The Role of Gut Dysbiosis in Autoimmune Disorders Among General Population

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ABSTRACT

Background: Gut dysbiosis has been increasingly implicated in the pathogenesis of autoimmune disorders, yet there is limited research on its role in General Population. Differences in genetic, environmental, and dietary factors necessitate region-specific studies to better understand microbiota-autoimmunity interactions.

Objective: To compare the gut microbiome composition between individuals with autoimmune disorders and healthy controls in a General population and identify microbiota alterations associated with autoimmune conditions.

Methods: A case-control study was conducted with 138 participants, comprising 69 individuals with autoimmune disorders and 69 matched healthy controls. Data were collected on demographics, clinical history, and dietary habits. Alpha diversity was evaluated using the Shannon index, and beta diversity was analyzed through Bray-Curtis dissimilarity. Statistical analyses included t-tests, chi-square tests, and logistic regression using SPSS version 25.

Results: Cases exhibited significantly lower Shannon diversity index scores (2.8 ± 0.4 vs. 3.2 ± 0.5, $p = 0.01$) and reduced Firmicutes-to-Bacteroidetes ratio (1.5 vs. 2.2, $p = 0.03$). Enrichment of Prevotella (12.4%) and Collinsella (8.5%) was observed in cases ($p < 0.001$). Logistic regression identified reduced microbial diversity as an independent predictor of autoimmune disorders (OR: 2.3, 95% CI: 1.2–4.4, $p = 0.03$).

Conclusion: Gut dysbiosis characterized by reduced microbial diversity and altered taxonomic composition was significantly associated with autoimmune disorders in a general population. These findings underscore the need for microbiome-targeted interventions in managing autoimmune conditions.

INTRODUCTION

The intricate relationship between gut dysbiosis and autoimmune disorders has garnered significant attention in recent medical research. Gut microbiota, a dynamic and diverse community of microorganisms inhabiting the gastrointestinal tract, plays a pivotal role in maintaining immune homeostasis and gut barrier integrity. Dysbiosis, defined as an imbalance in the gut microbial composition, disrupts this equilibrium, potentially compromising the intestinal barrier and promoting systemic inflammation through increased intestinal permeability, colloquially known as "leaky gut" (1, 3). Emerging evidence highlights the involvement of dysbiosis in the pathogenesis of several autoimmune conditions, including rheumatoid arthritis, type 1 diabetes, and multiple sclerosis, with studies demonstrating altered microbial compositions in affected individuals compared to healthy controls (2, 4).

The mechanisms underpinning the connection between gut microbiota and autoimmunity are multifaceted and context-dependent. Dysbiosis influences the immune system through the modulation of gut-associated lymphoid tissues, alterations in T-cell differentiation, and production of microbial metabolites such as short-chain fatty acids and other bioactive compounds. These interactions may exacerbate inflammatory responses and alter immune tolerance, setting the stage for autoimmunity (5, 7). Moreover, the aryl hydrocarbon receptor has been identified as a crucial mediator in host-microbiota interactions, influencing immune regulation and barrier function, thereby further implicating dysbiosis in autoimmune disease progression (8).

General Population present unique opportunities for studying gut microbiota and autoimmune diseases due to their genetic predispositions, dietary habits, and environmental exposures. While studies often identify consistent patterns of dysbiosis across autoimmune conditions, population-specific variations underscore the need for tailored approaches in research and therapeutic strategies (9, 11). For instance, environmental factors such as dietary practices and urbanization have been suggested to influence microbial diversity and composition in these populations, potentially modulating their susceptibility to autoimmunity (12, 15).

Understanding the gut microbiota's role in autoimmunity has opened avenues for novel therapeutic interventions. Microbiome-modulating strategies, including the use of probiotics, prebiotics, fecal microbiota transplantation, and dietary modifications, have shown promise in restoring microbial balance and alleviating disease symptoms (6, 14).

However, the heterogeneity of microbiota profiles across individuals necessitates personalized treatment approaches, incorporating genetic, environmental, and lifestyle factors to optimize efficacy (16, 18).

Despite advancements, significant gaps remain in elucidating the specific microbial alterations and their causal roles in autoimmune pathogenesis. Future research must aim to integrate longitudinal microbiome profiling with mechanistic studies to better understand host-microbiota interactions and their implications in autoimmunity. The development of diagnostic tools and biomarkers based on microbial signatures also holds potential for early detection and targeted interventions in autoimmune diseases (10, 17). By addressing these challenges, the field can move closer to leveraging the gut microbiota for preventive and therapeutic innovations in managing autoimmune disorders (19, 24).

MATERIAL AND METHODS

This case-control study was designed to explore the relationship between gut dysbiosis and autoimmune disorders in general population conducted at Social Security Hospital Gujranwala, Pakistan. The study recruited 138 participants, including individuals diagnosed with autoimmune disorders (cases) and healthy controls matched for age, gender, and socio-demographic characteristics. Participants were selected through purposive sampling from outpatient clinics and community settings. The diagnosis of autoimmune disorders was confirmed by a qualified physician based on established clinical and laboratory criteria. Healthy controls were recruited from the same geographic region and screened to ensure the absence of autoimmune or other chronic inflammatory conditions. Written informed consent was obtained from all participants before enrollment.

Ethical approval for the study was secured from the institutional review board of the participating institution, and all procedures were conducted in accordance with the Declaration of Helsinki and relevant local ethical guidelines. Participants were provided with detailed information about the study objectives, procedures, potential risks, and benefits, and they were assured of the confidentiality of their personal and medical information. Participation was voluntary, and participants could withdraw at any time without any implications for their ongoing care. Data collection involved comprehensive demographic and clinical assessments. A structured questionnaire was used to collect data on age, gender, dietary habits, physical activity, medication use, and medical history. Stool samples were obtained from all participants under standardized conditions, with instructions provided to ensure proper sample collection, storage, and transportation. Samples were stored at −80°C until further analysis. DNA was extracted from stool samples using a commercially available kit, following the manufacturer's protocol. The gut microbiome composition was analyzed through 16S rRNA gene sequencing, targeting the V3–V4 hypervariable regions. To assess differences in gut microbiome composition, alpha and beta diversity metrics were calculated, and taxonomic profiles were compared between cases and controls. Data analysis was conducted using SPSS version 25. Descriptive statistics were used to summarize demographic and clinical characteristics. Continuous variables were expressed as means with standard deviations or medians with interquartile ranges, depending on normality, while categorical variables were presented as frequencies and percentages. Between-group comparisons were performed using independent-samples t-tests, Mann-Whitney U tests, or chi-square tests, as appropriate. Associations between gut microbiota and autoimmune disorders were evaluated using logistic regression analysis, adjusting for potential confounders such as age, gender, and dietary habits. A p-value of <0.05 was considered statistically significant.

To ensure reliability and reproducibility, quality control measures were implemented throughout the study, including the use of standardized protocols for sample collection, processing, and sequencing, as well as rigorous data verification and validation processes. The findings of this study aim to contribute to the growing understanding of the role of gut dysbiosis in autoimmune disorders and to inform future research and therapeutic strategies tailored to General Population.

RESULTS

The study included a total of 138 participants, comprising 69 cases (individuals with autoimmune disorders) and 69 healthy controls. The demographic, clinical, and microbiome diversity characteristics of the participants are summarized in Table 1. The mean age of participants was comparable between cases and controls, with no significant differences observed in gender distribution or body mass index (BMI).

Table 1: Demographic and Clinical Characteristics of Participants

Characteristic	Cases (n = 69)	Controls (n = 69)	p-value
Age (years, mean ± SD)	42.3 ± 12.5	41.8 ± 13.1	0.82
Gender (Male: Female)	35:34	36:33	0.87
BMI (kg/m², mean ± SD)	24.7 ± 3.4	24.5 ± 3.6	0.74
Dietary Fiber Intake (g/day, mean ± SD)	18.5 ± 5.2	21.2 ± 6.1	0.03*
Medication Use (%)	78.3	18.8	<0.001*

*$p < 0.05$ indicates statistical significance.

Analysis of gut microbiota composition revealed significant differences in alpha and beta diversity between cases and controls. Alpha diversity, assessed using the Shannon diversity index, was significantly lower in cases compared to controls, indicating reduced microbial diversity in individuals with autoimmune disorders ($p = 0.01$). Beta diversity analysis, based on Bray-Curtis dissimilarity,

Table 2: Microbial Diversity and Taxonomic Differences

Microbiome Metric	Cases (n = 69)	Controls (n = 69)	p-value
Shannon Diversity Index (mean ± SD)	2.8 ± 0.4	3.2 ± 0.5	0.01*
Dominant Phylum (%) - Firmicutes	52.1	62.3	0.02*
Dominant Phylum (%) - Bacteroidetes	34.7	28.5	0.04*
Firmicutes: Bacteroidetes Ratio	1.5	2.2	0.03*
Genera Enriched in Cases (%)	Prevotella (12.4), Collinsella (8.5)	Not detected	<0.001*

*p < 0.05 indicates statistical significance.

demonstrated distinct clustering of cases and controls, suggesting significant differences in microbial community structure (Figure 1). Specific taxa associated with dysbiosis were identified in cases. Reduced abundance of beneficial genera such as Faecalibacterium and Roseburia was observed, while potentially pro-inflammatory genera, including Prevotella and Collinsella, were significantly enriched in individuals with autoimmune disorders ($p < 0.001$). These findings align with previous evidence linking gut dysbiosis to immune dysregulation.

Logistic regression analysis revealed that reduced microbial diversity (odds ratio [OR]: 2.3, 95% confidence interval [CI]: 1.2–4.4) and enrichment of Prevotella (OR: 3.1, 95% CI: 1.5–6.4) were independently associated with autoimmune disorders after adjusting for confounders ($p < 0.05$). The results support the hypothesis that gut dysbiosis is a significant factor in the pathogenesis of autoimmune disorders in General Population. Further research is warranted to elucidate the causal mechanisms and explore microbiome-targeted interventions for these conditions.

DISCUSSION

The findings of this study highlighted significant differences in gut microbiota composition and diversity between individuals with autoimmune disorders and healthy controls in a general population. Reduced alpha diversity, represented by a lower Shannon diversity index, and distinct clustering in beta diversity analysis underscored the presence of gut dysbiosis in cases compared to controls. These observations are consistent with prior research linking decreased microbial diversity with autoimmune diseases, such as rheumatoid arthritis, type 1 diabetes, and multiple sclerosis, where dysbiosis was identified as a potential driver of immune dysregulation and chronic inflammation (7, 9). The study further identified an enrichment of specific pro-inflammatory genera, including Prevotella and Collinsella, and a relative reduction in beneficial taxa such as Faecalibacterium and Roseburia among cases. These taxa-specific alterations align with previous evidence suggesting that certain microbial compositions promote inflammatory pathways, disrupt intestinal homeostasis, and modulate immune responses in favor of autoimmunity (14-16).

The observed reduction in the Firmicutes-to-Bacteroidetes ratio in cases also supported a dysbiotic profile, which has been implicated in immune-mediated diseases due to its role in gut barrier integrity and metabolite production (2, 17). This study provided novel insights into the microbiome-autoimmunity interplay specific to General Population, a group often underrepresented in microbiome research. Differences in dietary habits, environmental exposures, and genetic predispositions likely contributed to the unique microbiota patterns observed in this population, emphasizing the need for population-specific studies to inform targeted interventions (16). The lower dietary fiber intake among cases, as revealed in this study, may have exacerbated dysbiosis, as fiber-rich diets are known to support microbial diversity and the production of anti-inflammatory metabolites (13).

Despite its strengths, this study had limitations that should be acknowledged. The cross-sectional design precluded the determination of causal relationships between gut dysbiosis and autoimmune disorders. The sample size, while sufficient for preliminary analyses, may have limited the detection of subtler microbiota differences. Additionally, while rigorous methods were employed for microbiota analysis, the reliance on 16S rRNA sequencing provided only taxonomic information and not functional insights into the microbial communities. Future studies incorporating metagenomic or metabolomic approaches would provide a more comprehensive understanding of the functional implications of dysbiosis (14).

The study's strength lay in its robust matching of cases and controls for confounding factors such as age, gender, and socio-demographics, as well as the use of validated protocols for sample collection and analysis. Moreover, it filled a critical knowledge gap by focusing on General Population, whose unique genetic and environmental profiles necessitate tailored research efforts. However, the lack of longitudinal data limited the ability to assess microbiota changes over time or their response to therapeutic interventions (13). This research reinforced the potential of microbiota-targeted interventions as adjunctive strategies for managing autoimmune disorders. Dietary modifications to increase fiber intake, probiotics to restore beneficial taxa, and fecal microbiota transplantation to rebalance microbial communities represent promising therapeutic avenues. Personalized approaches, considering genetic, environmental, and microbial profiles, were recommended for future clinical applications (11, 24).

CONCLUSION

In conclusion, this study confirmed the presence of significant gut dysbiosis in individuals with autoimmune disorders in a General population, consistent with global findings. These results underscored the importance of microbiome research in understanding autoimmune pathogenesis and developing novel therapeutic strategies. Future longitudinal studies with larger sample sizes and integrated omics approaches are warranted to unravel the

complex microbiota-immune interactions and translate these findings into effective clinical interventions.

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