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Research Article

Role of Gut Microbiome in Susceptibility to Infection: A Study from Tertiary Care Centre

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A B S T R A C T

Introduction: The gut microbiome is a key regulator of immune function and host defense. Dysbiosis of gut microbial communities has been associated with impaired immune responses and increased susceptibility to infections. This study aimed to assess the relationship between gut microbiome composition and susceptibility to infection.

Materials and Methods: This prospective observational study included 100 adults, comprising 50 infection-susceptible participants and 50 age- and sex-matched healthy controls. Individuals with recent antibiotic or probiotic use were excluded. Stool samples were analyzed using 16S rRNA gene sequencing (V3–V4 regions). Microbial diversity was assessed using Shannon, Simpson, and Chao1 indices, and phylum-level composition was compared between groups.

Results: Infection-susceptible participants showed significantly reduced gut microbial diversity compared with controls ($p < 0.001$). A dysbiotic microbial profile was observed, characterized by reduced Firmicutes and Bacteroidetes and increased Proteobacteria ($p < 0.05$). Baseline demographic characteristics were comparable between the two groups.

Conclusion: Reduced gut microbial diversity and altered microbial composition were significantly associated with susceptibility to infection. These findings highlight the gut microbiome's role in host immune defense and suggest a potential role for microbiome profiling in infection risk assessment.

Keywords: gut microbiome, infection susceptibility, dysbiosis, microbial diversity, immune regulation

Introduction

The human gut microbiome comprises a highly diverse and metabolically active community of microorganisms that play a fundamental role in maintaining host homeostasis. Beyond their established role in digestion and nutrient metabolism, gut microbial communities exert profound effects on immune

system development, regulation of inflammatory responses, and maintenance of intestinal epithelial barrier integrity. Disruption of this finely balanced ecosystem, commonly referred to as dysbiosis, has been increasingly implicated in heightened susceptibility to infections as well as immune-mediated and inflammatory disorders.[1,2] A key protective function of the gut microbiome lies in its ability to provide colonization resistance against pathogenic microorganisms. Commensal bacteria competitively inhibit pathogen growth by occupying ecological niches, competing for nutrients, and producing antimicrobial metabolites. Additionally, the gut microbiota modulates epithelial tight junctions, mucus secretion, and antimicrobial peptide production, thereby strengthening the physical and biochemical barriers that prevent pathogen invasion.[3] Alterations in microbial composition have been shown to compromise epithelial barrier integrity, resulting in increased intestinal permeability and enhanced translocation of pathogenic organisms and microbial products.[4]

The gut microbiome also plays a central role in shaping both innate and adaptive immune responses. Microbial-derived metabolites, such as short-chain fatty acids (SCFAs), have been shown to promote immune tolerance by inducing and expanding regulatory T cells, thereby maintaining immune equilibrium and preventing excessive inflammatory responses that may predispose individuals to infection.[5,6] Experimental studies have further shown that specific commensal taxa, including indigenous Clostridium species, are critical for immune education and mucosal immune homeostasis.[6] Dysbiosis-associated immune dysregulation has been linked to increased susceptibility to infectious complications in both experimental models and clinical settings. Altered microbiota profiles have been associated with exaggerated inflammatory responses following viral infections, such as norovirus-induced mucosal inflammation, particularly in immunocompromised hosts.[7] Similarly, disease-associated microbiome alterations observed in chronic liver disease and viral hepatitis highlight the systemic immunological consequences of gut microbial imbalance, which may predispose affected individuals to recurrent or severe infections.[1,8]

Recent evidence has also highlighted the protective role of specific beneficial microbes in enhancing host resistance to infection and tissue injury. For instance, Akkermansia muciniphila has been shown to reduce peritonitis severity and promote intestinal wound healing through immune-dependent mechanisms, underscoring the therapeutic potential of targeted microbiome modulation.[9] These findings have prompted growing interest in microbiota-based interventions, including probiotics and supplementation with microbial metabolites, as novel strategies to reduce infection susceptibility and improve host immune resilience.[10] Despite significant advances, the precise microbial signatures and mechanistic pathways linking gut microbiome composition to infection susceptibility remain incompletely understood. Further investigation into microbiome-immune-pathogen interactions is essential to identify predictive biomarkers and develop microbiome-targeted preventive and therapeutic approaches against infectious diseases.

Materials and Methodology

This study was a prospective observational study conducted at a tertiary care teaching hospital. The objective was to assess the role of gut microbiome composition in determining susceptibility to infections. The study protocol was reviewed and approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrollment. A total of 100 participants were included in the study. The sample size was determined based on feasibility and previous microbiome-based observational studies assessing differences in gut microbial diversity between infected and non-infected individuals. Participants were equally distributed into two groups:

- **Infection-susceptible group:** 50 participants with clinically and microbiologically confirmed infections
- **Control group:** 50 age- and sex-matched healthy individuals without active infection

Study Population

Adult participants aged 18 years and above were recruited from inpatient and outpatient services. Participants were classified into the infection-susceptible group or the control group based on clinical evaluation and laboratory findings.

Inclusion Criteria

- Adults aged ≥18 years
- Willingness to provide written informed consent
- For infection group: laboratory-confirmed bacterial or viral infection
- For control group: absence of current or recent infection

Exclusion Criteria

- Use of antibiotics, probiotics, or prebiotics within the preceding 4 weeks
- History of inflammatory bowel disease or gastrointestinal malignancy
- Immunodeficiency states or ongoing immunosuppressive therapy
- Chronic liver disease, chronic kidney disease, or malignancy
- Pregnancy or lactation

Clinical Data Collection

Demographic and clinical data, including age, sex, comorbid conditions, medication history, dietary habits, and infection-

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related parameters, were collected using a structured pro forma. In the infection group, details on infection type, site, and severity, as well as microbiological culture results, were recorded.

Sample Collection

Fresh fecal samples were collected from all participants under sterile conditions using standardized stool collection containers. For infected patients, samples were collected prior to initiation of antimicrobial therapy whenever feasible. Samples were immediately transported to the laboratory and stored at −80°C until further analysis.

DNA Extraction and Gut Microbiome Analysis

Genomic DNA was extracted from stool samples using a commercially available DNA extraction kit according to the manufacturer's instructions. DNA quality and concentration were assessed using spectrophotometric methods. Gut microbiome profiling was performed using 16S rRNA gene sequencing, targeting the V3–V4 hypervariable regions. Sequencing libraries were prepared following standard protocols and sequenced on a next-generation sequencing platform. Bioinformatic analysis included quality filtering, operational taxonomic unit (OTU) clustering, and taxonomic classification using validated reference databases.

Microbial Diversity and Composition Analysis

- Alpha diversity indices (Shannon index, Simpson index, and Chao1 index) were calculated to assess within-sample microbial diversity.
- Beta diversity was assessed using principal coordinate analysis (PCoA) to evaluate differences in microbial community structure between the two groups.
- Relative abundance of predominant bacterial phyla and genera was compared between infection-susceptible participants and controls.

Outcome Measures

The primary outcome was the difference in gut microbiome diversity and composition between infection-susceptible individuals and healthy controls. Secondary outcomes included identification of specific microbial taxa associated with increased or reduced susceptibility to infections.

Statistical Analysis

Statistical analysis was performed using the appropriate statistical software, SPSS. 25. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution. Categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the Student's t-test or Mann–Whitney U test for continuous variables and Chi-square or Fisher's exact test for categorical variables. Differences in microbiome diversity indices were analyzed using non-parametric tests. A p-value <0.05 was considered statistically significant.

Results

A total of 100 participants were enrolled in the present study, comprising 50 infection-susceptible participants and 50 healthy controls. The baseline demographic and clinical characteristics of the study population are summarized in Table 1. The mean age of participants in the infection-susceptible group was 45.2 ± 13.1 years, while that of the control group was 43.6 ± 12.8 years. Statistical analysis revealed no significant difference in age distribution between the two groups ($p = 0.54$), indicating appropriate age matching. Sex distribution was also comparable between the two groups, with males constituting 56.0% of the infection-susceptible group and 52.0% of the control group ($p = 0.69$). The prevalence of comorbidities, such as diabetes mellitus and hypertension, was higher in the infection-susceptible group than in controls; however, these differences were not statistically significant ($p = 0.32$ and $p = 0.42$, respectively). None of the participants in either group reported recent antibiotic or probiotic use, thereby minimizing potential confounding effects on gut microbiome composition. Overall, the baseline characteristics were comparable between the two study groups (Table 1). All collected fecal samples yielded genomic DNA of sufficient quality for sequencing and downstream bioinformatic analysis. Sequencing quality control and filtering steps ensured reliable taxonomic assignment across all samples. The resulting data were included in both study groups for diversity and compositional analyses. Comparison of gut microbiome alpha diversity indices between infection-susceptible participants and healthy controls is presented in Table 2. A significant reduction in microbial diversity was observed in the infection-susceptible group across all evaluated indices. The median Shannon diversity index was significantly lower among infection-susceptible participants [3.1 (IQR: 2.7–3.5)] compared to controls [3.9 (IQR: 3.5–4.3)] ($p < 0.001$), indicating reduced microbial richness and evenness in individuals susceptible to infection. Similarly, the Simpson index, which reflects community dominance, was significantly lower in the infection-susceptible group [0.72 (IQR: 0.65–0.79)] compared to the control group [0.85 (IQR: 0.81–0.89)] ($p < 0.001$). The Chao1 index, a measure of estimated species richness, was also markedly reduced in the infection-susceptible group [210 (IQR: 185–240)] when compared with healthy controls [280 (IQR: 255–310)] ($p < 0.001$). Collectively, these findings demonstrate a consistent and statistically significant reduction in gut microbial diversity among participants with increased susceptibility to infection (Table 2). The relative abundance of major gut microbial phyla in the two study groups is detailed in Table 3. At the phylum level, infection-susceptible participants exhibited

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a significantly lower proportion of Firmicutes (38.6 ± 9.4%) compared to healthy controls (48.9 ± 10.1%) ($p < 0.001$). A similar reduction was observed in Bacteroidetes, with infection-susceptible participants showing a mean relative abundance of 29.4 ± 8.6%, compared with 35.7 ± 9.2% in controls ($p = 0.002$).In contrast, the relative abundance of Proteobacteria was significantly higher in the infection-susceptible group (21.1 ± 7.9%) compared to the control group (10.8 ± 5.4%) ($p < 0.001$). Actinobacteria also demonstrated a modest but statistically significant increase in infection-susceptible participants (6.3 ± 3.1%) compared to controls (3.9 ± 2.4%) ($p = 0.01$). Minor phyla categorized as "Others" were similarly elevated in the infection-susceptible group ($p = 0.003$). These findings indicate a shift toward a dysbiotic gut microbial profile in participants susceptible to infection, characterized by depletion of beneficial commensals and enrichment of potentially pathogenic taxa (Table 3). Participants exhibiting lower alpha diversity indices and altered phylum-level composition were predominantly observed in the infection-susceptible group. Reduced microbial diversity, along with increased Proteobacteria abundance, was consistently associated with increased infection susceptibility. Conversely, healthy controls demonstrated higher microbial diversity and a more balanced phylum-level distribution, suggesting a protective gut microbial profile.

Table 1.Baseline Demographic and Clinical Characteristics of the Study Population

Parameter	Infection-Susceptible Group (n = 50)	Control Group (n = 50)	p-value (n = 100)
Age (years), Mean ± SD	45.2 ± 13.1	43.6 ± 12.8	0.54
Sex (Male/Female), n	28 (50%) / 22 (50%)	26 (50%) / 24 (50%)	0.69
Diabetes Mellitus, n (%)	12 (24.0)	8 (16.0)	0.32
Hypertension, n (%)	10 (20.0)	7 (14.0)	0.42

Table 2.Comparison of Gut Microbiome Alpha Diversity Indices Between Study Groups

Alpha Diversity Index	Infection-Susceptible Group (n = 50) Median (IQR)	Control Group (n = 50) Median (IQR)	p-value
Shannon Index	3.1 (2.7–3.5)	3.9 (3.5–4.3)	<0.001
Simpson Index	0.72 (0.65–0.79)	0.85 (0.81–0.89)	<0.001
Chao1 Index	210 (185–240)	280 (255–310)	<0.001

Table 3.Relative Abundance of Major Gut Microbial Phyla in the Study Population

Phylum	Infection-Susceptible Group (%) Mean ± SD	Control Group (%) Mean ± SD	p-value
Firmicutes	38.6 ± 9.4	48.9 ± 10.1	<0.001
Bacteroidetes	29.4 ± 8.6	35.7 ± 9.2	0.002
Proteobacteria	21.1 ± 7.9	10.8 ± 5.4	<0.001
Actinobacteria	6.3 ± 3.1	3.9 ± 2.4	0.01
Others	4.6 ± 2.0	1.7 ± 1.2	0.003

Discussion

In the present study, baseline demographic variables were comparable between infection-susceptible participants and healthy controls (Table 1). The mean age of the infection-susceptible group was 45.2 ± 13.1 years, compared to 43.6 ± 12.8 years in controls ($p = 0.54$), with no significant difference in sex distribution (56.0% vs. 52.0% males, $p = 0.69$). This comparability ensured that observed microbiome differences were not confounded by age or sex, both of which are known determinants of gut microbial composition. Comparable demographic matching has been emphasized in prior microbiome studies across disease states. For example, Bayal et al. (2019)[11] analyzed 16S rDNA profiles from leprosy patients and healthy controls from India, ensuring age- and sex-matched cohorts to demonstrate that microbial alterations were disease-associated rather than demographic-driven. Although their study focused on the skin microbiome, they reported clear microbial differences between diseased and healthy individuals despite demographic similarity, reinforcing the importance of baseline comparability—an approach mirrored in our study design. Similarly, Bergot et al. (2020)[12] reviewed multiple cohort studies in rheumatoid arthritis where age- and sex-matching was critical to demonstrate

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that microbiome shifts were linked to immune-mediated pathology rather than demographic bias. Thus, the demographic equivalence in our cohort strengthens the validity of subsequent microbiome comparison. A major finding of our study was a significant reduction in gut microbiome alpha diversity among infection-susceptible participants (Table 2). The median Shannon diversity index was 3.1 (IQR: 2.7–3.5) in the infection-susceptible group, significantly lower than 3.9 (IQR: 3.5–4.3) observed in healthy controls ($p < 0.001$). Likewise, the Simpson index was reduced (0.72 vs. 0.85, $p < 0.001$), and the Chao1 richness index was markedly lower (210 vs. 280, $p < 0.001$), indicating diminished microbial richness and evenness. Although none of the cited studies directly assessed gut microbiome diversity in infection susceptibility per se, multiple studies support the biological relevance of reduced microbial diversity. Bernard et al. (2002)[13] demonstrated that microbial metabolites—particularly butyrate—significantly influenced immune cell differentiation. In their in-vitro experiments using human monocyte-derived dendritic cells and macrophages, butyrate exposure altered antigen presentation capacity, cytokine production, and maturation markers, indicating that the loss of butyrate-producing commensals (often associated with reduced diversity) can impair immune responsiveness. Similarly, Bautzova et al. (2018)[14], while studying constipation-predominant IBS, reported that altered microbial metabolic pathways led to increased levels of inflammatory lipid mediators such as 5-oxoETE, which activated MAS-related G-protein–coupled receptor D and enhanced nociceptive signaling. Although their endpoint was nociception rather than infection, their findings underscore that reduced or altered microbial diversity changes host immune and inflammatory signaling, a mechanism likely relevant to infection susceptibility observed in our cohort.Phylum-level analysis revealed a distinct dysbiotic pattern in infection-susceptible participants (Table 3). Firmicutes were significantly reduced ($38.6 \pm 9.4\%$) compared to controls ($48.9 \pm 10.1\%$, $p < 0.001$), while Bacteroidetes were also lower ($29.4 \pm 8.6\%$ vs. $35.7 \pm 9.2\%$, $p = 0.002$). In contrast, Proteobacteria were markedly increased in the infection-susceptible group ($21.1 \pm 7.9\%$) compared to healthy controls ($10.8 \pm 5.4\%$, $p < 0.001$). This Proteobacterial expansion is a well-recognized marker of dysbiosis and inflammatory stress. Bayal et al. (2019)[11] reported enrichment of potentially pathogenic taxa in leprosy patients compared to healthy controls, with reduced representation of commensal bacterial groups. Although their study analyzed skin microbiota, the disease-associated shift toward pathogenic taxa parallels our observation of Proteobacteria expansion in infection-susceptible individuals. Further mechanistic insight is provided by Bergot et al. (2020)[12], who summarized evidence that reductions in Firmicutes—particularly taxa involved in short-chain fatty acid production—are associated with immune dysregulation in rheumatoid arthritis. These authors highlighted that reduced Firmicutes abundance correlated with impaired regulatory immune pathways and increased inflammatory activity, mechanisms that plausibly overlap with increased infection susceptibility observed in our study. In addition, Budden et al. (2019)[15] demonstrated that alterations in the microbiome, particularly increased Proteobacteria, were associated with impaired host defense and heightened inflammatory responses in chronic respiratory diseases. Their review emphasized that Proteobacteria expansion reflects microbial instability and loss of immune-protective commensals, supporting our finding that elevated Proteobacteria may predispose individuals to infectious pathology.

Limitations

The observational design of this study precluded establishing a causal relationship between gut microbiome dysbiosis and infection susceptibility. The use of 16S rRNA sequencing limited functional and metabolomic characterization, and the single-center sample size may restrict the generalizability of the findings.

Conclusion

This study demonstrated that individuals susceptible to infection had significantly reduced gut microbial diversity and a dysbiotic shift characterized by enrichment of Proteobacteria, compared with healthy controls. These findings highlight the crucial role of gut microbiome composition in modulating host immune defense and susceptibility to infection, suggesting the potential utility of microbiome profiling in infection risk assessment.

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