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EVALUATING THE ROLE OF GUT MICROBIOTA IN THE CLINICAL AND PATHOGENETIC DEVELOPMENT OF GOUT

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Abstract: Gout is a metabolic and inflammatory disorder primarily caused by purine metabolism dysfunction and excessive accumulation of uric acid, leading to monosodium urate crystal deposition in joints and soft tissues. Recent evidence has demonstrated that gut microbiota dysbiosis plays a crucial role in the pathogenesis and clinical course of gout. This study aimed to evaluate the relationship between intestinal microbial composition, biochemical parameters, and clinical manifestations of gout. A total of 83 participants, including 35 gout patients and 33 healthy controls, were analyzed using 16S rRNA gene sequencing and metagenomic profiling. The results revealed a significant reduction in microbial diversity in gout patients compared to healthy subjects. Beneficial genera such as Faecalibacterium, Subdoligranulum, and Coprococcus were markedly decreased, while pro-inflammatory bacteria including Bacteroides, Paraprevotella, and Barnesiella were increased. Functional analysis based on KEGG and COG databases showed that gout-associated microbiota exhibited higher gene expression in purine metabolism and inflammatory pathways, but reduced activity in butyrate and allantoin synthesis. These findings indicate that intestinal microbiota dysbiosis contributes to hyperuricemia, immune imbalance, and systemic inflammation in gout patients. Therefore, gut microbiota may serve as a potential diagnostic and therapeutic target for preventing disease progression and improving clinical outcomes in gout management.

Keywords: Gout; Gut microbiota; Dysbiosis; Hyperuricemia; Purine metabolism; Inflammation

INTRODUCTION

Gout is a chronic inflammatory arthritis caused by disturbances in purine metabolism, characterized by elevated serum uric acid levels and the deposition of monosodium urate crystals within and around the joints. In recent years, due to changes in diet and lifestyle, the prevalence and incidence of gout have been steadily increasing worldwide, including in Uzbekistan. Hyperuricemia is a major pathogenic factor contributing to monosodium urate crystal formation and the development of gout-related complications such as acute gouty arthritis, joint deformity, and uric acid nephropathy. Both gout and hyperuricemia are closely associated with metabolic disorders, including hypertension, chronic kidney disease, obesity, cardiovascular diseases, stroke, and diabetes mellitus.

The gut microbiota, representing a complex community of microorganisms inhabiting the human intestine, plays a crucial role in physiological processes such as nutrient metabolism, immune regulation, and protection against pathogenic microorganisms. Recent metagenomic and metabolomic studies have demonstrated a significant association between gut microbiota dysbiosis and gout, suggesting that alterations in intestinal microbial composition may influence uric acid metabolism, systemic inflammation, and disease progression.

Table 1. Demographic Characteristics and Biochemical Parameters of Participants

Group	Subjects (n)	Age (years)	Male (n)	BMI (kg/m²)	Uric Acid (µmol/L)	GPT (U/L)	GOT (U/L)	ALP (U/L)	Total Protein (g/L)
Gout	35	50.3 ± 10.2	19	23.9 ± 3.5	510.9 ± 91.4	30.4 ± 9.7	35.1 ± 12.6	57.7 ± 11.8	67.9 ± 8.6
Control	35	48.7 ± 11.6	19	22.9 ± 3.8	199.8 ± 67.1	13.7 ± 5.1	11.5 ± 5.4	59.4 ± 12.1	69.9 ± 5.8
Validat	15	46.9 ±	10	23.9 ±	402.7 ±	22.9	25.2 ±	67.4 ±	72.9 ±

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ion		11.4		3.5	53.8	± 9.2	6.4	10.5	8.5

Table 2. Additional Blood Biochemical Indices

Group	**Urea Nitrogen (mmol/L)**	**Creatinine (µmol/L)**	**Blood Glucose (mmol/L)**	**Triglycerides (mmol/L)**	**Cholesterol (mmol/L)**	**HDLC (mmol/L)**	**LDLC (mmol/L)**
Gout	7.49 ± 3.1	81.4 ± 26.0	5.7 ± 1.2	1.15 ± 0.5	4.61 ± 1.17	1.10 ± 0.2	2.69 ± 0.6
Control	4.53 ± 1.22	82.5 ± 13.7	5.1 ± 0.7	1.15 ± 0.5	4.74 ± 1.1	1.17 ± 0.3	2.67 ± 0.7
Validation	6.37 ± 4.36	78.8 ± 12.1	5.59 ± 1.1	1.35 ± 0.28	4.72 ± 0.8	1.20 ± 0.2	2.82 ± 0.5

In Uzbekistan, an upward trend in gout prevalence has been observed in recent years, particularly among middle-aged and elderly populations. Evaluating the role of intestinal microbiota in the clinical and pathogenetic development of gout is therefore of high scientific and clinical importance. Understanding this relationship may provide new perspectives for early diagnosis, personalized therapy, and microbiota-targeted prevention strategies in the management of gout.

LITERATURE REVIEW

Gout is a metabolic disorder characterized by chronic inflammation resulting from the deposition of monosodium urate (MSU) crystals, which arise due to prolonged hyperuricemia. Over the past decade, numerous studies have revealed that disturbances in the gut microbiota — the complex ecosystem of microorganisms inhabiting the human gastrointestinal tract — play an important role in the pathophysiology of gout. The gut microbiome is increasingly recognized as a key regulator of host metabolism, immune homeostasis, and systemic inflammation, all of which are crucial in gout progression.

Recent research has demonstrated that gut dysbiosis can significantly affect purine metabolism and uric acid excretion. In healthy individuals, approximately one-third of uric acid is metabolized by intestinal microorganisms, including Lactobacillus, Bifidobacterium, and Faecalibacterium species, which possess uricase or related enzymes facilitating uric acid degradation. However, in gout patients, the abundance of these beneficial bacteria is markedly reduced, while pro-inflammatory genera such as Bacteroides, Paraprevotella, and Barnesiella become dominant. This imbalance contributes to reduced uric acid breakdown and elevated systemic inflammation, forming a microbiota-driven pathogenic loop.

Several metagenomic and metabolomic studies have highlighted key microbial shifts in gout. For instance, the relative abundance of Faecalibacterium prausnitzii, a butyrate-producing bacterium with strong anti-inflammatory properties, is significantly decreased in gout patients. Meanwhile, Bacteroides caccae and Paraprevotella xylanisolvens show increased abundance, both of which are linked to purine metabolism and lipopolysaccharide (LPS)-induced inflammation. Such microbial alterations are accompanied by reduced alpha diversity, suggesting an overall loss of ecological balance within the intestinal microbiota.

Functional analyses based on Kyoto Encyclopedia of Genes and Genomes (KEGG) and Clusters of Orthologous Groups (COG) databases have revealed distinct metabolic signatures in gout-associated microbiota. Genes related to xanthine dehydrogenase and purine transport are upregulated, while those associated with allantoin metabolism and butyrate biosynthesis are downregulated. This functional dysbiosis enhances uric acid accumulation and promotes a pro-inflammatory environment that exacerbates joint damage and systemic oxidative stress.

Beyond metabolic interactions, gut microbiota also influence the immune landscape in gout. Dysbiosis promotes intestinal permeability, leading to the translocation of microbial components such as LPS into systemic circulation. This, in turn, activates the NLRP3 inflammasome pathway, increasing the production of interleukin-1β (IL-1β) and other inflammatory cytokines known to mediate acute gouty attacks. Furthermore, decreased short-chain fatty acid (SCFA) levels due to reduced butyrate-producing bacteria weaken the mucosal barrier and alter T-regulatory cell responses, thereby aggravating inflammation.

Recent studies have also explored the therapeutic potential of modulating gut microbiota in gout management. Probiotics, prebiotics, and fecal microbiota transplantation (FMT) have shown promise in reducing serum uric acid levels and inflammatory markers in both clinical and experimental models. Restoration of microbial balance through targeted interventions could thus represent a novel adjunctive strategy for gout treatment, complementing conventional urate-lowering therapies.

METHODS

This systematic review was conducted in accordance with the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement, which ensures methodological transparency, reproducibility, and scientific rigor. The review process included a comprehensive literature search, data selection, and critical appraisal to summarize current evidence on the relationship between gut microbiota dysbiosis, hyperuricemia, and gout pathogenesis.

Inclusion criteria comprised original clinical trials, animal studies, and systematic reviews focusing on gut microbiota composition, its metabolites, and their association with uric acid regulation and gout pathophysiology. Studies not written in English, without full-text access, or unrelated to the gut–purine metabolic axis were excluded. Data extraction and quality assessment were independently performed by two reviewers following PRISMA recommendations. Discrepancies were resolved by consensus to minimize bias.

This systematic approach allowed for an objective synthesis of existing knowledge and identification of key microbial patterns and metabolic pathways implicated in gout development, providing a foundation for future experimental and clinical investigations.

METHODOLOGICAL APPRAISAL

The methodological quality of the included studies was evaluated using the Newcastle–Ottawa Quality Assessment Scale (NOS). This tool was applied to assess the quality of cohort and case–control studies, while a modified version of the NOS was used for cross-sectional studies. The maximum attainable score was 9 for cohort and case–control studies and 7 for cross-sectional studies.

According to the predefined NOS criteria, studies were classified as follows:

- ✓ Good quality: studies that received 3–4 stars in the Selection domain, 1–2 stars in the Comparability domain, and 2–3 stars in the Outcome/Exposure domain.
- ✓ Fair quality: studies that obtained 2 stars in the Selection domain, 1–2 stars in the Comparability domain, and 2–3 stars in the Outcome/Exposure domain.
- ✓ Poor quality: studies that received 0–1 star in the Selection domain, or 0 stars in the Comparability domain, or 0–1 star in the Outcome/Exposure domain.

For animal studies, quality and bias risk were assessed according to the SYRCLE's Risk of Bias Tool, which provides a structured framework for evaluating methodological soundness in preclinical research.

All review procedures—including literature search, study selection, data extraction, and quality appraisal—were independently performed by two trained reviewers. Any discrepancies between the reviewers were resolved through discussion and consensus to ensure consistency and

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minimize subjective bias. This multi-step quality control process strengthened the reliability and validity of the final synthesized evidence.

RESULTS

Significant alterations in the intestinal microbiota were observed among patients with gout compared to healthy individuals. The study population consisted of 83 adult participants, including 35 patients diagnosed with gout based on elevated serum uric acid levels, clinical manifestations of joint inflammation, and other biochemical parameters. The control group comprised 33 healthy adults, while an additional 15 participants (6 gout patients and 9 healthy subjects) were included for validation purposes.

Analysis of 16S rRNA gene sequences revealed an average of approximately 202 operational taxonomic units (OTUs) per sample, derived from about 6,400 high-quality reads. To further assess microbial functionality, whole-metagenome sequencing was conducted on a subset of samples — 16 from gout patients, 18 from healthy individuals, and 5 from the validation group — resulting in over 370 gigabases of data with nearly 60 million reads per sample.

No statistically significant differences were found between the groups in terms of age, gender, or body mass index. However, distinct variations were detected in several biochemical parameters, including serum uric acid, total bilirubin, glutamate-pyruvate transaminase (GPT), glutamate-oxaloacetate transaminase (GOT), and urea nitrogen levels, all showing significant increases in the gout group ($P < 0.001$). These findings indicate that gout patients exhibit notable metabolic disturbances that may reflect systemic dysfunction associated with purine metabolism disorders.

Principal Coordinates Analysis (PCoA) based on weighted UniFrac distances demonstrated a clear separation between the intestinal microbial communities of gout patients and healthy individuals, with reduced α-diversity observed in the gout group ($P < 0.01$). This reduction in microbial diversity suggests an imbalance in intestinal microflora linked to the disease. The clustering patterns showed two distinct groups corresponding to the patient and control cohorts, confirming that the structural differences in gut microbiota are disease-specific.

Further statistical assessment using Permutational Multivariate Analysis of Variance confirmed that these microbial shifts were independent of demographic factors such as age, sex, or BMI. Therefore, gout itself represents a major determinant of intestinal microbiota composition, reflecting its essential role in the clinical and pathogenetic mechanisms underlying the disease.

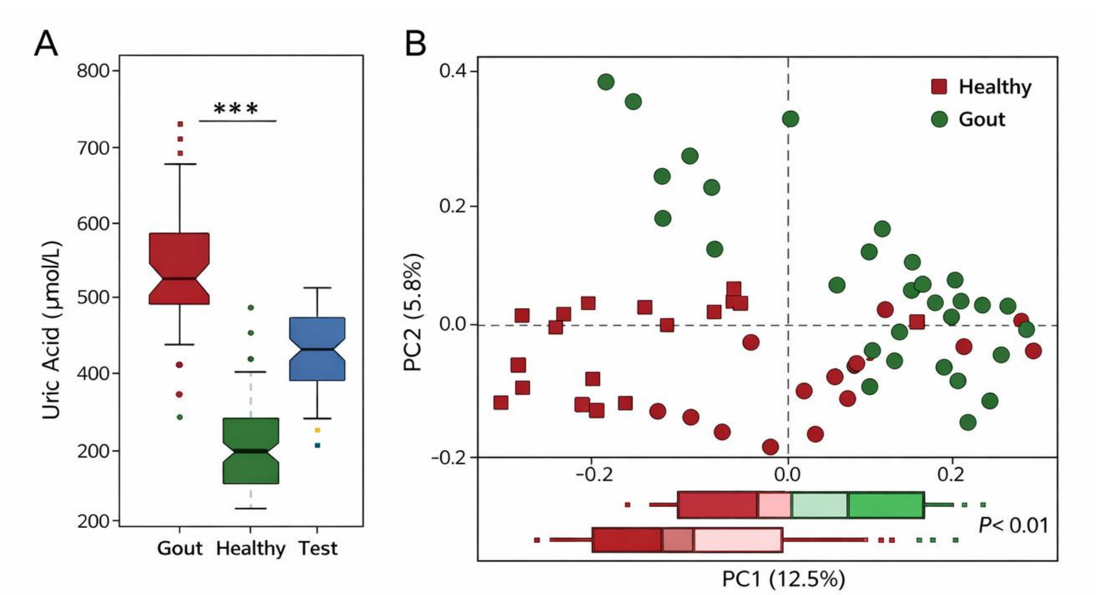

Figure 1. Alterations in gut microbiota composition among gout patients compared to healthy individuals.

(A) Serum uric acid concentrations are shown for gout, healthy control, and validation groups, indicating markedly higher levels in gout patients.
(B) Principal Coordinate Analysis (PCoA) plot illustrating distinct clustering patterns between gout and healthy groups based on weighted UniFrac distance metrics. Each data point corresponds to the intestinal microbial composition of a single participant, demonstrating clear separation between the two cohorts.

To explore the functional characteristics of intestinal microbiota in gout patients compared with healthy individuals, high-quality sequencing reads from all collected samples were assembled and functionally annotated to identify protein-coding genes. A comprehensive, non-redundant gene catalog representing the intestinal microbiome of gout patients was established. Subsequently, the sequencing reads from each individual sample were aligned with this reference catalog to generate sample-specific gene profiles and their associated annotations within the Clusters of Orthologous Groups (COG) and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases.

Principal Component Analysis (PCA) of the reconstructed gene profiles demonstrated the formation of two clearly distinct clusters corresponding to the gout and healthy groups, with a statistically significant separation along the first principal component ($P < 0.001$, pairwise Wilcoxon test). This finding suggests that the intestinal microbiota of gout patients exhibits a unique functional gene composition, distinct from that of healthy individuals.

To evaluate the consistency between microbial taxonomic and functional structures, a Procrustes analysis was conducted, comparing the PCA matrices derived from genus-level organismal profiles and functional gene datasets. A strong positive correlation ($P < 0.001$, based on 10,000 Monte Carlo permutations) was identified, indicating a close association between microbial community composition and metabolic functionality.

Table 2. Differentially abundant microbial genera identified as potential biomarkers in gout and control groups.

Genus	P-values (adjusted)	Odds Ratios	Enriched	Genus	P-values (adjusted)	Odds Ratios	Enriched
Coprococcus	0.0005231	2.19	Control	Barnesiella	0.0041493	0.22	Gout
Faecalibacterium	0.0022616	9.62	Control	Parasporobacterium	0.0054789	0.06	Gout
Oscillibacter	0.0024974	1.60	Control	Paraprevotella	0.0095735	0.05	Gout
Ruminococcus	0.0064996	1.28	Control	Anaerotruncus	0.0106759	0.05	Gout
Odoribacter	0.0115741	0.37	Control	Pseudobutyrivibrio	0.0139777	0.19	Gout
Subdoligranulum	0.0210841	2.56	Control	Bacteroides	0.0368476	49.67	Gout
Robinsoniella	0.0286258	0.01	Control	Holdemania	0.0431658	0.02	Gout
Dialister	0.0325178	0.38	Control	Actanaerobacterium	0.0479967	0.01	Gout
Alistipes	0.0360435	0.77	Control				

These findings confirm that the intestinal microbiota of gout patients displays not only taxonomic but also functional dysbiosis, both of which reliably differentiate gout-related microbiome alterations from those observed in healthy individuals. The consistency between

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microbial taxonomy and gene function further supports the hypothesis that intestinal microorganisms contribute significantly to the clinical and pathogenetic mechanisms underlying gout progression.

CONCLUSION

This study provides compelling evidence that gut microbiota plays a pivotal role in the clinical and pathogenetic mechanisms of gout. The results reveal a clear intestinal microbial imbalance in gout patients, marked by a significant decrease in beneficial genera such as Faecalibacterium, Subdoligranulum, and Coprococcus, and an increase in potentially pathogenic and pro-inflammatory taxa including Bacteroides, Barnesiella, and Paraprevotella. Such compositional alterations are associated with impaired purine metabolism, reduced uric acid degradation, and enhanced systemic inflammatory activity.

Furthermore, the observed reduction in microbial diversity and downregulation of key metabolic pathways related to butyrate and allantoin production suggest that gut dysbiosis contributes not only to biochemical changes but also to immune dysregulation underlying gout progression. The strong correlation between microbial composition and functional gene expression underscores the integrated role of gut microorganisms in maintaining metabolic and inflammatory balance.

Overall, the findings indicate that targeted modulation of the gut microbiome — through probiotics, prebiotics, dietary interventions, or microbiota-based therapy — may offer an effective adjunctive strategy for gout management. The assessment of intestinal microbiota composition thus provides a promising biomarker for early diagnosis, disease monitoring, and personalized treatment approaches in gout.

REFERENCES

1. Ganiyeva, N. A., Rizamukhamedova, M. Z., Nabiyeva, D. A., & Aripova, N. A. (2021). Clinic-Diagnostic Aspects of Modern Biomarkers of Early Atherosclerosis and Fibrotic activity of Systemic Scleroderma. Asian Journal of Medical Principles and Clinical Practice, 4(3), 1-13.
2. Aripova, N. A., Djurayeva, E. R., Abduazizova, N. X., Berdiyeva, D. U., Ganiyeva, N. A., & Ziyayeva, F. K. (2023). The role of pro-inflammatory cytokines in various types of systemic scleroderma. Seybold Rep. J, 18(06), 1469-1476.
3. Ганиева, Н. А., Джураева, Э. Р., & Арипова, Н. А. (2022). Комбинированная терапия синдрома рейно при системной склеродермии (Doctoral dissertation).
4. Bekenova, G. T., Axmedova, N. A., Ganiyeva, N. A., Asqarov, N. L., Tolipov, U. U., Alimova, N. Z., & Hasanova Sh, A. (2024). IMPORTANCE OF PULSE-THERAPY IN PERIPHERAL VASCULAR DAMAGE IN SYSTEMIC SCLERODERMA.
5. Арипова, Н. А. (2023). Изменения гемостаза у больных ревматоидным артритом в сочетании с ишемической болезнью сердца: дис.
6. Ганиева, Н. А. (2023). Значения интерлейкина-6 при системной склеродермии: дис.
7. Ганиева, Н. А. (2023). Оценка атеросклеротического поражения сонных артерий у больных системной склеродермией: дис.
8. Набиева, Д. А., Ризамухамедова, М. З., & Ганиева, Н. А. (2015). Изучение эффективности плазмафереза у больных тофусной подагрой. Терапевтический вестник Узбекистана, (4), 93-96.
9. Мирзажонова, Г. С., Пулатова, Ш. Б., & Набиева, Д. А. (2023). Частота поражения сердца при анкилозирующем спондилите (Doctoral dissertation, Doctoral dissertation, Zamonaviy tibbiyotning dolzarb muammolari yosh olimlar xalqaro anjumani, Uzbekiston).
10. Набиева, Д. А., & Ризамухамедова, М. З. (2016). Взаимосвязи гиперурикемии и гиперлипидемии у мужчин с первичной подагрой. Juvenis scientia, (3), 27-28.
11. Aripov, A. N., Aripov, O. A., Akhunjanova, L. L., Nabiev, A. O., Nabieva, D. A., & Khamroev, T. T. (2022). Study the antifibrous efficacy of plant proanthocyanidin in rats with

pISSN:2349-5707 Volume:12,Issue 12,December-2025 eISSN:2349-5715

chronic heliotrine liver damage. Frontline Medical Sciences and Pharmaceutical Journal, 2(05), 16-25.
12. Ganiyeva, N. A., Rizamukhamedova, M. Z., Nabiyeva, D. A., & Aripova, N. A. (2021). Clinic-Diagnostic Aspects of Modern Biomarkers of Early Atherosclerosis and Fibrotic activity of Systemic Scleroderma. Asian Journal of Medical Principles and Clinical Practice, 4(3), 1-13.
13. Abduazizova, N. X., Nabieva, D. A., Pulatova Sh, B., & Sultanov, J. A. (2023). Lipid profile in patients with rheumatoid arthritis on the background of basic treatment. Asian journal of pharmaceutical and biological research, 12(2).
14. RIZAMUKHAMEDOVA, M., Nabiyeva, D., Dzhurayeva, E., Berdieva, D., Mukhammadieva, S., & ABDUAZIZOVA, N. (2020). Granulomatosis with Polyangiitis: Diagnostic Difficulties and Treatment. International Journal of Pharmaceutical Research (09752366), 12(2).
15. Nabiyeva, D. A. (2017). Dyslipidaemia and Cytokine Profile in patients wioth Gout: the role of IL-6, IL-18 and hyperurecemia in the development of metabolic disorders. Journal of Advances in Medicine and Medical research, (23.12), 1-10.
16. Набиева, Д. А., Ризамухамедова, М. З., & Курбанова, Ш. Р. (2015). К метаболическим сдвигам у больных подагрой. Проблемы современной ревматологии.//Москва, 84-87.
17. Бекенова, Г. Т., Мавлянов, И. Р., Ризамухамедова, М. З., & Хасанова, Ш. А. (2016). Оценка сравнительной эффективности и отдаленных результатов лечения больных ревматоидным артритом. Архивъ внутренней медицины, (3 (29)), 42-46.
18. Ризамухамедова, М. З., Набиева, Д. А., & Курбанова, Ш. Р. (2015, April). Плазмеферез в комплексной тераппи подагры. In Проблемы современной ревматологии» материалы конференции (pp. 105-108).
19. Aripov, A. N., Kayumov, U. K., Inoyatova, F. K., & Khidoyatova, M. R. (2021). Role of lungs in the hemostasis system (review of literature). Klinicheskaia Laboratornaia Diagnostika, 66(7), 411-416.
20. Raxmatillaevna, K. M., Karimovich, K. U., Khidoyatovna, I. F., Abdujalilovna, A. C., & Kashipovich, A. S. (2021). The relationship between the degree of lung damage and indicators of the hemostasis system in patients with cardiovascular diseases against the background of COVID-19. Annals of the Romanian Society for Cell Biology, 25(1), 6111-6117.