbalances in CKD, providing potential new pathways for improving patient outcomes. To confirm their effectiveness, further research and standardized protocols are needed.

4. DISCLOSURE

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