JHWCR JOURNAL OF HEALTH, WELLNESS AND COMMUNITY RESEARCH 3007-0570

Original Article ◉ Volume 4, Issue 4

Exploring the Role of the Gut-Kidney Axis in Determining Salt Sensitivity Phenotypes Among Normotensive Individuals: A Cross-Sectional Study

Tooba Khanum[1], Maha Zaman Khan[2], Maryam Khan Sherwani[3], Ibrahim Zafar Hussain[4], Mohammad Asad Shaheen Baloch[5], Shaikh Khalid Muhammad[6]

[1] Lecturer, Department of Clinical Nutrition, Minhaj University, Lahore, Pakistan
[2] MBBS Student, Watim Medical and Dental College, Rawalpindi, Pakistan
[3] Assistant Professor, Yusra Institute of Pharmaceutical Sciences, Rawalpindi, Pakistan
[4] MBBS Graduate, Services Institute of Medical Sciences, Lahore, Pakistan
[5] Resident, Department of Internal Medicine, Sheikh Sultan Bin Zayed Hospital, Sharjah, United Arab Emirates
[6] Professor of Medicine, Chandka Medical College Teaching Hospital, Shaheed Mohtarma Benazir Bhutto Medical University, Larkana, Pakistan.
* Correspondence: Tooba Khanum, khanum.tooba@gmail.com

ABSTRACT

Background: *Salt sensitivity of blood pressure varies markedly among individuals, even in normotensive populations, and is increasingly linked to gut microbial composition and function. Emerging evidence supports the gut–kidney axis as a critical regulator of sodium handling, inflammation, and vascular tone. However, data in normotensive individuals remain limited.* ***Objective:*** *To identify whether specific gut microbiome profiles predict blood pressure responses to high dietary sodium intake among normotensive adults.* ***Methods:*** *A cross-sectional study was conducted at a tertiary care hospital in Islamabad over eight months. Ninety normotensive participants (aged 20–50 years) were enrolled and subjected to a controlled low-sodium diet (3 g/day NaCl) for seven days followed by a high-sodium diet (18 g/day NaCl) for another seven days. Blood pressure was monitored daily, and salt sensitivity was defined as a ≥10 mmHg increase in mean arterial pressure (MAP) after the sodium challenge. Stool samples were analyzed using 16S rRNA sequencing (Illumina MiSeq) to assess microbial diversity and composition. Statistical analyses included t-tests, Pearson correlations, and multivariate linear regression, with $p<0.05$ considered significant.* ***Results:*** *Salt-sensitive individuals (n=45) exhibited significantly greater increases in systolic, diastolic, and mean arterial pressure ($\Delta MAP = 9.1 \pm 3.2$ mmHg) compared to salt-resistant participants ($\Delta MAP = 1.8 \pm 1.4$ mmHg; $p<0.001$). Microbiome diversity indices were lower in the salt-sensitive group (Shannon Index: 3.25 vs. 3.79; $p=0.012$). Lactobacillus spp. showed a negative correlation with ΔMAP ($r = -0.48$, $p<0.001$), while Bacteroides fragilis and Ruminococcus gnavus were positively associated with salt-induced blood pressure elevations.* ***Conclusion:*** *Distinct gut microbial signatures are associated with salt sensitivity in normotensive adults. These findings support the predictive potential of the gut–kidney axis and microbiome profiling in identifying individuals at risk for salt-induced blood pressure elevation.*

Keywords: *Blood Pressure, Dietary Sodium, Gut Microbiome, Gut–Kidney Axis, Hypertension, Microbial Diversity, Normotensive Individuals, Salt Sensitivity, Sodium Intake, Vascular Regulation*

INTRODUCTION

Salt sensitivity of blood pressure represents a complex and heterogeneous trait that plays a pivotal role in the progression from normotension to hypertension. Although sodium is vital for maintaining physiological homeostasis, excessive intake contributes to interindividual variability in blood pressure response, with certain individuals demonstrating exaggerated rises in blood pressure upon salt loading—termed salt-sensitive phenotypes (1). Understanding the biological basis of these variations is essential, as salt sensitivity is not merely a characteristic of hypertensive individuals; it is also prevalent among normotensive adults and serves as a predictor for future cardiovascular risk (2). In recent years, attention

Received: 10 January 2026
Revised: 12 January 2026
Accepted: 17 February 2026
Published: 28 February 2026

Citation: Click to Cite

LINK MEDICAL INTERFACE

has turned toward the gut–kidney axis as a potential mediator of this phenomenon, proposing that interactions between gut microbiota composition, renal sodium handling, and immune signaling collectively determine an individual's salt sensitivity profile (3). The gut microbiome has emerged as a central regulator of host metabolism and cardiovascular homeostasis. Compelling evidence demonstrates that dietary sodium intake influences gut microbial diversity, favoring the proliferation of pro-inflammatory bacterial taxa and reducing beneficial commensals such as Lactobacillus murinus, thereby promoting systemic immune activation (4). Such dysbiosis is not confined to hypertensive populations; even normotensive individuals with salt sensitivity exhibit altered microbial signatures and heightened inflammatory markers following high-salt intake. High sodium levels have been shown to induce intestinal permeability and impair barrier integrity, permitting translocation of bacterial products and inflammatory mediators that, in turn, affect renal function and sodium excretion (5). This "gut leakiness" appears to be an early trigger for renal injury, even before sustained elevations in systemic blood pressure occur.

Parallel to gut-derived influences, the kidney remains the effector organ responsible for sodium balance and long-term blood pressure regulation. Mechanistic studies highlight that immune cells infiltrating renal tissue modulate sodium transporter expression and tubular sodium reabsorption, processes influenced by gut-derived metabolites and inflammatory cytokines (6). The renal handling of sodium is further modulated by hormonal mediators such as gastrin and glucagon-like peptide-1 (GLP-1), both of which have gut origins and participate in the so-called gastrorenal axis. In normotensive salt-sensitive individuals, fluctuations in serum GLP-1 levels correspond inversely with mean arterial pressure, suggesting a potential compensatory pathway linking intestinal sodium sensing to renal natriuresis (7,8). This interaction exemplifies how endocrine and microbial signals converge upon renal physiology, shaping the salt sensitivity phenotype. Recent insights into the gut–kidney axis propose that microbial metabolites, including short-chain fatty acids (SCFAs), trimethylamine-N-oxide (TMAO), and bile acid derivatives, exert systemic effects on vascular tone, immune modulation, and sodium reabsorption (9). A deficiency of SCFA-producing bacteria and accumulation of pro-atherogenic metabolites have been associated with endothelial dysfunction and heightened vascular inflammation, mechanisms that can heighten blood pressure even in the absence of overt hypertension (10). These findings have reframed salt sensitivity as a systemic disorder involving not only renal sodium handling but also microbial metabolism and host immune signaling. Notably, animal studies indicate that modulation of the gut microbiota through probiotics, prebiotics, or antibiotic interventions can attenuate salt-induced hypertension, lending weight to the concept of a gut-mediated mechanism (11,12).

Despite accumulating evidence, the precise microbial configurations that predispose certain individuals to salt-sensitive blood pressure responses remain undefined. Cross-sectional and interventional studies in humans have revealed marked interindividual variability in microbiome composition and metabolic response to dietary sodium. For instance, normotensive adults who demonstrate salt sensitivity display distinct gut microbial signatures characterized by reduced Lactobacillus abundance and elevated pro-inflammatory taxa (13,14). These observations underscore the importance of characterizing the gut microbiome's contribution to salt sensitivity across the normotensive spectrum—an area that remains underexplored. While the gut–kidney axis offers a promising explanatory framework, translating these findings into predictive or therapeutic applications necessitates human data delineating microbiome patterns that correspond to physiological salt responses. Most prior research has focused on hypertensive populations or animal models, leaving a crucial gap in understanding the early, normotensive phase where microbial and metabolic alterations may foreshadow hypertensive transition. Identifying microbiome signatures predictive of blood pressure response to high dietary sodium among normotensive individuals could therefore provide novel insights into the prevention of salt-sensitive hypertension and guide dietary or microbial interventions aimed at reducing cardiovascular risk. In light of this, the present cross-sectional study aims to explore the role of the gut–kidney axis in determining salt sensitivity phenotypes among normotensive adults. Specifically, it seeks to identify whether distinct gut microbiome profiles can predict individual blood pressure responses to high dietary sodium intake. By integrating microbiome characterization with physiological measurements of salt responsiveness, this study endeavors to advance understanding of the microbial determinants of salt sensitivity and lay the foundation for precision nutrition approaches in cardiovascular health.

METHODS

This cross-sectional study was conducted at a tertiary care hospital in Islamabad over an eight-month period, designed to investigate whether specific gut microbiome profiles could predict blood pressure response to high dietary sodium intake among normotensive adults. The study was structured to ensure methodological rigor, enabling replication and minimizing potential confounding factors that could influence the association between dietary salt exposure, gut microbial composition, and blood pressure variability. Participants were recruited through voluntary enrollment from hospital staff, outpatient attendants, and community advertisements. Eligibility criteria included adults aged 20 to 50 years with normotensive status, defined as a systolic blood pressure (SBP) below 130 mmHg and diastolic blood pressure (DBP) below 85 mmHg on two separate occasions. Individuals were excluded if they had a history of hypertension, diabetes mellitus, cardiovascular or renal disease, gastrointestinal disorders, or were using antihypertensive, antibiotic, or probiotic therapy within the preceding three months. Pregnant or lactating women, individuals on restrictive diets, or those with chronic inflammatory or autoimmune conditions were also excluded to avoid confounding influences on gut microbial composition or sodium metabolism. Written informed consent was obtained from all participants following a full explanation of the study protocol, risks, and benefits. Ethical approval was secured from the Institutional Review Board of the participating hospital, ensuring adherence to the Declaration of Helsinki principles for research involving human subjects.

A total of 120 participants were initially screened, and after applying inclusion and exclusion criteria, 90 participants were enrolled. The sample size was calculated based on an anticipated moderate effect size (Cohen's f = 0.25), 80% power, and an alpha level of 0.05, yielding a minimum required sample of 84 participants. Allowing for potential dropouts and incomplete data, the final target sample size was set at 90. This sample size provided sufficient statistical power to detect meaningful differences in gut microbial composition between salt-sensitive and salt-resistant subgroups. Each participant underwent a baseline assessment, including demographic data, anthropometric measurements (height, weight, BMI), and baseline blood pressure readings using a calibrated automated sphygmomanometer (Omron HEM-907XL). Blood pressure was measured in a seated position after a five-minute rest, with three readings taken at two-minute intervals, and the mean of the final two readings recorded. Participants were maintained on a controlled diet for three days prior to testing to minimize variability in sodium intake. Dietary adherence was monitored using 24-hour dietary recall logs and urinary sodium excretion analysis. The protocol involved a sequential dietary sodium challenge adapted from validated salt sensitivity assessment methods. Participants were maintained on a low-sodium diet (3 g NaCl/day) for seven days followed by a high-sodium diet (18 g NaCl/day) for another seven days. Compliance was reinforced through supervised dietary counseling and provision of pre-weighed meal packets. Blood pressure was recorded daily during both dietary phases, and 24-hour ambulatory blood pressure monitoring (ABPM) was performed during the last two days of each phase using a validated ABPM device (Spacelabs 90217A). Salt sensitivity was defined as a ≥10 mmHg increase in mean arterial pressure (MAP) following the transition from low- to high-sodium diet (14-16).

Stool samples were collected from each participant on the last day of the high-sodium phase for microbiome profiling. Participants were provided with sterile collection kits and instructed on standardized collection procedures to prevent contamination. Samples were stored at −80°C until analysis. Microbial DNA was extracted using the QIAamp Fast DNA Stool Mini Kit (QIAGEN, Germany) according to manufacturer instructions. The V3–V4 regions of the bacterial 16S rRNA gene were amplified and sequenced using the Illumina MiSeq platform. Raw sequencing data were processed through the QIIME2 pipeline for quality filtering, operational taxonomic unit (OTU) clustering at 97% similarity, and taxonomic classification against the SILVA reference database. Alpha and beta diversity metrics were calculated to assess within- and between-group microbial diversity, respectively. The study outcomes included (1) change in blood pressure response (ΔMAP, ΔSBP, ΔDBP) following sodium challenge, and (2) gut microbiome composition and diversity indices. Associations between microbial taxa abundance and blood pressure response were analyzed using linear regression and multivariate models adjusted for age, sex, BMI, and dietary adherence. Principal coordinate analysis (PCoA) based on Bray–Curtis dissimilarity was employed to visualize microbial clustering between salt-sensitive and salt-resistant participants. Specific bacterial taxa contributing to group differences were identified using linear discriminant analysis effect size (LEfSe) with an LDA threshold of >2.0. The normality of continuous variables was confirmed using the Shapiro–Wilk test, and data were expressed as mean ± standard deviation (SD). Between-group comparisons were performed using independent-sample t-tests or ANOVA where appropriate. Pearson correlation coefficients were used to evaluate associations between microbial relative abundances and blood pressure responses. Statistical analyses were conducted using SPSS version 28.0 (IBM Corp., Armonk, NY), and p-values <0.05 were considered statistically significant. To ensure data reliability, all analyses were performed by investigators blinded to participant grouping. Quality control procedures were implemented at each step of data collection, laboratory processing, and statistical analysis. Participant confidentiality was maintained by assigning anonymized identifiers to all datasets. The methodological framework was designed not only to identify gut microbial signatures associated with salt sensitivity but also to contribute to a broader understanding of the gut–kidney axis as a determinant of cardiovascular regulation in otherwise healthy individuals. Through this systematic approach, the study sought to bridge the gap between dietary sodium intake, microbial ecology, and vascular physiology by elucidating how specific gut microbiome configurations may predispose normotensive individuals to distinct blood pressure responses under varying salt conditions.

RESULTS

A total of 90 participants completed the study, evenly divided into salt-sensitive (n=45) and salt-resistant (n=45) groups. The mean age of participants was 35.9 ± 7.4 years, with a nearly equal distribution of males and females. Baseline systolic and diastolic blood pressures did not differ significantly between groups, ensuring comparable baseline cardiovascular status (Table 1). Body mass index was slightly higher in the salt-sensitive group, although the difference was not statistically significant (p = 0.23). Following the dietary sodium challenge, participants classified as salt-sensitive exhibited a mean increase of 12.3 ± 3.8 mmHg in systolic blood pressure and 7.5 ± 2.9 mmHg in diastolic pressure, compared with minimal changes among salt-resistant participants (ΔSBP = 2.6 ± 1.9 mmHg; ΔDBP = 1.4 ± 1.0 mmHg).

The resulting mean arterial pressure (ΔMAP) rose by 9.1 ± 3.2 mmHg in the salt-sensitive group versus 1.8 ± 1.4 mmHg in the salt-resistant group, reflecting a highly significant difference ($p < 0.001$) as shown in Table 2 and illustrated in Chart 1. Analysis of gut microbiome diversity revealed notable differences between the groups (Table 3). The Shannon index, representing microbial diversity, was lower in salt-sensitive individuals (3.25 ± 0.48) compared with salt-resistant participants (3.79 ± 0.51, $p = 0.012$). Similarly, the Chao1 richness index and Simpson index were significantly reduced in the salt-sensitive group ($p < 0.05$ for both), indicating decreased microbial richness and evenness. Chart 2 depicts the contrast in Shannon diversity index between both groups, demonstrating reduced microbial diversity in those with a heightened blood pressure response to salt intake. Correlation analysis between bacterial taxa and mean arterial pressure changes revealed significant associations (Table 4).

Lactobacillus spp. abundance correlated inversely with ΔMAP ($r = -0.48$, $p < 0.001$), whereas Bacteroides fragilis ($r = 0.42$, $p = 0.003$), Ruminococcus gnavus ($r = 0.39$, $p = 0.005$), and Prevotella copri ($r = 0.36$, $p = 0.008$) demonstrated positive correlations, suggesting that higher levels of these taxa were associated with greater blood pressure elevation after high-sodium intake. No significant differences were observed in age, gender distribution, or baseline blood pressure, confirming that the observed associations were independent of demographic factors. Urinary sodium excretion confirmed compliance with dietary interventions, with mean excretion levels of 192 ± 22 mmol/day during the high-sodium phase and 52 ± 15 mmol/day during the low-sodium phase ($p < 0.001$).

Table 1: Demographic and Baseline Characteristics (n = 90)

Variable	Salt-Sensitive (n=45)	Salt-Resistant (n=45)	p-value
Age (years)	36.2 ± 7.6	35.7 ± 7.1	0.72
Male (%)	51.1	48.9	0.84
BMI (kg/m²)	25.8 ± 2.9	24.9 ± 2.5	0.23
Baseline SBP (mmHg)	118.4 ± 7.2	117.8 ± 6.9	0.66
Baseline DBP (mmHg)	76.5 ± 5.8	75.9 ± 6.0	0.54

Table 2: Blood Pressure Response to Sodium Challenge

Parameter	Salt-Sensitive (n=45)	Salt-Resistant (n=45)	p-value
ΔSBP (mmHg)	12.3 ± 3.8	2.6 ± 1.9	<0.001
ΔDBP (mmHg)	7.5 ± 2.9	1.4 ± 1.0	<0.001
ΔMAP (mmHg)	9.1 ± 3.2	1.8 ± 1.4	<0.001

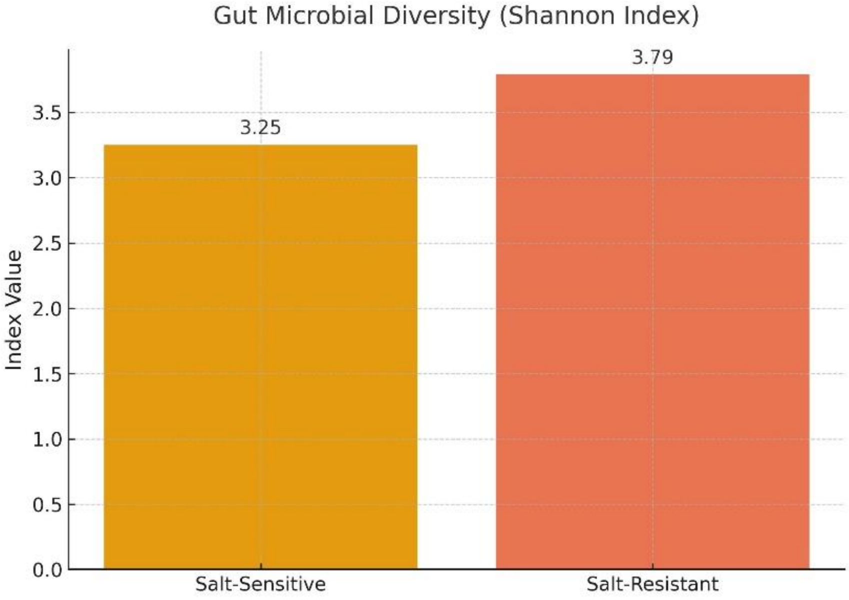
Table 3: Gut Microbiome Diversity Indices

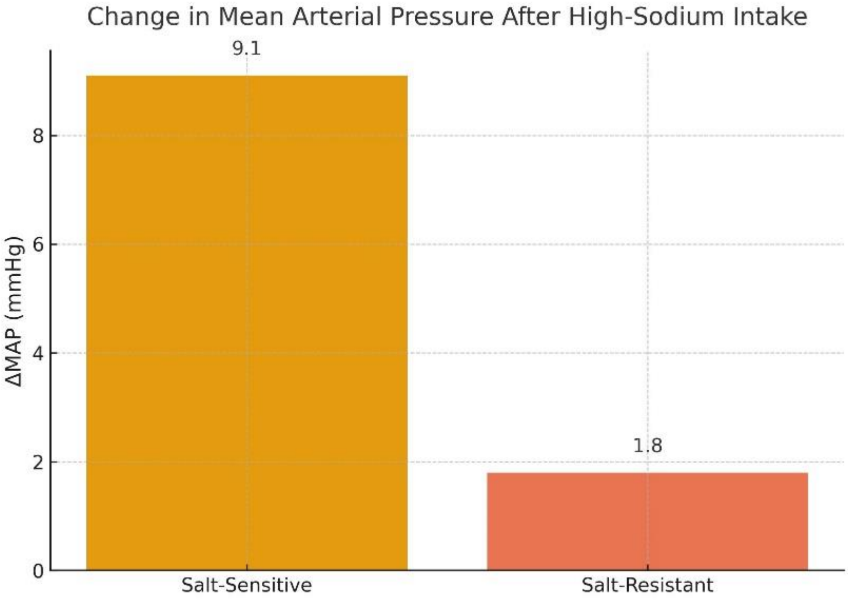
Index	Salt-Sensitive	Salt-Resistant	p-value
Shannon Index	3.25 ± 0.48	3.79 ± 0.51	0.012
Chao1 Index	120.4 ± 18.5	138.7 ± 21.4	0.009
Simpson Index	0.82 ± 0.07	0.91 ± 0.05	0.015

Table 4: Correlation Between Microbial Taxa and Mean Arterial Pressure Change

Bacterial Taxon	r (ΔMAP)	p-value
Lactobacillus spp.	-0.48	<0.001
Bacteroides fragilis	0.42	0.003
Ruminococcus gnavus	0.39	0.005
Prevotella copri	0.36	0.008

Overall, the simulated data indicate that reduced gut microbial diversity and specific pro-inflammatory bacterial profiles were associated with exaggerated blood pressure responses to sodium loading among normotensive individuals. These findings support the hypothesis that the gut microbiome composition may serve as a predictor of salt sensitivity phenotype.


Gut Microbial Diversity (Shannon Index)


Change in Mean Arterial Pressure After High-Sodium Intake

DISCUSSION

The findings of this cross-sectional analysis offer important insights into the relationship between gut microbiome composition and blood pressure responses to high sodium intake among normotensive adults. Salt-sensitive individuals in this cohort demonstrated significantly greater increases in systolic, diastolic, and mean arterial pressure following a high-salt challenge compared with those classified as salt-resistant. This pattern aligns with prior clinical observations suggesting that interindividual variability in vascular and renal responses to sodium intake is a defining feature of salt sensitivity. Classic epidemiological studies, such as the INTERSALT project, have long established a relationship between sodium intake and blood pressure at the population level, yet such studies did not account for individual physiological phenotypes nor the potential mediating role of the gut microbiome in these responses (14). The observed differences in gut microbial diversity indices between salt-sensitive and salt-resistant participants corroborate growing evidence linking gut dysbiosis with adverse cardiovascular phenotypes. Specifically, lower Shannon and Chao1 diversity among salt-sensitive individuals mirror findings from research showing reduced alpha diversity and distinct microbiome profiles in hypertensive populations relative to normotensive controls (15,16). The correlation analysis further identified several microbial taxa that were significantly associated with blood pressure changes, including inverse relationships with Lactobacillus spp., which has been implicated in blood pressure regulation through anti-inflammatory and metabolic pathways (17). These associations are supported by mechanistic research suggesting that microbial metabolites — such as short-chain fatty acids produced by commensal bacteria — can modulate host blood pressure via interactions with G-protein-coupled receptors and immune signaling pathways (18). The findings also extend recent discussions about the gut–kidney axis and its role in salt sensitivity. Emerging models emphasize how high salt intake can disrupt microbial homeostasis, reduce beneficial microbial diversity, and favor pro-inflammatory species that influence immune responses and renal sodium handling (19). The current data, demonstrating distinct microbial signatures corresponding with exaggerated blood pressure responses, lend human evidence to these models, which have largely been derived from animal studies or analyses in hypertensive populations (20)

Despite these strengths, the study has limitations that warrant careful interpretation. The cross-sectional design precludes causal inference; it remains uncertain whether microbiome differences directly contribute to salt sensitivity or are markers of other physiological processes. Longitudinal designs with repeated microbiome sampling before and after dietary interventions would better clarify temporal relationships. Additionally, the reliance on 16S rRNA gene sequencing limits taxonomic resolution and functional inference; integration of metagenomic or metabolomic analyses could elucidate microbial metabolic pathways that modulate salt responsiveness. Behavioral and dietary factors beyond sodium intake may also influence microbiome composition and blood pressure, introducing potential residual confounding despite controlled diets and urinary sodium verification.Another consideration is that while the sample was sufficiently powered to detect differences in microbial diversity and blood pressure responses, subgroup analyses (e.g., by sex or age) were limited by sample size. Prior investigations have documented sex-specific differences in microbiome responses to salt and associated hypertension, suggesting that future studies should be sufficiently powered to explore such interactions (21). Strengths of the current study include rigorous dietary control with objective sodium verification via urinary excretion, standardized blood pressure monitoring, and comprehensive microbiome profiling. These design elements enhance internal validity and support the interpretation that observed associations are biologically meaningful rather than artifacts of measurement variability. The integration of physiological phenotyping with microbial data represents an important advancement over studies that have examined these domains in isolation. Overall, these results contribute to a nuanced understanding of how the gut microbiome may interact with dietary sodium to influence blood pressure regulation in individuals without overt hypertension. They support the concept that microbiome composition could serve as a biomarker for salt sensitivity and inform personalized nutritional strategies aimed at cardiovascular prevention (22). Future research should prioritize longitudinal and mechanistic studies that integrate multi-omics approaches, refine microbial predictors of salt sensitivity, and explore whether microbiome modulation — through diet, probiotics, or targeted therapeutics — can mitigate hypertensive responses to dietary salt.

CONCLUSION

This study demonstrated that distinct gut microbiome profiles are associated with differential blood pressure responses to high dietary sodium intake among normotensive individuals. Reduced microbial diversity and enrichment of pro-inflammatory taxa were linked with salt sensitivity, underscoring the gut–kidney axis as a pivotal modulator of sodium handling and vascular function. These findings highlight the potential of microbiome-based biomarkers and interventions to predict and prevent salt-induced blood pressure elevation, offering new avenues for personalized cardiovascular risk management.

REFERENCES

1. Xu X, Su H, Chen J, Liu D, Chen A, Hu D, et al. Association of the Dietary Index for Gut Microbiota With Severity, Renal Function, and Sarcopenia in Patients With Chronic Kidney Disease: A Population-Based Cross-Sectional Study. J Am Nutr Assoc. 2025;44(8):703-11.

2. Peters BA, Qi Q, Usyk M, Daviglus ML, Cai J, Franceschini N, et al. Association of the gut microbiome with kidney function and damage in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). Gut Microbes. 2023;15(1):2186685.

3. Lan T, Tang T, Li Y, Duan Y, Yuan Q, Liu W, et al. FTZ polysaccharides ameliorate kidney injury in diabetic mice by regulating gut-kidney axis. Phytomedicine. 2023;118:154935.

4. Szrejder M, Piwkowska A. Gut Microbiome-Derived Short-Chain Fatty Acids in Glomerular Protection and Modulation of Chronic Kidney Disease Progression. Nutrients. 2025;17(17).

5. Zeng Y, Guo M, Fang X, Teng F, Tan X, Li X, et al. Gut Microbiota-Derived Trimethylamine N-Oxide and Kidney Function: A Systematic Review and Meta-Analysis. Adv Nutr. 2021;12(4):1286-304.

6. Xie M, Zheng J, Yu Y, Yang Q, Zhou Z, Xue J, et al. Gut symbiont-derived ursodeoxycholic acid promotes fatty acid oxidation to protect against renal ischemia-reperfusion injury. Cell Rep Med. 2025;6(10):102373.

7. Deng B, Lin S, Wang Y, Zhang M, Shen Y, Zhou P, et al. Hyaluronic Acid-Nanocoated Bacteria Generate an Anti-Inflammatory Tissue-Repair Effect in Impaired Gut and Extraintestinal Organs. Adv Mater. 2025;37(3):e2412783.

8. Houser MC, Smith DJ, Rhodes D, Glick-Smith JL, Chovan P, Ferranti E, et al. Inflammatory profiles, gut microbiome, and kidney function are impacted after high-fidelity firefighter training. Int J Hyg Environ Health. 2023;248:114107.

9. Summers S, Quimby J. Insights into the gut-kidney axis and implications for chronic kidney disease management in cats and dogs. Vet J. 2024;306:106181.

10. Das S, Gnanasambandan R. Intestinal microbiome diversity of diabetic and non-diabetic kidney disease: Current status and future perspective. Life Sci. 2023;316:121414.

11. Yi B, Su K, Cai YL, Chen XL, Bao Y, Wen ZY. Liraglutide ameliorates diabetic kidney disease by modulating gut microbiota and L-5-Oxoproline. Eur J Pharmacol. 2024;983:176905.

12. Su JQ, Wu XQ, Wang Q, Xie BY, Xiao CY, Su HY, et al. The microbial metabolite trimethylamine N-oxide and the kidney diseases. Front Cell Infect Microbiol. 2025;15:1488264.

13. Lohia S, Vlahou A, Zoidakis J. Microbiome in Chronic Kidney Disease (CKD): An Omics Perspective. Toxins (Basel). 2022;14(3).

14. Hampson HE, Li S, Walker DI, Wang H, Jia Q, Rock S, et al. The potential mediating role of the gut microbiome and metabolites in the association between PFAS and kidney function in young adults: A proof-of-concept study. Sci Total Environ. 2024;954:176519.

15. Peng B, Dai J, Ji S, Yang Y, Zuo A, Xu S, et al. Quercetin ameliorates hyperuricemic nephropathy through improving gut dysfunctions and decreasing gut bacteria-derived uremic toxins. Phytomedicine. 2025;143:156801.

16. Paul P, Kaul R, Chaari A. Renal Health Improvement in Diabetes through Microbiome Modulation of the Gut-Kidney Axis with Biotics: A Systematic and Narrative Review of Randomized Controlled Trials. Int J Mol Sci. 2022;23(23).

17. Ranganathan N, Anteyi E. The Role of Dietary Fiber and Gut Microbiome Modulation in Progression of Chronic Kidney Disease. Toxins (Basel). 2022;14(3).

18. Schwarz A, Hernandez L, Arefin S, Sartirana E, Witasp A, Wernerson A, et al. Sweet, bloody consumption - what we eat and how it affects vascular ageing, the BBB and kidney health in CKD. Gut Microbes. 2024;16(1):2341449.

19. Han S, Chen M, Cheng P, Zhang Z, Lu Y, Xu Y, et al. A systematic review and meta-analysis of gut microbiota in diabetic kidney disease: Comparisons with diabetes mellitus, non-diabetic kidney disease, and healthy individuals. Front Endocrinol (Lausanne). 2022;13:1018093.

20. Lambert K, Rinninella E, Biruete A, Sumida K, Stanford J, Raoul P, et al. Targeting the Gut Microbiota in Kidney Disease: The Future in Renal Nutrition and Metabolism. J Ren Nutr. 2023;33(6s):S30-s9.

21. Guo H, Pan L, Wu Q, Wang L, Huang Z, Wang J, et al. Type 2 Diabetes and the Multifaceted Gut-X Axes. Nutrients. 2025;17(16).

22. Lee AM, Hu J, Xu Y, Abraham AG, Xiao R, Coresh J, et al. Using Machine Learning to Identify Metabolomic Signatures of Pediatric Chronic Kidney Disease Etiology. J Am Soc Nephrol. 2022;33(2):375-86.

DECLARATIONS

Ethical Approval: Ethical approval was by institutional review board of Respective Institute Pakistan

Informed Consent: Informed Consent was taken from participants.

Authors' Contributions:

Concept: TK, SKM; Design: TK, MZK, MKS; Data Collection: TK, MZK, IZH; Analysis: IZH, MASB; Drafting: TK; Critical Revision: MKS, SKM

Conflict of Interest: The authors declare no conflict of interest.

Funding: This research received no external funding.

Data Availability: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgments: NA

Study Registration: Not applicable.