JIMSR
Journal of Integrated Medical Sciences & Research

ORIGINAL ARTICLE
Volume 1 · Issue 1 · 2026

ARTICLE ID JIMSR-2026-001

Compositional Characteristics of the Gut Microbiome in Patients with Acute Uremia: A Study in India

Jaya Chandnani[1*], Ruhneet Kaur[2]

1 Department of Microbiology, Shri Shankaracharya Institute of Medical Sciences (SSIMS), Junwani, Bhilai, District Durg, Chhattisgarh 490020, India

2 Department of Microbiology, Rajmata Shrimati Devendra Kumari Singhdeo Government Medical College (RSDKS GMC), Ambikapur, District Surguja, Chhattisgarh 497001, India

Corresponding author: Jaya Chandnani, Senior Resident, Department of Microbiology, SSIMS, Junwani, Bhilai, District Durg, Chhattisgarh 490020, India · jaya.chandnani24@gmail.com

Abstract

Background: Acute uremia may disrupt intestinal barrier function and microbial composition through the gut-kidney axis, but evidence from Indian populations is limited. This study compared gut microbial composition, diversity, predicted function, and uremic-toxin associations in patients with acute uremia and healthy controls.

Methods: In this cross-sectional case-control study, 60 adults with acute uremia secondary to KDIGO stage 3 acute kidney injury and 60 age-, sex-, and BMI-matched healthy controls were enrolled. Stool samples obtained within 24-48 hours of admission underwent V3-V4 16S rRNA gene sequencing. QIIME 2 and SILVA-based analyses assessed alpha and beta diversity, differential taxonomic abundance, and predicted metabolic pathways. Serum urea, creatinine, indoxyl sulfate, and *p*-cresyl sulfate were measured.

Results: Acute uremia was associated with lower richness and alpha diversity (Chao1 and Shannon indices, both $p < 0.001$) and distinct beta-diversity clustering (PERMANOVA $p = 0.001$). Proteobacteria increased, whereas Firmicutes and the Firmicutes-to-Bacteroidetes ratio decreased. *Escherichia-Shigella*, *Klebsiella*, *Enterococcus*, *Streptococcus*, and *Clostridium perfringens* were enriched; *Faecalibacterium*, *Roseburia*, *Blautia*, *Bifidobacterium*, and *Coprococcus* were depleted. Indoxyl sulfate and *p*-cresyl sulfate correlated positively with Enterobacteriaceae and negatively with short-chain-fatty-acid-producing taxa. Predicted urease and indole-biosynthesis pathways were increased.

Conclusion: Acute uremia in this Indian cohort was associated with gut dysbiosis characterized by loss of microbial diversity and short-chain-fatty-acid producers, expansion of potential pathobionts, and associations with circulating uremic toxins. These findings support further evaluation of microbiota-targeted interventions in acute kidney injury.

Keywords: Acute kidney injury; Uremia; Gastrointestinal microbiome; Dysbiosis; Indoxyl sulfate; Short-chain fatty acids

1. Introduction

Acute uremia represents a life-threatening clinical syndrome resulting from a precipitous decline in renal function, commonly secondary to acute kidney injury (AKI) or acute-on-chronic renal decompensation [1]. The hallmark of uremia is the systemic accumulation of nitrogenous waste compounds—most notably urea, uric acid, and protein-bound uremic toxins—which disrupt cellular homeostasis, impair immune responsiveness, and induce systemic endothelial injury [2].

While management has historically focused on hemodialytic clearance and fluid-electrolyte restoration, recent translational insights emphasize the pivotal role of gastrointestinal physiology in the pathogenesis and amplification of uremic toxicity [3,4].

The human gastrointestinal tract harbors an intricate ecosystem of trillions of microorganisms, collectively termed the gut microbiome, which regulates mucosal immunity, nutrient processing, and metabolic homeostasis [5]. In health, a symbiotic state is maintained primarily by anaerobic organisms belonging to the phyla Firmicutes, Bacteroidetes, Actinobacteria, and Verrucomicrobia [6]. These bacteria ferment indigestible dietary fibers into short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate, which nourish colonocytes, reinforce tight junction proteins, and exert systemic anti-inflammatory actions [7].

Under conditions of acute renal failure, massive influxes of urea permeate the gastrointestinal lumen via enterohepatic circulation. Bacterial ureases convert luminal urea into ammonia and ammonium hydroxide, elevating

colonic pH and damaging the mucin layer and epithelial tight junctions [4,6]. This disruption of the intestinal barrier, often referred to as "leaky gut," facilitates the translocation of lipopolysaccharides (LPS) and bacterial products into the bloodstream, triggering systemic inflammatory response syndrome (SIRS) and further aggravating renal microvascular injury [1,8]. Furthermore, the altered colonic environment favors the proliferation of proteolytic bacteria over saccharolytic species, producing pre-toxins such as indole and *p*-cresol that are absorbed and converted by the liver into potent circulating toxins like indoxyl sulfate (IS) and *p*-cresyl sulfate (PCS) [9,10].

Although the "gut-kidney axis" has been investigated predominantly in chronic kidney disease (CKD) populations within Western and East Asian cohorts [6,11], baseline gut microbial structures are strongly influenced by geographical location, ethnicity, and regional dietary patterns [12]. Indian populations frequently exhibit distinct baseline microbiota profiles rich in *Prevotella* due to high dietary fiber and plant-based carbohydrate intake [13,14]. How these unique baseline microbial architectures respond to acute uremic stress remains understudied. Therefore, this study aimed to profile the compositional characteristics, diversity changes, and metabolic correlations of the gut microbiome in Indian patients presenting with acute uremia.

2. Materials and Methods

2.1 Study Design and Ethical Considerations

This prospective cross-sectional case-control study was conducted at Shri Shankaracharya Institute of Medical Sciences (SSIMS), Bhilai, Chhattisgarh, India, between January 2025 and December 2025. The Institutional Human Ethics Committee (IHEC) of SSIMS approved the study protocol prior to initiation. Written informed consent was obtained from all participants or their legally authorized representatives prior to sample enrollment, in accordance with the Declaration of Helsinki and ICMR National Ethical Guidelines (2017).

2.2 Patient Recruitment and Selection Criteria

A total of 60 adult patients (aged ≥ 18 years) presenting to the emergency or nephrology services with acute uremia secondary to AKI (KDIGO Stage 3) were consecutively recruited. KDIGO Stage 3 AKI was defined as any of the following: (1) increase in serum creatinine to ≥ 3.0 times baseline within 7 days; (2) increase in serum creatinine to ≥ 4.0 mg/dL (≥ 353.6 µmol/L); (3) initiation of renal replacement therapy. Acute uremia was defined as KDIGO Stage 3 AKI with blood urea nitrogen ≥ 60 mg/dL and/or presence of uremic symptoms.

Exclusion criteria

- Established end-stage renal disease (ESRD) on chronic maintenance hemodialysis or peritoneal dialysis prior to presentation.
- Active gastrointestinal malignancies, inflammatory bowel disease (IBD), or history of major bowel resection.
- Consumption of systemic broad-spectrum antibiotics, commercial probiotics, prebiotics, or immunosuppressive therapy within 4 weeks prior to hospital admission.
- Active acute gastroenteritis or underlying chronic liver cirrhosis.

Patients with pre-existing CKD (non-ESRD) were included if they met KDIGO Stage 3 criteria for acute deterioration. Pre-existing CKD was defined as eGFR < 60 mL/min/1.73 m² for ≥ 3 months prior to admission or documented structural kidney damage.

For comparison, 60 age-, sex-, and BMI-matched healthy individuals were recruited from outpatient clinics and community volunteer drives. Controls were frequency-matched to cases on age (± 5 years), sex (exact), and BMI (± 2 kg/m²). Healthy controls had normal renal function (eGFR > 90 mL/min/1.73 m²), no history of chronic medical illness, and no recent antibiotic or probiotic usage.

2.3 Sample Collection and Clinical Parameters

Fecal samples were collected from uremic patients within 24–48 hours of admission. Among the 60 patients, 37 (61.7%) had samples collected before any in-hospital antibiotic administration; 23 (38.3%) received empirical antibiotics before sample collection (ceftriaxone n = 12, piperacillin-tazobactam n = 7, meropenem n = 2, other n = 2; median time from first dose to collection: 18 hours, IQR 12–24 hours). A sensitivity analysis excluding these 23 patients confirmed that principal findings remained significant. Samples were collected in sterile, DNA-free containers, immediately transported on ice to the laboratory, aliquoted into cryovials, and frozen at −80°C until processing.

Clinical and demographic parameters including blood urea nitrogen (BUN), serum creatinine, serum electrolytes, serum albumin, complete blood counts, and C-reactive protein (CRP) were recorded at admission.

2.4 Serum Uremic Toxin Quantification

Total serum concentrations (free plus protein-bound fractions) of indoxyl sulfate (IS) and *p*-cresyl sulfate (PCS) were quantified using High-Performance Liquid Chromatography (HPLC) coupled with fluorescence detection (Agilent Technologies 1260 Infinity II), following protein precipitation with acetonitrile according to validated protocols adapted from Meijers et al. [15]. The assay was validated with intra-day CV < 5%, inter-day CV < 8%, and recovery 92–105%. Serum concentrations are reported in μmol/L.

2.5 DNA Extraction and 16S rRNA High-Throughput Sequencing

Total genomic DNA was extracted from 200 mg of stool using the QIAamp PowerFecal Pro DNA Kit (Qiagen, Hilden, Germany) following the manufacturer's instructions. DNA concentration and purity were assessed using a NanoDrop 2000 Spectrophotometer (Thermo Fisher Scientific) and Qubit 4.0 Fluorometer (Invitrogen). The hypervariable V3–V4 regions of the bacterial 16S rRNA gene were amplified using universal primers:

Forward (341F): 5'-CCTACGGGNGGCWGCAG-3'
Reverse (805R): 5'-GACTACHVGGGTATCTAATCC-3'

Amplicon libraries were prepared using the Illumina Metagenomic Sequencing Library Preparation protocol, dual-indexed with Nextera XT Index Kit, and sequenced on an Illumina MiSeq platform (Illumina, San Diego, CA, USA) utilizing 2 × 300 bp paired-end chemistry.

2.6 Bioinformatic and Statistical Analysis

Raw fastq reads were demultiplexed and processed using Quantitative Insights Into Microbial Ecology 2 (QIIME 2, version 2023.9). Quality filtering, denoising, dereplication, and chimera removal were executed using the DADA2 pipeline to generate Amplicon Sequence Variants (ASVs). Taxonomic classification of ASVs was performed using a Naive Bayes classifier trained on the SILVA 138.1 reference database at 99% identity.

Alpha diversity metrics (Chao1, Observed Features, Shannon index, and Faith's Phylogenetic Diversity) were calculated after rarefying samples to an even depth. Beta diversity was evaluated using weighted and unweighted UniFrac distance matrices, visualized via Principal Coordinate Analysis (PCoA).

Statistical evaluations were conducted in R software (v4.3.2). Continuous parametric variables were expressed as mean ± standard deviation (SD) and compared using Student's *t*-test. Non-parametric data were presented as median with interquartile range (IQR) and analyzed via the Mann-Whitney U test. Differences in beta-diversity matrices were tested using Permutational Multivariate Analysis of Variance (PERMANOVA/ADONIS, 999 permutations). Differential abundance of taxa between groups was analyzed using Analysis of Compositions of Microbes with Bias Correction (ANCOM-BC) and Linear Discriminant Analysis Effect Size (LEfSe; logarithmic LDA score threshold > 3.5). Spearman's rank correlation was performed to correlate microbial abundance with serum parameters. p-value < 0.05 (adjusted for false discovery rate [FDR] where applicable) was considered statistically significant.

2.7 Bias Control

Potential confounding by age, sex, and BMI was addressed through frequency matching. Consecutive case recruitment and prespecified exclusion criteria were used to reduce selection bias, and the potential influence of antibiotics administered after hospital admission was examined in a sensitivity analysis.

3. Results

3.1 Baseline Demographic and Clinical Profile

The demographic features and clinical biochemical characteristics of the acute uremia cohort (n = 60) and healthy control cohort (n = 60) are summarized in Table 1. Both groups were well-matched regarding age (51.4 ± 12.3 vs. 49.8 ± 11.6 years), sex distribution (58.3% vs. 56.7% male), and BMI (23.5 ± 3.1 vs. 23.1 ± 2.8 kg/m²). As anticipated, patients with acute uremia demonstrated elevated levels of blood urea nitrogen, serum creatinine, C-reactive protein, and circulating uremic toxins (IS and PCS) compared to healthy controls ($p < 0.001$ for all).

Among the 60 acute uremia cases, 19 (31.7%) had pre-existing CKD (Stage 3a: 8; Stage 3b: 7; Stage 4: 4). No significant interaction between CKD status and microbiome composition was observed (PERMANOVA $p = 0.34$).

Table 1. Baseline clinical and biochemical parameters of study participants

Parameter	Healthy Controls (n = 60)	Acute Uremia (n = 60)	p-value
Age (years)	49.8 ± 11.6	51.4 ± 12.3	0.462
Sex (Male/Female)	34/26	35/25	0.854
Body Mass Index (kg/m²)	23.1 ± 2.8	23.5 ± 3.1	0.458
Serum Creatinine (mg/dL)	0.84 ± 0.18	6.72 ± 2.41	< 0.001
Blood Urea Nitrogen (mg/dL)	13.2 ± 3.4	88.5 ± 26.3	< 0.001
C-Reactive Protein (mg/L)	1.8 ± 0.9	42.6 ± 18.5	< 0.001
Serum Indoxyl Sulfate (µmol/L)	1.24 ± 0.45	48.3 ± 16.2	< 0.001
Serum *p*-Cresyl Sulfate (µmol/L)	3.15 ± 1.12	62.8 ± 21.4	< 0.001

Values are mean ± SD or counts. *p*-values are from Student's *t*-test or the chi-square test, as appropriate.

3.2 Loss of Microbial Diversity in Acute Uremia

Profiling of 16S rRNA sequences demonstrated a sharp decrease in gut microbial richness and diversity in acute uremia. Within-sample (α-diversity) indices revealed significant reductions in uremic patients relative to controls:

- Chao1 Richness Index: 214.5 (IQR 178–245) vs. 342.1 (IQR 310–385), $p < 0.001$
- Shannon Diversity Index: 3.82 ± 0.54 vs. 5.21 ± 0.42, $p < 0.001$
- Faith's Phylogenetic Diversity: 12.4 ± 2.1 vs. 21.8 ± 3.2, $p < 0.001$

Between-sample diversity (β-diversity) analysis showed structural divergence between the intestinal communities of uremic patients and healthy controls. Principal Coordinate Analysis (PCoA) based on weighted UniFrac distances demonstrated distinct spatial separation along the primary axis (PC1 explaining 38.4% of variance; PERMANOVA $F = 28.4$, $p = 0.001$).

3.3 Taxonomic Restructuring at Phylum and Family Levels

Analysis of taxonomic profiles revealed structural alterations across multiple taxonomic ranks. At the phylum level, healthy Indian controls displayed a profile dominated by Firmicutes (51.2%), Bacteroidetes (38.6%), Actinobacteria (5.4%), and Proteobacteria (3.8%).

In contrast, patients with acute uremia exhibited:

- A marked expansion of Proteobacteria (21.4% vs. 3.8%, FDR-adjusted $p < 0.001$)
- A decline in Firmicutes (34.1% vs. 51.2%, FDR-adjusted $p < 0.001$)
- A shift in the Firmicutes-to-Bacteroidetes (F/B) ratio from 1.33 in healthy controls to 0.89 in uremic patients ($p = 0.004$)

At the family level, uremic samples showed significant enrichments in Enterobacteriaceae ($p < 0.001$), Streptococcaceae ($p < 0.001$), and Enterococcaceae ($p = 0.002$). Conversely, obligate anaerobic families responsible for fiber fermentation and mucosal health were depleted, including Ruminococcaceae ($p < 0.001$), Lachnospiraceae ($p < 0.001$), and Bifidobacteriaceae ($p < 0.01$).

3.4 Genus-Level Biomarkers and Functional Pathways

Linear Discriminant Analysis Effect Size (LEfSe) identified key taxa discriminating the two groups (Figure 1).

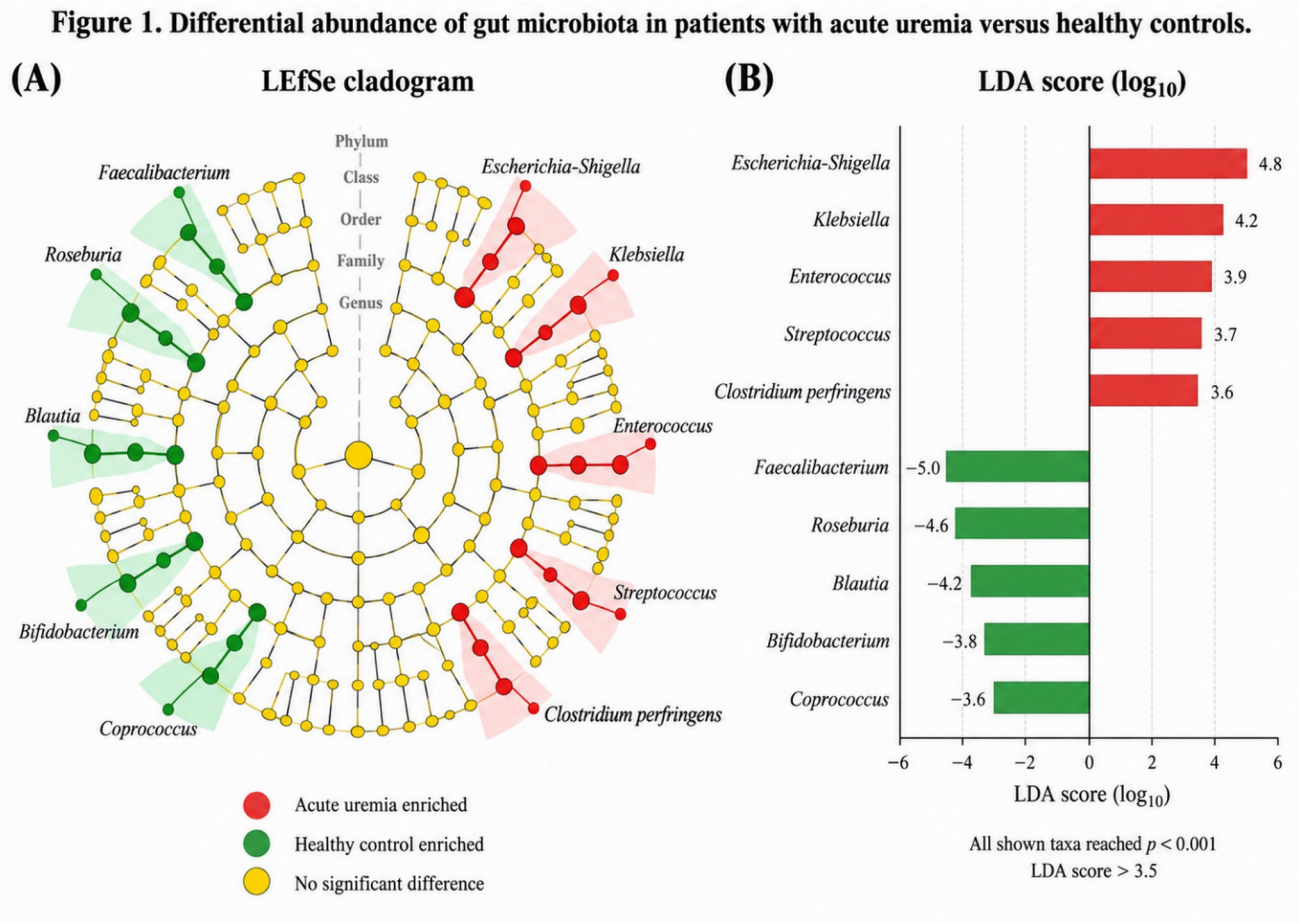

Figure 1. Differential abundance of gut microbiota in patients with acute uremia versus healthy controls. (A) Linear Discriminant Analysis Effect Size (LEfSe) cladogram showing taxonomic hierarchy from phylum to genus level. Red regions indicate taxa enriched in acute uremia; green regions indicate taxa enriched in healthy controls; yellow indicates taxa with no significant difference. (B) LDA score bar plot showing discriminative taxa with LDA score > 3.5 (log10). Bars extending to the right represent taxa enriched in acute uremia (*Escherichia-Shigella*, *Klebsiella*, *Enterococcus*, *Streptococcus*, and *Clostridium perfringens*); bars extending to the left represent taxa depleted in acute uremia (*Faecalibacterium*, *Roseburia*, *Blautia*, *Bifidobacterium*, and *Coprococcus*). All shown taxa reached $p < 0.001$.

Enriched in Acute Uremia (LDA score > 3.5, p < 0.001):

- *Escherichia-Shigella*
- *Klebsiella*
- *Enterococcus*
- *Streptococcus*
- *Clostridium perfringens*

Depleted in Acute Uremia (LDA score > 3.5, p < 0.001):

- *Faecalibacterium* (specifically *Faecalibacterium prausnitzii*)
- *Roseburia*
- *Blautia*
- *Bifidobacterium*
- *Coprococcus*

Functional profiling via PICRUSt2 mapped to MetaCyc pathways indicated significant upregulation of genes encoding microbial ureases (e.g., EC 3.5.1.5), tryptophanase (EC 4.1.99.1, involved in indole biosynthesis), and tyrosine phenol-lyase in the uremic microbiome. Conversely, pathways involved in short-chain fatty acid biosynthesis (acetyl-CoA pathway and pyruvate fermentation to propionate/butyrate) were downregulated ($p < 0.001$). These functional predictions should be interpreted with caution as they are inferred from 16S rRNA gene data rather than directly measured.

3.5 Correlations Between Microbiota and Clinical Parameters

Spearman rank correlation analysis demonstrated associations between specific bacterial genera and circulating biochemical indicators of uremia (Table 2).

Table 2. Spearman rank correlation coefficients (ρ) between key bacterial genera and biochemical markers

Bacterial Genus	Blood Urea Nitrogen	Serum Creatinine	Indoxyl Sulfate	p-Cresyl Sulfate	C-Reactive Protein
Escherichia-Shigella	+0.64***	+0.58***	+0.71***	+0.62***	+0.53***
Klebsiella	+0.52***	+0.49***	+0.55***	+0.48***	+0.41**
Enterococcus	+0.43**	+0.38**	+0.41**	+0.39**	+0.36**
Faecalibacterium	−0.61***	−0.55***	−0.68***	−0.63***	−0.48***
Roseburia	−0.54***	−0.51***	−0.59***	−0.57***	−0.42**
Bifidobacterium	−0.46**	−0.42**	−0.48**	−0.45**	−0.35*

Significance: *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$. p-values are FDR-adjusted for multiple comparisons.

4. Discussion

This study provides a detailed 16S rRNA sequencing-based characterization of the gut microbiome in Indian patients with acute uremia secondary to severe AKI. The data demonstrate that acute uremia is accompanied by intestinal dysbiosis characterized by a severe loss of microbial diversity, expansion of aerobic and facultative anaerobic pathobionts (Proteobacteria), and collapse of beneficial SCFA-producing commensals (Firmicutes).

Our findings align with and build upon global studies of the gut-kidney axis in renal injury [1,6,11]. The observed reduction in α-diversity reflects a disrupted colonic microenvironment. Under normal physiological conditions, the colonic lumen maintains a low oxygen tension that favors strict anaerobic fermenters. In acute uremia, the rapid flux of urea into the gut lumen and its breakdown into ammonia by bacterial ureases elevates luminal pH and disrupts epithelial mucosal integrity [2,4]. The resulting tissue hypoxia, microvascular ischemia, and mucosal edema create a niche favorable for facultative anaerobes—notably Enterobacteriaceae (e.g., *Escherichia-Shigella*, *Klebsiella*)—at the expense of obligate anaerobes like *Faecalibacterium prausnitzii* [3,10].

A key observation in this study is the correlation between specific microbial taxa and circulating protein-bound uremic toxins (indoxyl sulfate and *p*-cresyl sulfate). Indoxyl sulfate is derived from dietary tryptophan, which is converted by bacterial tryptophanase into indole, subsequently absorbed and sulfated in the liver [9,16]. *p*-Cresyl sulfate originates from the bacterial fermentation of tyrosine and phenylalanine into *p*-cresol [10]. The expansion of Enterobacteriaceae and *Clostridium* species, which harbor high tryptophanase and amino acid decarboxylase activity, was associated with elevated serum IS and PCS levels in our patient cohort. These toxins are known to induce renal tubular cell apoptosis, interstitial fibrosis, and vascular endothelial damage, potentially establishing a destructive feedback loop that hampers renal recovery [8,9].

Conversely, the depletion of SCFA-producing organisms (*Faecalibacterium*, *Roseburia*, *Blautia*) highlights the loss of homeostatic signals. SCFAs, particularly butyrate, serve as the primary energy source for colonocytes and reinforce intestinal tight junction complexes (Claudin-1, Occludin, ZO-1) [7]. Butyrate also interacts with G-protein-coupled receptors (GPR41/GPR43) on immune cells to inhibit NF-κB pathways, suppressing pro-inflammatory cytokine expression [5]. The marked loss of SCFA producers observed in our cohort may contribute to systemic hyper-inflammation (elevated CRP) and intestinal hyperpermeability in acute uremia.

The findings from this Indian cohort offer a regional perspective. Indian populations typically possess a baseline microbiome enriched in *Prevotella* and plant-starch fermenting machinery due to high dietary carbohydrate and fiber contents [13,14]. Despite this dietary baseline, acute uremic stress induced shifts that mirror those seen in Western cohorts, including Proteobacteria overgrowth and Firmicutes suppression [6]. This suggests that acute uremic toxicity acts as a strong environmental driver capable of overcoming baseline geographical microbial variations.

4.1 Therapeutic Implications

These results point toward potential adjuvant therapeutic approaches targeting the gut-kidney axis in acute uremia:

- **Targeted Prebiotics and Synbiotics:** Administration of fiber formulations paired with SCFA-producing strains (e.g., *Bifidobacterium* spp., *Lactobacillus* spp.) may help restore intestinal barrier integrity and suppress pathobiont growth [17,18].
- **Oral Uremic Toxin Adsorbents:** Intestinal adsorbents such as AST-120 (spherical carbon adsorbent) can bind luminal indole and pre-toxins, reducing systemic IS load and potentially attenuating renal damage [9,19].

- **Urease Inhibitors and Microbiome Editing:** Selective inhibition of bacterial ureases or targeted bacteriophage therapy against expansion-prone Enterobacteriaceae offers potential pathways to stabilize colonic pH and prevent epithelial breakdown [3,16].

4.2 Limitations

Several limitations should be considered when interpreting our findings:

- **Cross-Sectional Design:** The cross-sectional nature precludes definitive conclusions regarding causality—whether gut dysbiosis directly accelerates acute uremia or is solely a secondary metabolic consequence.
- **16S rRNA Resolution:** 16S rRNA gene sequencing offers limited taxonomic resolution at the species and strain levels compared to shotgun metagenomic sequencing, and functional pathways were predicted rather than directly sequenced.
- **Dietary Confounders:** While healthy controls were matched for demographic parameters, precise daily dietary nutrient logging was not performed during the acute phase of illness.
- **Antibiotic Exposure:** Although pre-admission antibiotic use was an exclusion criterion, 38.3% of patients received in-hospital antibiotics before sample collection. Sensitivity analysis suggested this did not drive the observed dysbiosis, but residual confounding cannot be excluded.

5. Conclusion

Patients with acute uremia in India display gut microbial dysbiosis marked by reduced α-diversity, an altered Firmicutes-to-Bacteroidetes ratio, expansion of pathobionts (Enterobacteriaceae, Streptococcaceae), and depletion of beneficial SCFA producers (*Faecalibacterium*, *Roseburia*, *Bifidobacterium*). The abundance of pathobionts correlates with circulating levels of indoxyl sulfate, *p*-cresyl sulfate, and systemic inflammatory markers. Therapeutic interventions aimed at modulating the gut microbiome present a promising strategy to mitigate uremic toxicity and improve clinical outcomes in acute renal failure.

Declarations

Ethics approval and consent to participate: This study was approved by the Institutional Human Ethics Committee of Shri Shankaracharya Institute of Medical Sciences, Bhilai, Chhattisgarh, India. Written informed consent was obtained from all participants or their legally authorized representatives before enrollment, in accordance with the Declaration of Helsinki.

Consent for publication: Not applicable. The article does not contain identifiable individual participant data.

Data availability: The raw 16S rRNA gene sequencing reads are not publicly available because institutional data-governance policies require a formal data-sharing agreement. De-identified processed data (OTU/ASV tables, taxonomic assignments, and metadata) and R scripts are available from the corresponding author on reasonable request. Requests will be reviewed by the Institutional Human Ethics Committee and the corresponding author to ensure participant privacy. Raw sequence data may be shared under a formal data-transfer agreement for non-commercial research.

Conflicts of interest: The authors declare no conflicts of interest.

Funding: No external funding was received. The research was conducted using institutional resources.

Author contributions: Jaya Chandnani: conceptualization, methodology, investigation, data curation, formal analysis, writing - original draft, writing - review and editing, and project administration. Ruhneet Kaur: conceptualization, methodology, validation, resources, writing - review and editing, and supervision. Both authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Acknowledgements: The authors thank the patients and healthy volunteers who participated in this study; the Department of Nephrology and Emergency Department at SSIMS for assistance with participant recruitment; and the laboratory staff for technical assistance with 16S rRNA sequencing and bioinformatics analysis.

AI-assisted technology declaration: The authors did not use artificial intelligence tools for the design, data collection, analysis, interpretation, or drafting of this manuscript.

References

1. Chou YT, Kan WC, Shiao CC. Acute kidney injury and gut dysbiosis: a narrative review focus on pathophysiology and treatment. Int J Mol Sci. 2022;23(7):3658. doi:10.3390/ijms23073658.

2. Rysz J, Franczyk B, Ławiński J, Olszewski R, Ciałkowska-Rysz A, Gluba-Brzózka A. The impact of CKD on uremic toxins and gut microbiota. Toxins (Basel). 2021;13(4):252. doi:10.3390/toxins13040252.

3. Cao C, Zhu H, Yao Y, Zeng R. Gut dysbiosis and kidney diseases. Front Med (Lausanne). 2022;9:829349. doi:10.3389/fmed.2022.829349.

4. Ramezani A, Massy ZA, Meijers B, Evenepoel P, Vanholder R, Raj DS. Role of the gut microbiome in uremia: a potential therapeutic target. Am J Kidney Dis. 2016;67(3):483-496. doi:10.1053/j.ajkd.2015.09.027.

5. Kobayashi T, Iwata Y, Nakade Y, Wada T. Significance of the gut microbiota in acute kidney injury. Toxins (Basel). 2021;13(6):369. doi:10.3390/toxins13060369.

6. Vaziri ND, Wong J, Pahl MV, Piceno YM, Yuan J, DeSantis TZ, et al. Chronic kidney disease alters intestinal microbial flora. Kidney Int. 2013;83(2):308-315. doi:10.1038/ki.2012.345.

7. Andrade-Oliveira V, Amano MT, Correa-Costa M, Castoldi A, Felizardo RJ, de Almeida DC, et al. Gut bacteria products prevent acute kidney injury through gut-kidney axis regulation. J Am Soc Nephrol. 2015;26(8):1877-1888. doi:10.1681/ASN.2014060575.

8. Meijers BK, Evenepoel P. The gut-kidney axis: indoxyl sulfate, p-cresyl sulfate and CKD progression. Nephrol Dial Transplant. 2011;26(3):759-761. doi:10.1093/ndt/gfq818.

9. Niwa T. Uremic toxicity of indoxyl sulfate. Nagoya J Med Sci. 2010;72(1-2):1-11.

10. Gryp T, Vanholder R, Vaneechoutte M, Glorieux G. p-Cresyl sulfate. Toxins (Basel). 2017;9(2):52. doi:10.3390/toxins9020052.

11. Wang X, Yang S, Li S, Zhao L, Hao Y, Qin J, et al. Aberrant gut microbiota alters host metabolome and impacts renal failure in humans and rodents. Gut. 2020;69(12):2131-2142. doi:10.1136/gutjnl-2019-319766.

12. Yatsunenko T, Rey FE, Manary MJ, Trehan I, Dominguez-Bello MG, Contreras M, et al. Human gut microbiome viewed across age and geography. Nature. 2012;486(7402):222-227. doi:10.1038/nature11053.

13. Dhakan DB, Maji A, Sharma AK, Saxena R, Pulikkan J, Grace T, et al. The unique composition of Indian gut microbiome, gene catalogue, and associated faecal metabolome deciphered using multi-omics approaches. Gigascience. 2019;8(3):giz004. doi:10.1093/gigascience/giz004.

14. Bhute S, Pande P, Shetty SA, Shete A, Sharma A, Sivapalasingam S, et al. Molecular characterization and meta-analysis of gut microbial communities illustrate enrichment of Prevotella and Megasphaera in Indian subjects. Front Microbiol. 2016;7:660. doi:10.3389/fmicb.2016.00660.

15. Meijers BK, Bammens B, de Loor H, Evenepoel P, Verbeke K, Vanrenterghem Y. Free p-cresol is associated with cardiovascular disease in hemodialysis patients. Kidney Int. 2008;73(10):1174-1180. doi:10.1038/ki.2008.31.

16. Devlin AS, Marcobal A, Dodd D, Nayak RR, Banerjee NA, Lober U, et al. Modulation of a circulating uremic solute via rational genetic manipulation of the gut microbiota. Cell Host Microbe. 2016;20(6):709-715. doi:10.1016/j.chom.2016.10.021.

17. Ranganathan N, Ranganathan P, Friedman EA, Joseph A, Delano B, Goldfarb DS, et al. Pilot study of probiotic dietary supplementation for promoting healthy kidney function in patients with chronic kidney disease. Adv Ther. 2010;27(9):634-647. doi:10.1007/s12325-010-0059-9.

18. Rossi M, Johnson DW, Morrison M, Pascoe EM, Coombes JS, Forbes JM, et al. Synbiotics easing renal failure by improving gut microbiology (SYNERGY): a randomized trial. Clin J Am Soc Nephrol. 2016;11(2):223-231. doi:10.2215/CJN.05240515.

19. Schulman G, Berl T, Beck GJ, Remuzzi G, Ritz E, Arita K, et al. Randomized placebo-controlled EPPIC trials of AST-120 in CKD. J Am Soc Nephrol. 2015;26(7):1732-1746. doi:10.1681/ASN.2014010042.