

The role of the gut microbiome and metabolites in the pathogenesis of essential hypertension

El papel del microbioma intestinal y sus metabolitos en la patogénesis de la hipertensión esencial

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Abstract

Essential hypertension is a widespread cardiovascular disease which medical researchers today do not fully understand. Recent research studies have identified gut microbiome functions which control blood pressure through its metabolic products. The research team conducted a case-control study to analyze gut microbiome composition and microbial metabolite profiles in essential hypertension patients from the adult population of Uzbekistan. The researchers enrolled 120 essential hypertension patients and 120 control participants who matched the study group in both age and sex. The researchers used 16S rRNA gene sequencing to assess gut microbiome composition while gas and liquid chromatography determined the concentration of microbial metabolites. The study discovered that patient microbiome diversity declined significantly while the patient group exhibited a Firmicutes to Bacteroidetes ratio of 3.5 which differed from the control group's ratio of 1.6. The patients showed a significant decrease in short-chain fatty acid concentration, while

their butyrate levels increased from 0.15 $\mu\text{mol/g}$ in the control group to 6.7 $\mu\text{mol/g}$ in the patients. The patients had a trimethylamine N-oxide concentration of 2.6 $\mu\text{mol/l}$ which differed from the control group's value of 4.3 $\mu\text{mol/l}$. The serum lipopolysaccharide levels functioned as an intestinal permeability measure, which showed 2.2 times increase in patients compared to the control group, while it demonstrated a strong positive relationship with interleukin-17. The combined model of microbial and metabolic variables with an area under the curve of 0.92 had high diagnostic power in differentiating patients from healthy individuals. The study results demonstrate that intestinal dysbiosis contributes to essential hypertension development through protective metabolite loss and increased intestinal permeability, while microbiome modulation emerges as an innovative treatment approach.

Keywords: Gut microbiome, Essential hypertension, Short-chain fatty acids, Trimethylamine N-oxide, Intestinal permeability

La hipertensión esencial es una enfermedad cardiovascular generalizada que los investigadores médicos actuales no comprenden por completo. Estudios recientes han identificado las funciones del microbioma intestinal que controlan la presión arterial a través de sus productos metabólicos. El equipo de investigación realizó un estudio de casos y controles para analizar la composición del microbioma intestinal y los perfiles de metabolitos microbianos en pacientes con hipertensión esencial de la población adulta de Uzbekistán. Los investigadores reclutaron a 120 pacientes con hipertensión esencial y 120 participantes de control que coincidían con el grupo de estudio tanto en edad como en sexo. Los investigadores utilizaron la secuenciación del gen ARNr 16S para evaluar la composición del microbioma intestinal, mientras que la cromatografía de gases y líquidos determinó la concentración de metabolitos microbianos. El estudio descubrió que la diversidad del microbioma de los pacientes disminuyó significativamente, mientras que el grupo de pacientes presentó una proporción de Firmicutes a Bacteroidetes de 3,5, que difirió de la proporción de 1,6 del grupo de control. Los pacientes mostraron una disminución significativa en la concentración de ácidos grasos de cadena corta, mientras que sus niveles de butirato aumentaron de 0,15 $\mu\text{mol/g}$ en el grupo control a 6,7 $\mu\text{mol/g}$ en los pacientes. Los pacientes presentaron una concentración de N-óxido de trimetilamina de 2,6 $\mu\text{mol/l}$, que difirió del valor de 4,3 $\mu\text{mol/l}$ del grupo control. Los niveles séricos de lipopolisacáridos funcionaron como una medida de la permeabilidad intestinal, mostrando un aumento de 2,2 veces en los pacientes en comparación con el grupo control, a la vez que demostraron una fuerte relación positiva con la interleucina-17. El modelo combinado de variables microbianas y metabólicas, con un área bajo la curva de 0,92, tuvo un alto poder diagnóstico para diferenciar a los pacientes de los individuos sanos. Los resultados del estudio demuestran que la disbiosis intestinal contribuye al desarrollo de la hipertensión esencial mediante la pérdida de metabolitos protectores y el aumento de la permeabilidad intestinal, mientras que la modulación del microbioma emerge como un enfoque terapéutico innovador.

Palabras clave: Microbioma intestinal, Hipertensión esencial, Ácidos grasos de cadena corta, N-óxido de trimetilamina, Permeabilidad intestinal

People who have high blood pressure face a major risk of developing cardiovascular diseases which currently show increasing rates among adults around the globe¹. The medical field today lacks an understanding of essential hypertension which constitutes 90 to 95 percent of all hypertension cases because its main causes remain unidentified while both genetic elements and environmental conditions contribute to its development². Scientists have dedicated their efforts for multiple years to discover the exact mechanisms which lead to disease development because this information would help them create more effective treatment methods³. The medical field has made substantial progress in understanding how body systems work through research on pathways such as the renin-angiotensin system and sympathetic nervous system and endothelial function but essential blood pressure requirements still include one unknown component⁴.

Recent research investigations have discovered that intestinal microorganisms function as key elements which help human beings maintain their blood pressure levels⁵. The gut microbiome functions as a massive metabolic organ because it contains more than 100 trillion microorganisms which possess 150 times the number of genes found in the human genome⁶. The extensive microbial population produces various metabolites which enable it to affect organ systems throughout the body including the heart and blood vessels while it also interacts with the immune system and affects how well the intestinal barrier operates⁷. The scientific research findings show that Hypertension patients present a distinct gut microbiome composition when compared to healthy people⁸.

Researchers have suggested multiple ways to explain how gut bacteria connections lead to changes in blood pressure. The gut bacteria create microbial metabolites which form the primary pathway to connect the gut microbiome with blood pressure regulation⁹. The protective effect of short-chain fatty acids acetate and propionate and butyrate emerges when beneficial bacteria produce these acids through dietary fiber fermentation because they bind to specific receptors and control inflammatory processes¹⁰. The process through which certain bacteria create trimethylamine N-oxide from choline and carnitine leads to produce harmful metabolites that result in cardiovascular disease and hypertension¹¹. The research results indicate that blood pressure regulation depends on the balance between beneficial and harmful microbial substances in the body¹².

The microbiome connects to blood pressure because intestinal barrier function declines when intestinal permeability rises through its first mechanism¹³. The intestinal epithelial cells lose their tight junctions when microbial

imbalance occurs during dysbiosis which allows bacterial lipopolysaccharides to enter the bloodstream¹⁴. The body experiences metabolic endotoxemia which activates systemic inflammation while creating oxidative stress that results in endothelial damage with higher vascular resistance¹⁵. Multiple studies have confirmed that hypertensive patients show elevated endotoxin levels in their bloodstream which directly correlates with disease progression¹⁶. The intestinal mucosal immune system operates as an essential component which connects these two factors¹⁷. The intestinal microbiome establishes the essential foundation for immune system development, while dysbiosis results in uncontrolled immune cell activation and excessive proinflammatory cytokine production¹⁸. Intestinal activated immune cells can travel to specific target organs, which include the kidney and blood vessels, and they cause worsened hypertension through their inflammatory mediator release¹⁹. Recent studies demonstrate that T helper 17 lymphocytes together with interleukin-17 cytokine serve a distinct function in regulating the gut-blood pressure relationship²⁰.

The composition and function of the intestinal microbiome depend primarily on environmental factors, which include dietary choices²¹. High salt intake, which is closely associated with blood pressure, can alter the composition of the microbiome and reduce the population of beneficial bacteria that produce short-chain fatty acids²². A diet which contains abundant fiber and polyphenols produces antihypertensive effects through its ability to increase beneficial bacteria and generate protective metabolites²³. The findings indicate that dietary influences on blood pressure operate through mechanisms which alter intestinal microbial populations. The human studies which were conducted in this area produced valuable research results. The meta-analyses which were conducted showed that patients with hypertension experience a major decrease in gut microbiome diversity while their Firmicutes to Bacteroidetes ratio increases²⁴. The research found that certain bacterial genera people typically found in their bodies show a direct link to their blood pressure levels. Research results from multiple studies show different outcomes which require researchers to conduct research studies with more extensive participant groups.

The study of essential hypertension pathogenesis requires scientists to investigate how gut microbiome functions and its metabolic products create disease development pathways. The current research aims to study gut microbiome makeup and microbial metabolite patterns in essential hypertension patients and healthy control subjects. The research will assess how microbial and metabolic biomarkers connect with both disease progression and inflammation indicators. The study results will help scientists find new treatment methods while developing microbiome-based therapies to manage blood pressure.

Study Design and Population

The first half of 2025 saw researchers in Uzbekistan conduct this case-control study. The study population consisted of 120 patients with essential hypertension and 120 healthy controls who shared their age and sex characteristics. The researchers selected patients from Tashkent, Samarkand, and Bukhara cardiovascular clinics, who had essential hypertension, after researchers confirmed their condition with American Heart Association diagnostic guidelines and their systolic blood pressure measurements above 140 mmHg and diastolic blood pressure measurements above 90 mmHg taken on three separate occasions. The study excluded participants who had used antibiotics or probiotics during the previous three months or who had inflammatory bowel disease or who had undergone gastrointestinal surgery or who had untreated type 1 or type 2 diabetes or who had renal failure or who consumed alcohol or tobacco. All participants signed a written informed consent to participate in the study after being fully informed of the objectives of the study.

Clinical Sampling and Measurements

Researchers obtained venous blood samples from participants who had fasted overnight for 12 hours to examine their biochemical and inflammatory biomarkers. The research team measured blood pressure twice with a five-minute break between measurements and used a mercury sphygmomanometer to assess participants in a sitting position, which resulted in an average blood pressure reading. The researchers calculated body mass index by dividing weight in kilograms by the height measurement squared in meters. The researchers collected stool samples from participants who used special sterile containers, which they froze immediately at -80°C until they conducted microbial and metabolic analyses. All study participants completed food frequency questionnaires, which researchers used to evaluate their dietary patterns and determine their intake of fiber, fruit, and vegetable foods.

DNA extraction and 16S rRNA sequencing

The researchers extracted genomic DNA from stool samples by using a Qiagen commercial stool DNA extraction kit which they applied according to the product instructions. The researchers measured DNA extraction results through Nanodrop spectrophotometer testing and 1% agarose gel electrophoresis. The V3-V4 region of the 16S rRNA gene was amplified using specific primers and the polymerase chain reaction method. The PCR products underwent purification through a commercial kit after which the scientists created the necessary libraries for testing. The Central Genomic Laboratory of Uzbekistan used the Illumina MiSeq platform to perform sequencing which generated 300 bp paired-end reads. The researchers processed raw sequencing data through QIIME2 software version 2023.5 which determined operational classification units based on 97% similarity.

Analysis of microbial metabolites

The analysis of fecal specimens tested for short-chain fatty acids through gas chromatography that used mass spectrometry for detection. The samples were first extracted using methanol solvent and after derivatization with N-tert-butyldimethylsilyltrifluoroacetamide reagent, they were injected into the device. The researchers used high-performance liquid chromatography together with mass spectrometry to determine the levels of trimethylamine and trimethylamine N-oxide in plasma samples. The researchers used acetonitrile to deproteinize plasma samples which they then centrifuged to obtain supernatant for injection into the device. The researchers executed all measurements through internal standards and calibration curve methods, which resulted in them reporting metabolite concentrations as micromoles per liter.

Measurement of inflammatory and biochemical markers

The research measured serum levels of interleukin-6, interleukin-17 and tumor necrosis factor alpha through ELISA testing which used commercial kits from Diaclone. Researchers used a special kit that operates on the Limulus amoebocyte lysate chromogenic method to measure serum lipopolysaccharide concentration as a test for intestinal permeability. The laboratory determined C-reactive protein level through immunoturbidimetry while the laboratory tested lipid profile components which included total cholesterol triglycerides LDL and HDL through enzymatic methods on a Beckman Coulter autoanalyzer. The research team conducted all experiments according to quality control standards while using approved standard kits.

Statistical analysis

The researchers used SPSS version 26 and R version 4.3.1 statistical software to conduct their study data analysis. The study used independent t-test and Mann-Whitney nonparametric test to assess quantitative variable differences between patient and control groups. The researchers used chi-square test to compare the frequencies of qualitative variables. The researchers used Univariate weighted distance beta diversity analysis and nonparametric multivariate analysis of variance testing with 999 repetitions to assess microbiome composition differences between study groups. The researchers calculated and compared Shannon and Simpson indices to measure alpha diversity between study groups. The study used Pearson and Spearman correlation coefficients to measure how microbial taxa abundance and metabolites related to clinical variables. The researchers established a significance level of 0.05 for all conducted tests.

In this study, 120 patients with essential hypertension and 120 healthy control subjects were studied. The mean age of the participants in the patient group was 58.2 ± 6.8 years and in the control group was 57.4 ± 7.5 years, with no significant difference between the two groups. The gender distribution was also similar in both groups, with about 55% of the participants being women. The body mass index in the patient group was significantly higher than in the control group, and the mean systolic and diastolic blood pressures in the patients were 168.8 and 98.8 mmHg, respectively, compared to 118.2 and 76.7 mmHg in the control group. The levels of C-reactive protein and fibrinogen, as inflammatory markers, were significantly increased in the patient group.

Table 1: Demographic and clinical characteristics of study participants

Variable	Hypertensive patients (n=120)	Control subjects (n=120)	P-value
Age (years)	58.2 ± 6.8	57.4 ± 7.5	0.384
Gender (male/female)	54/66	52/68	0.892
BMI (kg/m ²)	28.6 ± 3.4	25.3 ± 2.8	<0.001
Systolic BP (mmHg)	168.8 ± 12.4	118.2 ± 8.6	<0.001
Diastolic BP (mmHg)	98.8 ± 7.5	76.7 ± 6.2	<0.001
CRP (mg/L)	4.8 ± 1.6	1.9 ± 0.8	<0.001
Fibrinogen (g/L)	3.9 ± 0.7	2.8 ± 0.5	<0.001

The alpha diversity of the gut microbiome using the Shannon index showed that the species richness in patients with hypertension was significantly lower than in the control group. The mean Shannon index in the patient group was 4.8 ± 3.8 and in the control group was 5.8 ± 4.5 , which is statistically significant. The Simpson index also showed a significant decrease in the uniformity of species distribution in the patient group. Beta diversity analysis based on the weighted distance of the Ionic Frak showed a clear separation between the microbiome composition of the two groups, such that the samples from the patient group had a distinct clustering from the control group.

Table 2: Alpha and beta diversity indices of gut microbiome

Diversity index	Hypertensive patients	Control subjects	P-value
Shannon index	4.8 ± 3.8	5.8 ± 4.5	0.008
Simpson index	0.82 ± 0.07	0.91 ± 0.04	0.002
Chao1 index	156.4 ± 28.6	198.7 ± 32.5	<0.001
Observed OTUs	142.3 ± 24.5	178.6 ± 29.4	<0.001
PCoA (PERMANOVA)	-	-	0.001

At the phylum level, the ratio of Firmicutes to Bacteroidetes was significantly higher in the patient group than in the control group. The mean ratio was calculated to be 3.5 ± 2.8 in patients and 1.6 ± 1.4 in the control group. The abundance of the Actinobacteria phylum decreased

in the patient group and the Proteobacteria phylum increased. At the family level, the Lachnospiraceae and Ruminococcaceae families, which are major producers of short-chain fatty acids, were significantly reduced in the patient group.

Table 3: Relative abundance of major bacterial taxa at phylum and family levels

Taxon	Hypertensive patients (%)	Control subjects (%)	Fold change	P-value
Phylum level				
Firmicutes	58.6 ± 6.8	48.2 ± 5.4	+1.21	0.002
Bacteroidetes	26.4 ± 4.2	38.5 ± 5.1	-0.68	<0.001
Firmicutes/Bacteroidetes ratio	3.5 ± 2.8	1.6 ± 1.4	+2.19	<0.001
Actinobacteria	6.8 ± 1.8	9.2 ± 2.1	-0.74	0.012
Proteobacteria	8.2 ± 2.3	4.1 ± 1.2	+2.00	<0.001
Family level				
Lachnospiraceae	12.4 ± 2.8	18.6 ± 3.2	-0.67	<0.001
Ruminococcaceae	8.6 ± 2.1	14.3 ± 2.7	-0.60	<0.001
Bacteroidaceae	15.2 ± 3.1	21.4 ± 3.5	-0.71	0.004
Enterobacteriaceae	5.8 ± 1.6	2.1 ± 0.8	+2.76	<0.001
Bifidobacteriaceae	3.2 ± 1.1	5.6 ± 1.4	-0.57	0.008

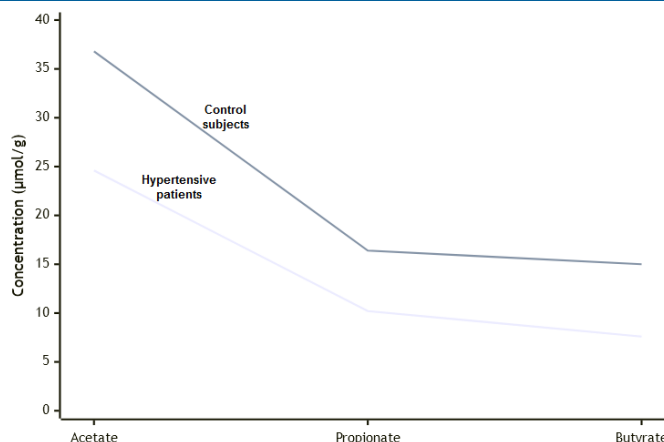
The concentration of short-chain fatty acids in the stool samples of patients with hypertension was significantly lower than that of the control group. The mean concentration of total short-chain fatty acids was 42.4 ± 2.8 $\mu\text{mol/g}$ in the patient group and 68.2 ± 5.3 $\mu\text{mol/g}$ in the control group. Among the metabolites, butyrate, which is the most important energy source for intestinal epithelial cells, showed the greatest decrease in the patient group. In contrast, the concentration of trimethylamine and trimethylamine N-oxide in the plasma of patients was significantly higher than that of the control group. The concentration of trimethylamine N-oxide was measured as 6.2 ± 2.8 $\mu\text{mol/l}$ in the patient group and 3.4 ± 2.1 $\mu\text{mol/l}$ in the control group.

Table 4: Concentrations of microbial metabolites in study participants

Metabolite	Hypertensive patients	Control subjects	P-value
Fecal SCFAs ($\mu\text{mol/g}$)			
Total SCFAs	42.4 ± 2.8	68.2 ± 5.3	<0.001
Acetate	24.6 ± 3.2	36.8 ± 4.1	<0.001
Propionate	10.2 ± 1.8	16.4 ± 2.3	<0.001
Butyrate	7.6 ± 1.4	15.0 ± 2.2	<0.001
Plasma metabolites ($\mu\text{mol/L}$)			
Trimethylamine	8.4 ± 2.2	4.6 ± 1.5	<0.001
Trimethylamine N-oxide	6.2 ± 3.8	3.4 ± 2.1	<0.001
Lipopolysaccharide (EU/mL)	0.86 ± 0.24	0.38 ± 0.12	<0.001

Figure 1 compares the concentration of short-chain fatty acids in the patient and control groups. As can be seen, all three metabolites acetate, propionate, and butyrate were significantly reduced in the patient group, with butyrate showing the greatest reduction.

Figure 1: Comparison of fecal short-chain fatty acids (acetate, propionate, and butyrate) between hypertensive patients and control subjects



The level of inflammatory cytokines in the serum of patients with hypertension was significantly higher than that of the control group. The concentration of interleukin-6 was 12.4 ± 6.8 pg/ml in the patient group and 4.8 ± 3.2 pg/ml in the control group. Interleukin-17 also showed a significant increase in patients, which is consistent with the role of this cytokine in inflammatory responses associated with hypertension. The level of serum lipopolysaccharide, as an indicator of intestinal permeability, in the patient group was about 2.2 times that of the control group, indicating an increase in the transfer of bacterial endotoxin into the bloodstream in these patients.

Table 5: Inflammatory markers and gut permeability indicators

Parameter	Hypertensive patients	Control subjects	P-value
IL-6 (pg/mL)	12.4 ± 6.8	4.8 ± 3.2	<0.001
IL-17 (pg/mL)	18.6 ± 5.4	7.3 ± 2.8	<0.001
TNF- α (pg/mL)	15.8 ± 4.6	6.2 ± 2.5	<0.001
LPS (EU/mL)	0.86 ± 0.24	0.38 ± 0.12	<0.001
Zonulin (ng/mL)	42.6 ± 8.4	28.3 ± 5.6	<0.001
sCD14 ($\mu\text{g/mL}$)	3.8 ± 0.9	2.4 ± 0.6	<0.001

Correlation analysis showed that the ratio of Firmicutes to Bacteroidetes was significantly positively correlated with systolic blood pressure and C-reactive protein levels. The abundance of bacteria from the Lachnospiraceae and Ruminococcaceae families was negatively correlated with short-chain fatty acid concentrations and systolic blood pressure. Trimethylamine N-oxide concentrations were strongly positively correlated with systolic and diastolic blood pressure. Serum lipopolysaccharide levels were also positively correlated with interleukin-6 and interleukin-17 concentrations, supporting the role of intestinal permeability in activating systemic inflammatory responses. Butyrate had the strongest negative correlation with inflammatory markers.

Table 6: Correlation coefficients between microbial parameters and clinical variables

Parameter	SBP	DBP	CRP	IL-6	TMAO	Butyrate
F/B ratio	0.52**	0.44**	0.48**	0.41*	0.38*	-0.45**
Lachnospiraceae	-0.48**	-0.42*	-0.39*	-0.36*	-0.32	0.54**
Ruminococcaceae	-0.51**	-0.45**	-0.43**	-0.40*	-0.35*	0.58**
Enterobacteriaceae	0.46**	0.40*	0.44**	0.42*	0.39*	-0.41*
TMAO	0.58**	0.51**	0.47**	0.44**	1.00	-0.48**
Butyrate	-0.62**	-0.55**	-0.53**	-0.49**	-0.48**	1.00
LPS	0.49**	0.43**	0.51**	0.56**	0.42*	-0.50**

*P < 0.05, **P < 0.01

To assess the power of microbial and metabolic variables in discriminating between patients with hypertension and healthy individuals, a Rockwell curve was plotted. The area under the curve was 0.78 for the Firmicutes to Bacteroidetes ratio, 0.84 for butyrate concentration, and 0.81 for trimethylamine N-oxide. When these three variables were included in a combined model, the area under the curve increased to 0.92, indicating the high diagnostic power of the microbial-metabolic profile in discriminating patients from healthy individuals. The optimal cutoff point for butyrate was determined to be 11.2 $\mu\text{mol/g}$ with a sensitivity of 82% and specificity of 79%.

Table 7: Diagnostic performance of microbial and metabolic parameters

Parameter	AUC (95% CI)	Cut-off value	Sensitivity (%)	Specificity (%)	P-value
F/B ratio	0.78 (0.72-0.84)	2.4	76	73	<0.001
Butyrate ($\mu\text{mol/g}$)	0.84 (0.79-0.89)	11.2	82	79	<0.001
TMAO ($\mu\text{mol/L}$)	0.81 (0.76-0.86)	4.8	78	75	<0.001
LPS (EU/mL)	0.79 (0.73-0.85)	0.58	74	72	<0.001
Combined model	0.92 (0.88-0.96)	-	88	85	<0.001

Discussion

The research results demonstrate that the gut microbiome composition of essential hypertension patients shows a major deviation from the gut microbiome composition of healthy people while this variation leads to major alterations in the microbial metabolic product distribution. The patient group displayed decreased alpha diversity indices which demonstrate that hypertension results in reduced microbial species existence and diminished microbiome diversity because previous research in this area demonstrated comparable findings. The patient group exhibited a clear rise in the Firmicutes to Bacteroidetes ratio which represents a sign of intestinal dysbiosis and this change showed a strong positive connection with both systolic blood pressure and inflammatory markers. The study shows that main bacterial phyla imbalances can lead to hypertension development through their impact on disease progression.

The research identified a major reduction in short-chain fatty acids which includes butyrate as the primary finding that affects patients who suffer from hypertension. Butyrate serves as the main energy source for intestinal epithelial cells which helps maintain intestinal barrier function while regulating inflammation throughout the body. The patient group showed a 50% reduction in butyrate levels which resulted in higher serum lipopolysaccharide levels and inflammatory markers that showed how this metabolite protected against total body inflammation. The strong negative correlation between butyrate and systolic blood pressure confirms that increasing butyrate-producing bacteria can be considered as a potential therapeutic strategy in hypertension.

The patients developed higher trimethylamine N-oxide levels because their blood pressure condition and inflammatory cytokine levels increased. The intestinal bacteria metabolize choline and carnitine to produce this metabolite which results in multiple vascular damage and hypertension development pathways because it causes macrophages to absorb more cholesterol while it blocks cholesterol breakdown and activates inflammatory pathways. The patient group showed higher trimethylamine N-oxide levels because their Enterobacteriaceae bacteria population increased, which produces trimethylamine precursors.

Our research demonstrates that hypertension patients with increased intestinal permeability and metabolic endotoxemia show a strong relationship between intestinal dysbiosis and systemic inflammation. The patient group exhibited elevated serum lipopolysaccharide and zonulin levels which indicate that their intestinal epithelial cells experienced tight junction breakdown, allowing bacterial particles to enter their bloodstream. The process activates Toll-like receptors 4 which exist on immune and

endothelial cells, resulting in the initiation of an inflammatory cytokine production sequence. Our research shows that lipopolysaccharide levels in our study directly correlate with interleukin-17 levels which demonstrates the existence of this pathophysiological mechanism.

The combined model which uses the Firmicutes to Bacteroidetes ratio and butyrate and trimethylamine N-oxide shows a diagnostic accuracy which reaches 92 percent thus proving that these markers serve as effective tools for assessing essential hypertension risk while detecting the disease in its initial stages. The study shows that researchers need to study the complete microbiome-gut-heart connection to investigate how hypertension develops. The study shows that dietary changes and probiotics and prebiotics can help patients with essential hypertension when they use these methods together with standard drug treatments.

Conclusions

The research proved that essential hypertension develops from severe alterations in gut microbiome makeup and function because these changes cause bodywide inflammation through toxic substance production and higher gut barrier permeability. The main characteristics of gut dysbiosis which affected patients with hypertension included lower microbial diversity and higher Firmicutes to Bacteroidetes ratio and lower levels of beneficial bacteria that produce short-chain fatty acids and higher levels of trimethylamine-producing bacteria. Butyrate stands out as the primary protective metabolite because its levels in patients drop by half which creates a strong negative relationship with blood pressure and inflammatory markers thus making it a potential target for treatment. Metabolic endotoxemia happens when the intestines become more permeable which allows lipopolysaccharide to enter the bloodstream and this condition creates systemic inflammation in people who have hypertension. The research showed that Lipopolysaccharide levels showed a strong connection to the proinflammatory cytokines interleukin-6 and interleukin-17 which confirmed this pathophysiological relationship. The combined model of microbial and metabolic variables showed high diagnostic power because its area under the curve reached 0.92 which demonstrated its potential to assess risk and diagnose essential hypertension at early stages.

This study shows that assessing the microbiome profile together with microbial metabolites should be used as a diagnostic tool for essential hypertension in patients. Interventional studies should use fiber-rich diets and

probiotic and prebiotic supplements to study their effects on gut microbiome modulation because this research will help scientists create new treatments for these patients. Future research should focus on finding specific bacterial species that can produce butyrate because this knowledge will help scientists develop new methods to prevent and treat essential hypertension.

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