GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 11 (344) ноябрь 2023

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
No 11 (344) 2023

Содержание:

GEORGIAN MEDICAL NEWS
No 11 (344) 2023

RELEVANCE FOR DIAGNOSIS, THERAPY, AND STRATEGIES OF GUT MICROBES DYSBIOSIS IN CHRONIC KIDNEY DISEASE: A SYSTEMATIC REVIEW

Amandeep Singh[1], Pravesh Kumar Sharma[2], Ashok Kumar Singh[3], Chhaya Agarwal[4], Geetika M. Patel[5], Kavina Ganapathy[6].

[1]*Professor, School of Pharmacy & Research, Dev Bhoomi Uttarakhand University, Dehradun, India.*

[2]*Associate Professor, Department of Pharmacy, Vivekananda Global University, Jaipur, India.*

[3]*Associate Professor, Department of General Surgery, Teerthanker Mahaveer University, Moradabad, Uttar Pradesh, India.*

[4]*Assistant Professor, Department of Biotechnology, Noida Institute of Engineering and Technology, Greater Noida, Uttar Pradesh, India.*

[5]*Associate Professor, Department of Community Medicine, Parul University, PO Limda, Tal. Waghodia, District Vadodara, Gujarat, India.*

[6]*Assistant Professor, Department of Biotechnology, School of Sciences, JAIN (Deemed-to-be University), Karnataka, India.*

Abstract.

Background: Dysbiosis and weakened gastrointestinal barrier function have been identified as potential regulators of Chronic Kidney Disease (CKD). The complex connection among gut micro biota and CKD is provided in this study, with particular attention to how inflammation contributes to the CKD path physiology. It establishes the inverse association between CKD and gut microbial dysbiosis by exploring the collision of CKD about the organization and capabilities of the gut micro biota.

Methods: The possibility of new diagnostic tools in measuring the dynamic changes within the gut microbial ecology illustrates the importance of accurately diagnosing gut micro biota abnormalities in CKD. Additionally, the study explores the targeted medicines that focus on gut micro biota in CKD. Using data from both human clinical trials and rat models, the study demonstrates the variety of therapeutic approaches and their ability to limit the rate of development of CKD and its accompanying problems.

Result: The study we performed was based on the Preferred Reporting Items for Systematic reviews and Meta Analyses (PRISMA) approach. The findings show the significance of investigating the relationship between gut micro biota and CKD, paving up the possibility for new therapeutic strategies to improve the patient outcomes and quality of life. The present understanding of CKD-induced modifications to the gut micro biota and the ensuing effects on gastrointestinal health, emphasizing studies, will be highlighted in this review.

Key words. Gastrointestinal, pathophysiology, diagnostic tools, human clinical trials, rat models.

Introduction.

The prevalence of CKD is a substantial worldwide health burden that has grown dramatically in the last several years as a result of aging populations and illnesses that are linked to it, such as metabolic syndrome, obesity, diabetes mellitus (DM), and arterial hypertension [1]. Patients with CKD frequently have altered gut microbiota, which is linked to low-grade chronic inflammation, oxidative stress (OS), and acute hemolysis (AH). The term CKD refers to a wide range of illnesses that impact the anatomy and functionality of the kidney. Kidney damage (albuminuria) or impaired kidney function glomerular filtration rate (GFR) are the two main criteria used to define CKD. Renal replacement treatment, including hemodialysis (HD), peritoneal dialysis, and kidney transplants, is becoming more prevalent yearly, making for 10-15% of all cases [2]. Organic waste products, especially those derived from nitrogen metabolism that the kidneys are ordinarily responsible for eliminating; accumulate due to the gradual loss of renal function. Still, early identification can help to avoid some of the negative effects of CKD. The most frequent causes of CKD globally are diabetes and hypertension [3].

Additional reasons could include polycystic kidney disease, pyelonephritis, and glomerulonephritis. Cardiovascular (CV) the primary cause of death is illness for persons with CKD. As the illness progresses, the risk of cardiovascular disease (CVD) increases exponentially. Hence, patients with CKD generally have a substantial CV burden when they start a renal replacement treatment [4]. Patients with ESRD may have up to 500 times the overall CV-related mortality rate. The frequency of CV events cannot be decreased, and the condition's progression can be slowed down by treatments aimed at classic CV risk factors such as diabetes, dyslipidemia, and hypertension. Thus, non-traditional risk factors for CKD rise in 66 bacteria [5].

Chronic inflammation, arterial calcification, sympathetic hyperactivity, and anaemia are examples of the prevalence of kidney function falls that have been connected to an increased risk of heart attacks and an accelerated phase of the illness [6]. Dysbiosis is used to illustrate an imbalance in the gut micro biota that leads to modifications in the gastrointestinal tract's regular functions and the creation of toxins that harm the organism. Many chronic illnesses, including CKD, can cause the dysbiosis condition [7]. Disbyosis, which is often observed in a uremic condition, actually causes the retention of uremic toxins, the majority of which are produced by an imbalance in the fermentation of nitrogen compounds relative to non-digestible carbohydrates, including ρ-cresyl and indoxylsulphate. In a few individuals, these toxins increase inflammation, dysmetabolism, and CVD, among other consequences of CKD [8]. Disbyosis condition is currently being acknowledged as a potential therapy target to prevent or mitigate CKD-related effects. An increasing amount of study indicates that individuals with CKD and ESRD have different microbiota composition. It was found that the abundance of up to 190 microbial operational taxonomic unitsvaried considerably [9]. Another study found that ESRD patients had greater levels compared to controls, of aerobic bacteria, including species of Enterobacteria and Escherichia Patients on hemodialysis had considerably greater counts of Clostridium perfringens among anaerobic bacteria

and lower counts of Bifidobacterium species [10]. Patients with CKD and ESRD have dysbiosis of the gut microbiota due to several causes. These include iron treatment, frequent use of antibiotics, reduced dietary fiber consumption and increased constipation, and inadequate protein absorption [11]. The study aims to identify possible indicators and molecular fingerprints for early diagnosis and prognosis evaluation by examining the unique modifications in the number of gut microbes associated with CKD. It also investigates how the CKD affects the gut microbiota's the structure and function clarifying the underlying processes that support the advancement of the illness. Figure 1 depicts the link between GUT and CKD.

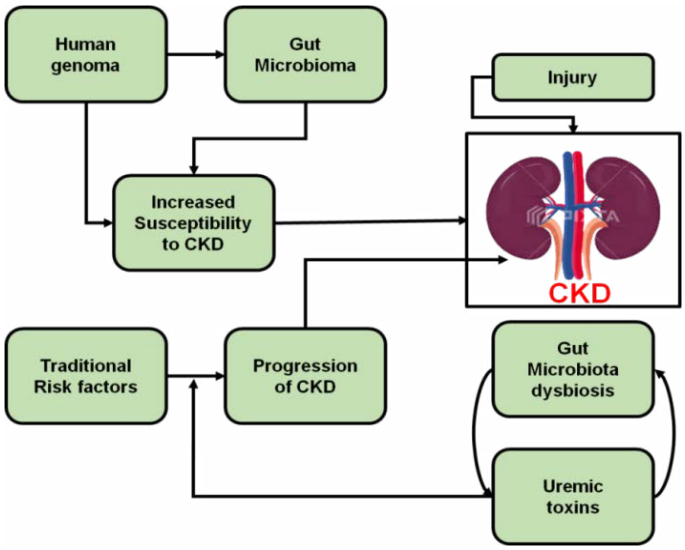

Figure 1. *Link between GUT and CKD.*

Therapeutic Approaches for Dysbiosis of the Gut Microbes in CKD.

GUT Microbiota.

In the human gastrointestinal system, there are billions of microorganisms, generally bacteria, that make up a diverse and abundant population. The production of vitamins and nutrients is one advantage of the human body's symbiotic relationship with the gut bacteria, defense against infections, modulation of host immunity, and the digestion of complex food macronutrients [12]. The phylum has two families that are prevalent in the colon, Lachnospiraceae and Ruminococcaceae, which together account for bacteria found in healthy adult fecal samples [13]. The genera Bacteroides and Prevotella are the dominant members of the phylum Bacteroidetes. The genus Bifidobacterium is the primary representative of the less common phylum Actinobacteria. Early experiences in life affect the gut microbiota's richness and variety, which indicates an appropriate constitution of the microbiota. Every person has a different ideal healthy composition, which may be attributed to their age, ethnic background, lifestyle, and dietary preferences [14]. Dietary habits have a significant influence on the structure of bacteria among these parameters. Prevotella-dominated microbiota is linked to diets high in fiber, whereas Bacteroides-dominated microbiota is linked to diets high in protein. It has also been proposed that artificial sweeteners, alcohol, and fermented meals could impact the makeup of bacteria [15].

The gastrointestinal as a cause of inflammation in CKD.

Dialysis patients have chronic inflammation across their whole gastrointestinal system (esophageal to colon). A study on animals has demonstrated that bacterial urease activity destroys the colon's tight epithelial junctions, and that cytokine production causes localized inflammation. However, it is significant because animals cannot degrade urea [16]. The low potassium and low phosphorus diets that CKD patients follow lead to inadequate intake of symbiotic bacteria and vegetable fiber. The bacteria that generate the enzyme urease breaks down urea into ammonia and ammonium hydroxide (NH4OH), which breaks down proteins with tight junctions [17]. Meanwhile, the balance between symbiotic bacteria is disrupted by the changed microbiome, which also poses competition for colonocytes' SCFA supply. This can cause inflammatory leukocytes to infiltrate and produce cytokines, compromising colonocyte integrity and the mucosal barrier. Gastrointestinal inflammation accelerates the breakdown of the epithelial barrier by promoting tight junction protein endocytosis [18]. Systemic inflammation eventually results from transferring uremic toxins, endotoxins, and bacterial byproducts. As kidney disease advances, serum urea concentrations rise along with alterations in the gut flora, creating a vicious cycle. The broad and ever-expanding list of uremic toxins and solutes is the primary reason why, despite the severity of uremia's effects and the many reviews conducted on the issue, the cellular and molecular processes at play in the formation of the illness remain mostly unexplained. During uremia, the levels of over 100 different solutes rise, although the exact source of most of them is still up for discussion [19].

The effects of CKD on GUT Microbiota.

The accumulation of uremic toxins is a characteristic of CKD, which is also often linked to mechanically disrupted alterations in the gastrointestinal tract, including intestinal wall edema and altered colonic transit [20]. Dietary restrictions and regular use of iron, phosphorus-binding medicines, and antibiotics are common in patients with CKD. These traits have the potential to cause dysbiosis and, inversely, to accelerate the illness's progression to more severe stages of chronic kidney disease. Uremic toxins are waste products that accumulate in the intestinal epithelium and blood when renal function deteriorates [21]. The revolutionize in the digestive system promote the establishment of microorganisms that may produce both urease or uricase enzymes and use urea as a source of energy. The cytosolic enzyme urease is responsible for catalyzing the conversion of urea into ammonia and carbon dioxide. Thus, a large increase in ammonia generation raises the pH of the gut, breaks down gut tight connections in the epithelium to cause enterocolitis [22]. The kidney is primarily charge of eliminating uric acid produced by the metabolism of purine; however, as renal function declines, the colon takes over as the principal site of uric acid excretion. Through the same mechanism, a high uric acid concentration increases the number of microorganisms [23].

Diagnosis of GUT in CKD.

To diagnose gut microbial dysbiosis in CKD, an in-depth investigation involving laboratory tests, clinical evaluations, and innovative techniques for examining the organization and functioning of the gut microbiota is required. The following methods are frequently used to diagnose gut microbial dysbiosis in CKD [24]. A comprehensive clinical evaluation that includes the patient's food habits, prescription usage, medical history, and gastrointestinal symptoms is the initial step in the diagnosis procedure. In individuals with CKD, gut microbe dysbiosis can be indicated by clinical signs such as uremia, abnormal bowel habits, and gastrointestinal disorders [25]. One of the most important aspects of detecting gut microbial dysbiosis involves examining stool samples to examine the construction of the gut microbiota. Metagenomic sequencing, "16S rRNA gene sequencing", and metabolomics analysis are a few examples of advanced techniques that are being used to discover particular microbial imbalances associated with CKD by providing exact data on the variation, prosperity, and functional capability of gut microbial communities [26].

GUT Microbiota strategic therapies on CKD.

As potential targets for therapy, researchers are becoming more interested in the gut microbiota and the chemicals it produces. Probiotics and prebiotics are the gut microbiota-targeted treatments most often used in clinical practice. When taken orally, probiotics live bacteria that have positive health effects [27]. Beneficial bacterial growth and activity can be enhanced by prebiotics. Synbiotics combine probiotics and prebiotics, which provide additional health benefits. Postbiotics, compounds created or leased by the gut microorganisms, have also shown beneficial effects on the host [28]. Figure 2 summarizes prospective therapeutics targeting the gut microbiota to address the developmental programming of CKD and connected comorbidities.

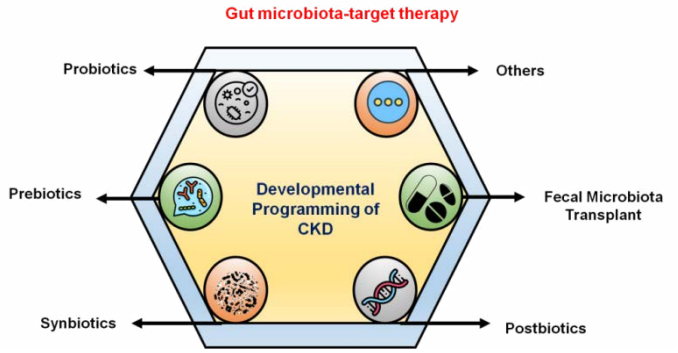

Figure 2. *GUT Microbiota-target therapy.*

Human Indications in Children with CKD.

The potential of gut microbiota modifications brought about by microbiome-targeted therapy to avoid the course of CKD and its related complication in children has yet to be thoroughly studied. For example, the butyrate-producing bacterium Clostridium butyricum is employed as a probiotic. In children with INS, oral treatment of the bacteria Clostridium butyricum during remission has been demonstrated to decrease the incidence of recurrence and the need for immunosuppressive medications [29]. Probiotic therapy's protective effects have been linked to increases in Treg cells and butyrate-producing microorganisms. However, there is strong evidence from animal research that targets gut microbiota to stop the course of the illness and its adverse repercussions.

Models of Animals for Strategic Therapy Using Gut Microbiota.

The potential benefits of gut microbiota strategic treatment to prevent and cure many disorders have generated much interest. Preclinical research often uses animal models to investigate the mechanisms and effectiveness of these medicines. The effects of early-life therapies aimed at targeting the gut microbiota have been investigated with various animal models. In advance of being used in clinical settings, these models play an important part in clarifying the underlying processes and proving the effectiveness and safety of certain treatment approaches [30]. Rats are useful models for examining the impact of early-life gut microbiota-targeted therapy because they are comparable to people physiologically. They provide light on the intricate relationships that exist between host metabolism, immunological response, neurobehavioral development, and the gut microbiota [31]. Table 1 summarizes probiotics and prebiotics in CKD in both humans and animals.

Results and Discussion.

This study was performed following the PRISMA standards. The investigations showed that many databases were necessary for a thorough representation of papers, demonstrating the reliability of systematic evaluations.1800 citations were found after the examination of the designated resources. 1545 citations remained for titles or an abstract screening after multiple entries (n=255) consisted of eliminated. In the end, 14 papers received inclusion in the current systematic evaluation after 645 documents were tested for inclusion in full text. Figure 3 displays the decision-making method's diagram.

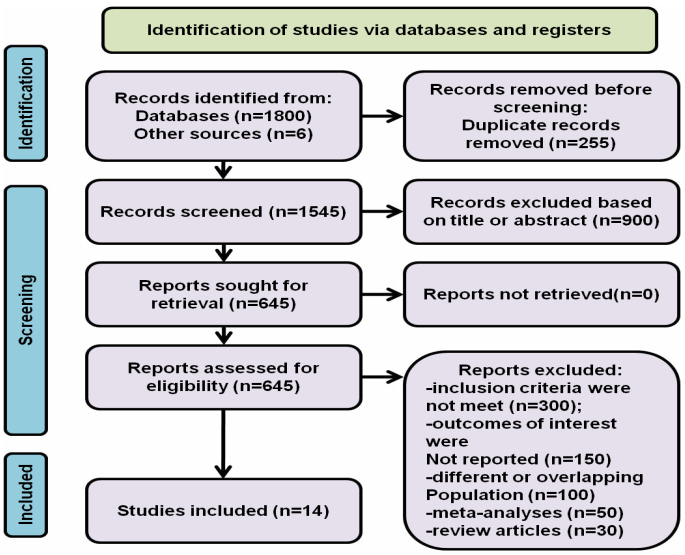

Figure 3. *Flow chart of some of the research included in the study.*

Table 1. *Investigation of prebiotics and probiotics in CKD.*

Kinds	Nutritional Intervention	Results	Reference
Prebiotics			
Rat	starch resistant to amylase in maize	Reduction of inflammation and oxidative stress. Delayed development of renal disease that is chronic.	[32]
Human	High fermentable fiber gum Arabic	Decrease in serum urea nitrogen that is significant. Considerable rise in the amount of nitrogen and bacterial bulk in the feces.	[33]
Mice	Fatty acids with a short chain	Decreased inflammation both locally and overall	[34]
Probiotics			
Rat	Alkalophilic urease-positive bacteria found in soil Pasteurisporosarcina	Lower levels of blood urea nitrogen. An increase in survival.	[35]
Human	B. longum, S. thermophilus, and L. acidophilus	Decrease of blood urea nitrogen levels significantly. higher quality-of-life ratings	[36]
Dog	VSL#3	The estimated glomerular filtration rate has increased significantly.	[37]
Synbiotics			
Human	Probinulneutro is a commercial symbiotic composition.	Extremely lower amount of ρ-cresol in whole plasma.	[38]
Human	Probiotics and Prebiotics	In the gut microbiota, the presence of Bifidobacterium was significantly improved by symbiotic treatments.	[39]
Human	Streptococcus thermophilus and Bifidobacterium longum	Decrease of the fluid urea nitrogen saturation significantly.	[40]

CKD is mostly caused by malfunctioning metabolic pathways, highlighting the illness's complexity. Forecasted analyses have shown distinct metabolic fingerprints across different CKD cohorts, emphasizing the complex relationship between changed metabolic pathways and disease development. In addition to expanding the scope of our understanding of the path physiology of CKD, these findings have made it possible to develop focused; therapeutic approaches specialized to the unique metabolic abnormalities typical of various phases of the disease. The investigators require creating individualized therapy plans that decrease the progress of CKD and enhance patient outcomes by understanding the complex metabolic nuances [41]. Figure 4 depicts the metabolic processes among individuals with CKD based on functional analysis predictions.

The Kidney Disease Outcomes Quality Initiative (KDOQI) classifies CKD into stages, with a large complication variation among these stages. From imbalances in electrolytes and hypertension in the beginning stages to anemia, bone problems, and cardiovascular difficulties in the latter stages, each step is linked to a unique spectrum of consequences. Comprehending the frequency of these complications at various stages of CKD is essential for implementing customized monitoring and management plans. This highlights the necessity of prompt interventions to reduce the risk of unfavourable consequences and enhance the general quality of life for patients with CKD [42]. Figure 5 depicts the frequency of problems based on the CKD stage determined by KDOQI.

Body weight (BW) changes were observed during five weeks in rats with CKD caused by oral gavages with adenine at a dose of 250 mg/kg BW/day. Compared to the control group, the CKD rats significantly lost body weight, with losses of around 22% and 31% observed in the third and fifth weeks, respectively. The animals' entire health is negatively impacted by the severe CKD disease, which is highlighted by this significant weight loss. Despite this, providing a synbiotic therapy to CKD rats appears to mitigate weight loss promisingly. With weight reductions of around 16% and 22% within third as well as fifth weeks, correspondingly, the synbiotic-treated CKD rats showed a comparatively easier fall in body weight than the control group. According to these results, using synbiotics could slow down the rate at which weight loss linked to CKD is progressing [44]. Figure 6 depictsthe rat's modifications in body weight.

In rats with CKD, a significant difference in indole levels was found between the rats with CKD and the control group. In particular, the indole level is superior in the CKD rats than in the control rats. Also, animals that were given adenine to cause CKD died by the tenth week, demonstrating the seriousness of the illness and its possible negative effects. However, the CKD rats' indole levels dropped when they were given synbiotics, returning them to levels observed in the control group. This decrease emphasizes the ability of synbiotic therapy to regulate indole metabolism in the setting of CKD. It raises the possibility that it may play a role in decreasing fecal indole levels [43]. Figure 7 depicts the amount of rat fecal indole time series.

An interdisciplinary field including gastroenterology, nephrology, and micro biome research is the effect of certain medications on the gut micro biota in patients with chronic kidney disease. The most accurate and customized information on the management of CKD and its possible impacts on the gut flora is usually obtained by consulting with medical specialists. Human study provides critical therapeutic relevance and assists in bridging the translational gap, even while animal models offer insightful information. According to the results of these human investigations, there is a complicated interaction between the gut micro biota and medications for CKD. Further study is required to understand the processes behind these interactions and how they affect patient care. As a whole, the data gathered from human research improves and contextualizes our knowledge of how different treatment approaches affect the gut micro biota within the intricate framework of chronic kidney disease.

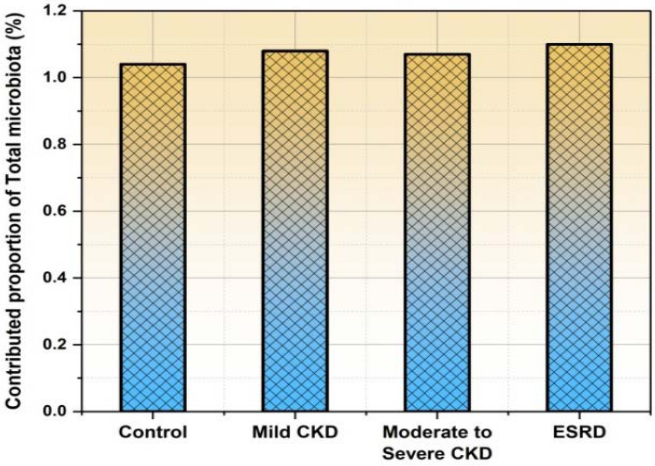

Figure 4. *Predicted functional analysis in CKD.*

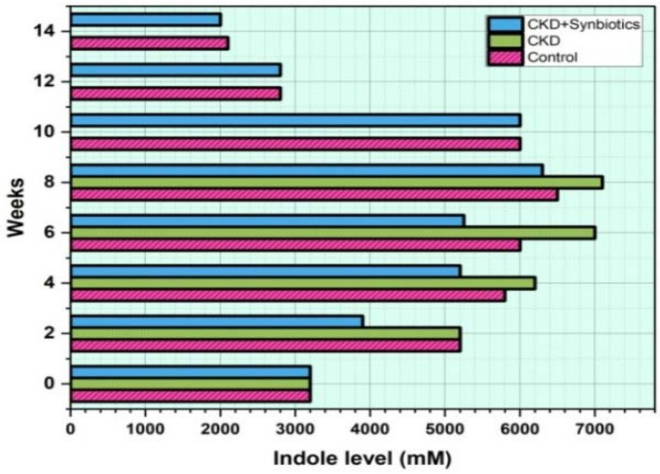

Figure 7. *The amount of rat fecal indole time-series.*

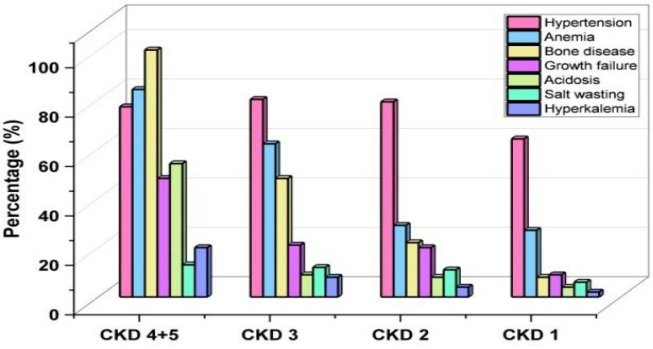

Figure 5. *Complications according to CKD stage prevalence.*

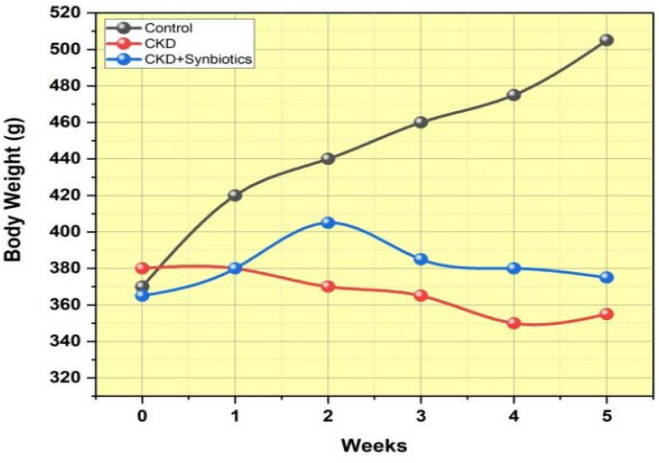

Figure 6. *The rat's modifications in body weight.*

Conclusion.

The term CKD indicates a progressive, long-term loss of kidney function. It is characterized by a progressive decline in the kidneys' capacity to remove waste from the circulation. This illness often progresses slowly, and the glomerular filtration rate estimate (eGFR) used to categorize the illness's severity into several phases. A dysbiotic condition caused by an increase in pathogenic germs and a decrease in helpful bacteria in the gut microbiome is often associated with CKD. Clinicians could be able to identify new biomarkers that support early CKD identification and prognosis evaluation by clarifying the complex relationships between gut microbial imbalances and CKD pathogenesis. Moreover, certain treatments, including probiotics and prebiotics, as well as dietary changes that target the gut microbiota, indicate possibilities in slowing the advancement of CKD and its side effects. The complex structure of the gut microbiome presents difficulties in accurately determining the particular microbial changes linked to CKD, which often results in inconsistent study outcomes. To generate individualized treatment plans for each patient, further study will help identify certain microbial signatures related to various phases of CKD.

REFERENCES

1. Kim SM, han Song I. The clinical impact of gut microbiota in chronic kidney disease. The Korean Journal of Internal Medicine. 2020;35:1305.
2. Zhao J, Ning X, Liu B, et al. Specific alterations in gut microbiota in patients with chronic kidney disease: an updated systematic review. Renal failure. 2021;43:102-12.
3. Rukavina Mikusic NL, Kouyoumdzian NM, Choi MR. Gut microbiota and chronic kidney disease: evidences and mechanisms that mediate a new communication in the

gastrointestinal-renal axis. Pflügers Archiv-European Journal of Physiology. 2020;472:303-20.
4. Hu X, Ouyang S, Xie Y, et al. Characterizing the gut microbiota in patients with chronic kidney disease. Postgraduate medicine. 2020;132:495-505.
5. Salguero MV, Al-Obaide MA, Singh R, et al. Dysbiosis of Gram-negative gut microbiota and the associated serum lipopolysaccharide exacerbates inflammation in type 2 diabetic patients with chronic kidney disease. Experimental and therapeutic medicine. 2019;18:3461-9.
6. Jazani NH, Savoj J, Lustgarten M, et al. Impact of gut dysbiosis on neurohormonal pathways in chronic kidney disease. Diseases. 2019;7:21.
7. Evenepoel P, Dejongh S, Verbeke K, et al. The role of gut dysbiosis in the bone–vascular axis in chronic kidney disease. Toxins. 2020;12:285.
8. Meijers B, Farré R, Dejongh S, et al. Intestinal barrier function in chronic kidney disease. Toxins. 2018;10:298.
9. Lun H, Yang W, Zhao S, et al. Altered gut microbiota and microbial biomarkers associated with chronic kidney disease. Microbiologyopen. 2019;8:e00678.
10. Hobby GP, Karaduta O, Dusio GF, et al. Chronic kidney disease and the gut microbiome. American Journal of Physiology-Renal Physiology. 2019;316:F1211-7.
11. Chi M, Ma K, Wang J, et al. The immunomodulatory effect of the gut microbiota in kidney disease. Journal of immunology research. 2021;2021:1-6.
12. Feng YL, Cao G, Chen DQ, et al. Microbiome–metabolomics reveals gut microbiota associated with glycine-conjugated metabolites and polyamine metabolism in chronic kidney disease. Cellular and molecular life sciences. 2019;76:4961-78.
13. Rinninella E, Raoul P, Cintoni M, et al. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms. 2019;7:14.
14. Wright AT. Gut commensals make choline too. Nature microbiology. 2019;4:4-5.
15. Plata C, Cruz C, Cervantes LG, et al. The gut microbiota and its relationship with chronic kidney disease. International Urology and Nephrology. 2019;51:2209-26.
16. Lim E, Hyun S, Lee JM, et al. Effects of education on low-phosphate diet and phosphate binder intake to control serum phosphate among maintenance hemodialysis patients: A randomized controlled trial. Kidney research and clinical practice. 2018;37:69.
17. Yang J, Lim SY, Ko YS, et al. Intestinal barrier disruption and dysregulated mucosal immunity contribute to kidney fibrosis in chronic kidney disease. Nephrology Dialysis Transplantation. 2019;34:419-28.
18. Yang T, Richards EM, Pepine CJ, et al. The gut microbiota and the brain–gut–kidney axis in hypertension and chronic kidney disease. Nature Reviews Nephrology. 2018;14:442-56.
19. Meijers B, Evenepoel P, Anders HJ. Intestinal microbiome and fitness in kidney disease. Nature reviews nephrology. 2019;15:531-45.
20. Koppe L, Fouque D, Soulage CO. The role of gut microbiota and diet on uremic retention solutes production in the context of chronic kidney disease. Toxins. 2018;10:155.
21. Cani PD. Human gut microbiome: hopes, threats and promises. Gut. 2018;67:1716-25.
22. Pittayanon R, Lau JT, Yuan Y, et al. Gut microbiota in patients with irritable bowel syndrome—a systematic review. Gastroenterology. 2019;157:97-108.
23. Shin A, Preidis GA, Shulman R, et al. The gut microbiome in adult and pediatric functional gastrointestinal disorders. Clinical Gastroenterology and Hepatology. 2019;17:256-74.
24. Mafra D, Borges N, Alvarenga L, et al. Dietary components that may influence the disturbed gut microbiota in chronic kidney disease. Nutrients. 2019;11:496.
25. Rovella V, Rodia G, Di Daniele F, et al. Association of gut hormones and microbiota with vascular dysfunction in obesity. Nutrients. 2021;13:613.
26. Noce A, Marrone G, Di Daniele F, et al. Impact of gut microbiota composition on onset and progression of chronic non-communicable diseases. Nutrients. 2019;11:1073.
27. Merra G, Noce A, Marrone G, et al. Influence of mediterranean diet on human gut microbiota. Nutrients. 2020;13:7.
28. Parada Venegas D, De la Fuente MK, Landskron G, et al. Short chain fatty acids (SCFAs)-mediated gut epithelial and immune regulation and its relevance for inflammatory bowel diseases. Frontiers in immunology. 2019:277.
29. Li F, Wang M, Wang J, et al. Alterations to the gut microbiota and their correlation with inflammatory factors in chronic kidney disease. Frontiers in cellular and infection microbiology. 2019;9:206.
30. Mazidi M, Shekoohi N, Covic A, et al. Adverse impact of Desulfovibrio spp. and beneficial role of Anaerostipes spp. on renal function: insights from a mendelian randomization analysis. Nutrients. 2020;12:2216.
31. Magruder M, Sholi AN, Gong C, et al. Gut uropathogen abundance is a risk factor for development of bacteriuria and urinary tract infection. Nature communications. 2019;10:5521.
32. Younes H, Egret N, Hadj-Abdelkader M, et al. Fermentable carbohydrate supplementation alters nitrogen excretion in chronic renal failure. Journal of renal nutrition. 2006;16:67-74.
33. Xie LM, Ge YY, Huang X, et al. Effects of fermentable dietary fiber supplementation on oxidative and inflammatory status in hemodialysis patients. International journal of clinical and experimental medicine. 2015;8:1363.
34. Arentsen T, Raith H, Qian Y, et al. Host microbiota modulates development of social preference in mice. Microbial ecology in health and disease. 2015;26:29719.
35. Borges NA, Carmo FL, Stockler-Pinto MB, et al. Probiotic supplementation in chronic kidney disease: a double-blind, randomized, placebo-controlled trial. Journal of Renal Nutrition. 2018;28:28-36.
36. Natarajan R, Pechenyak B, Vyas U, et al. Randomized controlled trial of strain-specific probiotic formulation (Renadyl) in dialysis patients. BioMed research international, 2014.
37. Lippi I, Perondi F, Ceccherini G, et al. Effects of probiotic VSL# 3 on glomerular filtration rate in dogs affected by chronic kidney disease: A pilot study. The Canadian Veterinary Journal. 2017;58:1301.
38. Guida B, Germanò R, Trio R, et al. Effect of short-term synbiotic treatment on plasma p-cresol levels in patients with

chronic renal failure: a randomized clinical trial. Nutrition, Metabolism and Cardiovascular Diseases. 2014;24:1043-1049.
39. McFarlane C, Ramos CI, Johnson DW, et al. Prebiotic, probiotic, and synbiotic supplementation in chronic kidney disease: a systematic review and meta-analysis. Journal of Renal Nutrition. 2019;29:209-220.
40. Pavan M. Influence of prebiotic and probiotic supplementation on the progression of chronic kidney disease. Minerva urologica e nefrologica= The Italian journal of urology and nephrology. 2014;68:222-226.
41. Zhuang R, Ge X, Han L, et al. Gut microbe–generated metabolite trimethylamine N-oxide and the risk of diabetes: A systematic review and dose-response meta-analysis. Obesity Reviews. 2019;20:883-94.
42. Zhong Z, Tan J, Tan L, et al. Modifications of gut microbiota are associated with the severity of IgA nephropathy in the Chinese population. International Immunopharmacology. 2020;89:107085.
43. Kim JE, Kim HE, Park JI, et al. The association between gut microbiota and uremia of chronic kidney disease. Microorganisms. 2020;8:907.
44. Kistler BM, Moore LW, Benner D, et al. The International Society of Renal Nutrition and Metabolism Commentary on the National Kidney Foundation and Academy of Nutrition and Dietetics KDOQI clinical practice guideline for nutrition in chronic kidney disease. Journal of Renal Nutrition. 2021;31:116-20.