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THE RELATIONSHIP BETWEEN GUT MICROBIOTA DYSBIOSIS AND PATHOMORPHOLOGICAL CHANGES IN THE DIGESTIVE SYSTEM MUCOSA IN METABOLIC SYNDROME

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Abstract

Metabolic syndrome (MetS) is a multifaceted disorder characterized by obesity, insulin resistance, dyslipidemia, and hypertension, often linked to gut microbiota dysbiosis and subsequent alterations in the intestinal barrier. This study investigates the relationships between gut microbiota disruption and pathomorphological changes in the mucous membrane of the digestive system among patients with MetS. Utilizing advanced sequencing and histological analyses, we demonstrate that dysbiosis, marked by reduced microbial diversity and shifts in bacterial taxa, correlates with increased intestinal permeability, mucosal inflammation, and epithelial damage. These findings highlight the role of microbial metabolites and endotoxemia in exacerbating MetS pathology, offering insights into potential microbiota-targeted interventions for improving gut barrier integrity and metabolic health.

Keywords: gut microbiota; Dysbiosis; Metabolic syndrome; Intestinal mucosa; Pathomorphology; Short-chain fatty acids; Endotoxemia; Barrier permeability; Inflammation; Microbial metabolites

Materials and Methods

This cross-sectional study enrolled 120 participants aged 40-65 years, divided into two groups: 60 patients diagnosed with metabolic syndrome (MetS) based on the International Diabetes Federation criteria (central obesity plus at least two of: elevated triglycerides, reduced HDL cholesterol, hypertension, or hyperglycemia) and 60 age- and sex-matched healthy controls. Exclusion criteria included recent antibiotic use, gastrointestinal surgery, or inflammatory bowel disease. Stool samples were collected for gut microbiota analysis using 16S rRNA gene sequencing on the Illumina MiSeq platform, targeting the V3-V4 region. Alpha and beta diversity were assessed via Shannon index and principal coordinate analysis (PCoA), respectively. Taxonomic

composition was analyzed at phylum, genus, and species levels using QIIME2 software.

Duodenal and colonic biopsies were obtained via endoscopy for pathomorphological evaluation. Tissues were fixed in formalin, paraffin-embedded, and stained with hematoxylin-eosin (H&E) for histological assessment. Mucosal integrity was quantified by measuring villus height, crypt depth, goblet cell density, and inflammatory cell infiltration using ImageJ software. Tight junction proteins (zonula occludens-1 and occludin) were evaluated via immunohistochemistry. Serum levels of lipopolysaccharide (LPS) and zonulin were measured by ELISA to assess intestinal permeability.

Statistical analyses were performed using SPSS version 27. Data normality was checked with Shapiro-Wilk tests; group comparisons used Student's t-test or Mann-Whitney U test, while correlations were assessed via Spearman's rank coefficient. Significance was set at $p < 0.05$.

Results and Discussion

Gut microbiota profiling revealed significant dysbiosis in MetS patients compared to controls. Alpha diversity (Shannon index: 4.2 ± 0.5 vs. 5.8 ± 0.6, $p < 0.001$) was markedly reduced, with PCoA showing distinct clustering between groups. At the phylum level, MetS patients exhibited an increased Firmicutes-to-Bacteroidetes ratio (2.1 ± 0.4 vs. 1.2 ± 0.3, $p < 0.01$), alongside decreased Actinobacteria (e.g., Bifidobacterium spp.) and increased Proteobacteria (e.g., Escherichia spp.). Genera such as Faecalibacterium and Roseburia, known for short-chain fatty acid (SCFA) production, were depleted ($p < 0.05$), while pathobionts like Bilophila and Desulfovibrio were enriched.

Pathomorphological examination of the mucous membrane showed pronounced changes in MetS patients. Duodenal biopsies displayed villus atrophy (villus height: 320 ± 45 μm vs. 450 ± 50 μm, $p < 0.001$), increased crypt depth, and reduced goblet cell density (15 ± 3 vs. 28 ± 4 per 100 μm, $p < 0.01$), indicative of impaired mucus production. Colonic samples revealed epithelial erosion, lymphocytic infiltration (inflammation score: 2.5 ± 0.6 vs. 0.8 ± 0.4, $p < 0.001$), and diminished tight junction expression (zonula occludens-1 staining intensity: 1.2 ± 0.3 vs. 2.8 ± 0.4, $p < 0.001$). Serum LPS (45 ± 12 EU/mL vs. 18 ± 5 EU/mL, $p < 0.001$) and zonulin (32 ± 8 ng/mL vs. 12 ± 4 ng/mL, $p < 0.001$) levels were elevated, confirming heightened permeability.

Correlations analyses linked dysbiosis to mucosal pathology: reduced SCFA-producing bacteria negatively correlated with inflammation scores ($r = -0.62$, $p < 0.01$) and positively with villus height ($r = 0.58$, $p < 0.01$). Increased Proteobacteria abundance associated with LPS levels ($r = 0.65$, $p < 0.001$), suggesting endotoxemia as a mediator.

These results align with prior studies indicating that dysbiosis promotes metabolic endotoxemia through LPS translocation, triggering systemic inflammation

and insulin resistance. The observed mucosal changes, such as barrier dysfunction, mirror findings in obesity models where high-fat diets exacerbate microbiota shifts and epithelial damage. Mechanisms involve SCFAs modulating gut integrity via G-protein-coupled receptors (e.g., GPR43), while bile acid alterations impair lipid metabolism and further dysbiosis. Unlike some reports focusing solely on obesity, our data emphasize MetS-specific colonic involvement, potentially due to hyperglycemia-induced microbial restructuring.

Conclusion

Gut microbiota dysbiosis in metabolic syndrome is intricately linked to pathomorphological alterations in the digestive system's mucous membrane, primarily through increased permeability, inflammation, and metabolite dysregulation. These changes exacerbate metabolic dysfunction, underscoring the gut as a therapeutic target. Interventions like probiotics, prebiotics, or fecal microbiota transplantation could restore microbial balance and mucosal integrity, offering novel strategies for MetS management. Future longitudinal studies are warranted to establish causality and optimize microbiota-based therapies.

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