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Gut microbiota in IgA nephropathy; a letter to the editor on recent data

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Abstract
Gut dysbiosis and intestinal barrier dysfunction are thought to contribute to the progression of IgA nephropathy (IgAN) by enhancing the production of galactose-deficient IgA1, which leads to the formation of nephrotoxic immune complexes. Furthermore, metabolites generated by an altered gut microbiome—such as indoxyl sulfate and trimethylamine N-oxide—can impair the intestinal barrier and activate mucosal immunity, playing a causal role in the disease's pathogenesis.

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Introduction

Gut microbiome plays a significant role in the pathogenesis of IgA nephropathy (IgAN) (1). Mendelian randomization studies have identified specific gut bacteria, such as Actinobacteria, that have a causal relationship with the risk of developing IgAN (1). Recent findings imply that alterations in the intestinal microbiome can directly contribute to the development of IgAN too (2). In addition, comparative studies have found differences in the intestinal microbiome composition amongst IgAN individuals and healthy subjects (3). Likewise, IgAN patients showed higher proportions of certain bacterial genera like Bacteroides, Escherichia-Shigella, and Ruminococcus in the gut, as well as increased bacterial DNA levels in the blood (4,5). Prior investigations show that, gut-kidney axis appears to be an important factor, in the integrity of the intestinal barrier (6). Disruption of the gut-kidney axis, potentially through gut dysbiosis, may facilitate the translocation of gut-derived antigens and bacteria into the circulation, triggering the autoimmune processes underlying IgAN (7). This letter aimed to take a short look at the recent data on the role of gut microbiota in aggravation of IgA nephropathy.

Search method

For this project, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ) and Embase, using different keywords like; Gut microbiome dysbiosis, gut-kidney axis, IgA nephropathy, gut microbiota and mesangial cells.

Gut microbiota alteration in IgAN

Patients with IgAN tend to have higher levels of certain bacteria in their gut (4). Meanwhile in these patients, a decreased abundance of beneficial bacteria like Bifidobacterium, Clostridium, Lactobacillus, and Enterococcus were detected (8). Additionally, increased Firmicutes/Bacteroidetes (F/B) ratio was detected (9). Likewise, in IgAN, p-cresyl sulfate, indole-3-acetic acid, phenylacetylglutamine, trimethylamine N-oxide, and indoxyl sulfate which are the metabolites produced by an altered gut microbiome, can disrupt the intestinal barrier (1,2). Previous studies showed that, these metabolites have been shown to have a causal relationship with the risk of developing IgAN (1,2). Furthermore, genes associated with IgAN are linked to the regulation of intestinal pathogens and the integrity of the intestinal barrier (10); since, disruption of the gut-kidney axis may facilitate autoimmunity and the production of aberrantly glycosylated IgA1 in this disease (11). Besides, high levels of gut-homing IgA+ B lymphocytes support the pathogenic role of intestinal mucosal hyperresponsiveness at this condition (12).

Gut microbiota influences mesangial cells

Patients with IgAN have higher levels of galactose-deficient IgA1 (Gd-IgA1) in their serum and urine compared to healthy controls (13). Moreover, urine Gd-IgA1 levels positively correlate with markers of disease severity; while, Gd-IgA1 is a key factor in the pathogenesis of IgAN (14). Gut dysbiosis and intestinal barrier dysfunction promote

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Implication for health policy/practice/research/ medical education

Alterations in the gut microbiome, including increased abundance of certain bacterial taxa and disruption of the gut-renal axis, are likely causal factors in the evolution of IgA nephropathy.

IgAN by enhancing Gd-IgA1 creation (15). Alterations in the intestinal microbiome affect the metabolism of microbiota-associated metabolites like polyunsaturated fatty acids (16). In contrast, specific gut metabolites, such as beta-hydroxybutyric acid were found to be associated with a reduced risk of IgAN (2). The recent study by Wang et al, showed higher levels of beta-hydroxybutyric acid were associated with a lower odds ratio for IgAN development (2). Notably, the study by Chang et al, in experimental models showed that, beta-hydroxybutyric acid had protective effects in kidney diseases, including IgAN (17). This substance also inhibits the deacetylation of key proteins involved in podocyte function and glomerular injury, such as nephrin, WT-1, and GSK3β (17). It is possible that, gut dysbiosis and intestinal barrier dysfunction would be primary events in IgAN pathogenesis (15). Both of these factors lead to increased production of Gd-IgA1, which forms nephrotoxic immune complexes that deposit in the glomeruli and drive disease progression (18,19).

Conclusion

Gut microbiome dysbiosis, increased intestinal permeability, translocation of gut-derived antigens and metabolites, and immune system dysregulation collectively contribute to the evolution of IgA nephropathy.

Conflicts of interest

The author declares that he has no competing interests.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the author utilized Perplexity to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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