CORRECTION OF MICROBIOTA CHANGES IN PATIENTS WITH CHRONIC KIDNEY FAILURE IN KHOREZM REGION

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Annotatsiya. Surunkali buyrak yetishmovchiligi (SBY) bemorlarida ichak mikrobiotasining buzilishi (disbioz) uremik toksinlar ishlab chiqarilishining ortishi va yallig‘lanish jarayonlarining kuchayishi orqali kasallikning og‘irlashishiga olib keladi. Xorazm viloyatida odatiy ovqatlanish odatlari mikrobiota tarkibiga bevosita ta’sir ko‘rsatadi. Tadqiqotmizning maqsadi SBY bo‘lgan bemorlarda mikrobiota o‘zgarishlarini ilmiy adabiyotlar asosida o‘rganish, ularni tuzatishga qaratilgan aralashuv usullarini baholash va Xorazm viloyatida o‘tkazilgan klinik kuzatuv natijalarini taqdim etish. 2013–2024 yillar oralig‘ida ilmiy manbalar tahlil qilindi. 30 nafar SBY bilan og‘rigan bemorlar ishtirokida 12 haftalik sinbiotik (Bifidobacterium longum, Lactobacillus acidophilus va inulin) va tolaga boy parhez asosida klinik kuzatuv o‘tkazildi. Davolashdan so‘ng foydali bakteriyalar soni oshdi, zararli toksinlar (indoksil sulfat, p-kresil sulfat) miqdori kamaydi, CRP va IL-6 kabi yallig‘lanish belgilari pasaydi, shuningdek, ichak faoliyati yaxshilandi. Mikrobiotani tuzatish usullari SBY bo‘lgan bemorlar uchun foydali bo‘lib, ularning umumiy ahvolini yaxshilashda yordam beradi. Xorazm sharoitida bunday yondashuvlar keng qo‘llanilishi zarur.

Kalit so‘zlar: surunkali buyrak kasalligi, mikrobiota, probiotiklar, sinbiotiklar, uremik toksinlar

Аннотация. Хроническая болезнь почек (ХБП) сопровождается нарушением состава кишечной микробиоты, что ведёт к увеличению продукции уремических токсинов и активации системного воспаления. В Хорезмском регионе характер питания влияет на микробиоту кишечника. Целью нашего исследования проанализировать изменения микробиоты при ХБП на основе научной литературы, оценить эффективность методов коррекции микробиоты, а также представить результаты клинического наблюдения, проведённого в Хорезмской области. Изучены данные из международных и национальных научных баз данных (2013–2024 гг.). Проведено клиническое наблюдение за 30 пациентами с ХБП (стадии 3–5), получавшими комбинированную терапию синбиотиком (Bifidobacterium longum, Lactobacillus acidophilus и инулин) и диетой, богатой пищевыми волокнами, в течение 12 недель. Отмечено увеличение количества полезных бактерий, снижение уровней уремических токсинов (иноксилсульфат, п-крезилсульфат), уменьшение воспалительных маркеров (CRP, IL-6), а также улучшение состояния желудочно-кишечного тракта. Коррекция микробиоты является эффективным дополнительным методом терапии у пациентов с ХБП. В условиях Хорезмского региона такие подходы заслуживают широкого внедрения.

Ключевые слова: хроническая болезнь почек, кишечная микробиота, пробиотики, синбиотики, уремические токсины

Abstract Chronic kidney disease (CKD) is associated with gut microbiota dysbiosis, which exacerbates disease progression through increased production of uremic toxins and systemic inflammation. The Khorezm region presents unique dietary and environmental factors influencing microbiota composition. To review current literature on microbiota alterations in CKD, evaluate therapeutic interventions, and present clinical observations on microbiota correction in CKD patients from the Khorezm region. Literature review combined with a prospective observational study of 30 CKD patients (stages 3–5) receiving probiotic and dietary interventions. Literature confirms dysbiosis characterized by decreased SCFA-producing bacteria and increased proteolytic species. Clinical observations showed that 12 weeks of probiotic and prebiotic supplementation combined with dietary fiber increase resulted in significant reduction of serum uremic toxins (indoxyl sulfate, p-cresyl sulfate), inflammatory markers (CRP, IL-6), and improvement in gastrointestinal symptoms. Targeted microbiota correction is effective in improving biochemical and clinical parameters in CKD patients in Khorezm. Larger controlled studies are recommended.

Key words: chronic kidney disease, gut microbiota, probiotics, synbiotics, uremic toxins

Introduction. Chronic kidney disease (CKD) progression is increasingly linked to alterations in gut microbiota that promote systemic inflammation and uremic toxicity. The gut microbiota of CKD patients typically shows a loss of beneficial SCFA-producing bacteria and overgrowth of proteolytic and endotoxin-producing species, aggravating renal dysfunction [1,5]. The Khorezm region’s unique dietary patterns, characterized by low fiber intake and high carbohydrate consumption, may exacerbate this dysbiosis[8,10]. While literature has extensively described these mechanisms, there is a paucity of clinical data from Central Asia, particularly the Khorezm region, regarding microbiota correction interventions [2]. This review integrates global evidence with a clinical observation study conducted in Khorezm, assessing the effectiveness of microbiota-targeted therapies.

Objective. To evaluate current scientific evidence on gut microbiota alterations and correction in CKD, and to observe clinical outcomes of probiotic, prebiotic, and dietary fiber interventions in CKD patients in the Khorezm region.

Materials and methods. A systematic literature search was conducted across multiple scientific databases, including local Uzbek scientific repositories, to capture both international and region-specific research related to gut microbiota alterations in chronic kidney disease (CKD). The search period spanned from 2013 to 2024 to ensure inclusion of the most recent advances. Inclusion criteria were restricted to human studies involving adult patients with CKD stages 2 through 5, with an emphasis on research detailing gut microbiota composition assessed via culture methods or molecular techniques such as 16S rRNA gene sequencing. Studies evaluating interventions aimed at modulating the microbiota—such as probiotic, prebiotic, synbiotic supplementation, dietary fiber, or oral adsorbents—were prioritized. Reviews without original data, animal-only studies, and reports focusing on acute kidney injury or dialysis patients were excluded to maintain clinical relevance to CKD populations.

Data extraction from eligible studies focused on the characterization of microbiota changes, types of interventions used, biochemical markers including serum uremic toxin levels (indoxyl sulfate and p-cresyl sulfate), inflammatory biomarkers (e.g., C-reactive protein and interleukin-6), clinical outcomes, and any region-specific factors influencing microbiota and treatment response [3].

A prospective observational study was conducted to assess the effects of microbiota-targeted therapy in CKD patients from the Khorezm region. Thirty adult patients, aged between 35 and 65 years, diagnosed with stage 3 to 5 CKD according to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, were recruited from nephrology outpatient clinics in Khorezm. Patients with ongoing dialysis treatment, recent (within 3 months) use of antibiotics, presence of active gastrointestinal diseases (such as inflammatory bowel disease, irritable bowel syndrome), or on

immunosuppressive therapy were excluded to avoid confounding factors affecting gut microbiota and inflammatory status [9].

All enrolled participants received a daily oral synbiotic formulation for a period of 12 weeks. The synbiotic preparation contained a combination of probiotic strains—Bifidobacterium longum and Lactobacillus acidophilus—alongside the prebiotic fiber inulin, selected for their documented efficacy in restoring beneficial gut flora and enhancing short-chain fatty acid production [4].

In parallel, patients underwent structured dietary counseling sessions aimed at increasing daily fiber intake to 25–30 grams, primarily through the incorporation of locally available high-fiber foods such as whole grains, legumes, and vegetables. Nutritional education focused on sustainable and culturally acceptable dietary modifications to support microbiota health [7,9].

Baseline assessments included detailed medical history, physical examination, and collection of blood and stool samples. Serum levels of uremic toxins—indoxyl sulfate (IS) and p-cresyl sulfate (PCS)—were quantified using high-performance liquid chromatography (HPLC) methods. Systemic inflammatory status was evaluated by measuring C-reactive protein (CRP) and interleukin-6 (IL-6) concentrations through enzyme-linked immunosorbent assay (ELISA). Gut microbiota composition was analyzed via 16S rRNA gene sequencing of stool samples, allowing taxonomic profiling and evaluation of microbial diversity indices. Additionally, participants completed validated gastrointestinal symptom questionnaires addressing common issues such as bloating, constipation, abdominal discomfort, and stool consistency. Following the 12-week intervention period, all assessments were repeated to evaluate changes in microbiota composition, biochemical markers, and clinical symptoms. The study protocol was reviewed and approved by the Institutional Review Board of the Khorezm Regional Medical Center. All participants provided written informed consent prior to enrollment, ensuring adherence to the Declaration of Helsinki and local ethical standards for human research [6].

Results. CKD-associated dysbiosis is typified by loss of *Bifidobacterium*, *Lactobacillus*, *Roseburia* spp. and increase in *Proteobacteria*, *Enterobacteriaceae* and *Clostridia* spp.Dysbiosis correlates with elevated serum IS and PCS, systemic inflammation, and progression to ESRD [6–12].Probiotic and synbiotic supplementation reduces uremic toxins and inflammation, improving gut barrier integrity [13–17].Dietary fiber enhances SCFA production, modulating immune responses and gut microbiota composition [18,19].Significant increase in relative abundance of *Bifidobacterium* (+25%, $p<0.01$) and *Lactobacillus* (+18%, $p<0.05$) post-intervention; decrease in *Proteobacteria* (-15%, $p<0.05$). Alpha diversity indices improved modestly. Mean serum IS reduced from 45.3 ± 8.2 mg/L to 32.7 ± 7.1 mg/L ($p<0.01$); PCS from 36.9 ± 7.4 mg/L to 25.6 ± 6.3 mg/L ($p<0.01$). CRP decreased from 7.5 ± 2.3 mg/L to 4.2 ± 1.9 mg/L ($p<0.05$); IL-6 from 12.1 ± 3.7 pg/mL to 7.9 ± 2.6 pg/mL ($p<0.05$). Significant improvement in bloating, constipation, and abdominal discomfort reported by 70% of patients. No adverse events related to supplementation noted.

Discussion. The observed clinical improvements align closely with literature findings, confirming that microbiota-targeted interventions can reduce systemic uremic toxins and inflammation in CKD patients. The Khorezm-specific dietary patterns, previously identified as low in fiber, were effectively modified through counseling, supporting microbiota recovery.

This study underscores the feasibility and clinical benefit of combined probiotic-synbiotic-dietary fiber therapy in real-world CKD management in Central Asia. Limitations include small sample size and lack of a control group; randomized controlled trials are warranted to confirm these preliminary findings.

Conclusion. Correction of gut microbiota dysbiosis through probiotic, synbiotic, and dietary fiber supplementation is a promising adjunctive therapy for CKD patients in the Khorezm region. Clinical observations demonstrate improved microbiota composition, reduced uremic toxins, and

decreased inflammation, highlighting the need for larger, controlled studies and integration into regional nephrology protocols.

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