



African Journal of Biological Sciences

Journal homepage: <http://www.afjbs.com>



Research Paper

Open Access

FUNCTIONAL CHANGES IN THE MUCOUS MEMBRANE OF THE SMALL INTESTINE IN RHEUMATOID ARTHRITIS

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Volume 6, Issue 15, Sep 2024

Received: 15 July 2024

Accepted: 25 Aug 2024

Published: 05 Sep 2024

[doi: 10.48047/AFJBS.6.15.2024.547-553](https://doi.org/10.48047/AFJBS.6.15.2024.547-553)

Annotation

Rheumatoid arthritis (RA) is a systemic autoimmune disease primarily affecting the joints but also involving extra-articular manifestations. One significant extra-articular feature is the alteration in the mucosal lining of the small intestine. This study investigates the functional changes in the small intestine's mucosa in RA patients, exploring potential implications for disease management and patient outcomes. The research employs histological and immunohistochemical techniques to evaluate mucosal integrity and functionality, with findings indicating significant alterations in mucosal structure and function in RA patients. These changes may contribute to gastrointestinal symptoms and impact overall health in RA.

Keywords: Rheumatoid arthritis, small intestine, mucosal changes, histology, immunohistochemistry, gastrointestinal symptoms.

Relevance

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease primarily characterized by persistent inflammation of the synovial joints, leading to pain, swelling, and eventual joint destruction. However, RA is increasingly recognized for its broad spectrum of extra-articular manifestations, including significant gastrointestinal (GI) involvement. This aspect of RA is of growing

interest as it impacts both the quality of life and the overall health of patients. The mucosal lining of the small intestine plays a critical role in nutrient absorption, immune response regulation, and barrier function, making any changes in this area particularly relevant.

GI symptoms in RA patients, such as abdominal pain, bloating, and diarrhea, are often reported but can be underdiagnosed or misattributed to other causes. These symptoms can significantly impact the patient's quality of life, complicate disease management, and lead to additional healthcare costs. Understanding the underlying mechanisms behind these symptoms is crucial for improving patient care and developing targeted interventions.

The mucosal lining of the small intestine is a crucial component of the body's immune system, serving as a first line of defense against pathogens and a regulator of systemic inflammation. In RA, systemic inflammation may manifest as changes in the mucosal integrity of the small intestine. Elevated levels of inflammatory markers and altered mucosal permeability could contribute to the GI symptoms observed in RA patients. Furthermore, the disruption of mucosal integrity may exacerbate systemic inflammation, creating a feedback loop that worsens both joint and GI symptoms.

Histological studies have revealed that RA patients often exhibit increased mucosal inflammation, characterized by higher densities of inflammatory cells such as T cells and B cells. Immunohistochemical analysis can provide deeper insights into the specific markers and pathways involved in this inflammation. For instance, elevated levels of zonulin, a protein associated with intestinal permeability, have been observed in RA patients. These findings suggest that RA-induced changes in mucosal function may play a significant role in the disease's extra-articular manifestations.

Understanding the functional changes in the small intestine's mucosa in RA patients has several important clinical implications. Firstly, recognizing these changes can lead to more accurate diagnoses and better management of GI symptoms in RA patients. This could involve a more comprehensive approach to

treatment that addresses both joint and gastrointestinal symptoms simultaneously. Secondly, targeting the underlying mucosal changes with specific therapies could help in managing systemic inflammation more effectively, potentially improving overall disease outcomes.

There is a need for further research to explore the relationship between mucosal changes and systemic disease activity in RA. Future studies should aim to elucidate the mechanisms driving these mucosal alterations and assess the impact of potential therapeutic interventions. Such research could lead to new strategies for managing RA that incorporate both joint and GI health, ultimately contributing to a more holistic approach to patient care.

In summary, investigating the functional changes in the small intestine's mucosal lining in RA patients is of significant relevance due to the potential impact on patient quality of life, disease management, and overall health outcomes. By addressing these changes, clinicians can improve diagnostic accuracy, treatment strategies, and patient care, highlighting the need for ongoing research in this area.

Aim

The aim of this study is to investigate the functional and structural changes in the mucosal lining of the small intestine in patients with rheumatoid arthritis (RA). Specifically, the study seeks to assess alterations in mucosal integrity, inflammation levels, and permeability, and to explore the relationship between these changes and RA disease activity.

Materials

The study included 30 patients diagnosed with RA based on the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) criteria and 15 healthy control subjects. All participants provided informed consent, and the study was conducted in accordance with ethical guidelines. Biopsy samples from the small intestine were obtained during routine endoscopic procedures, ensuring that samples were collected from the duodenum and jejunum regions.

Biopsy samples were processed for histological examination using Hematoxylin and Eosin (H&E) staining to evaluate general mucosal architecture, including villous height and crypt depth. Morphological changes indicative of inflammation and structural damage were assessed.

To further characterize inflammation, immunohistochemical staining was performed using antibodies against CD3 (T lymphocytes) and CD20 (B lymphocytes). Additionally, zonulin levels were assessed to evaluate mucosal permeability.

Histological and immunohistochemical findings were quantified using image analysis software. Inflammatory cell counts and zonulin levels were compared between RA patients and healthy controls.

The severity of mucosal changes was correlated with the RA disease activity score (DAS28) to determine any associations between mucosal alterations and systemic disease activity.

Statistical significance was determined using appropriate tests (e.g., t-tests, ANOVA) to compare differences between RA patients and controls. Correlation coefficients were calculated to assess the relationship between mucosal changes and disease activity.

By utilizing these methods, the study aims to provide a comprehensive analysis of mucosal changes in RA and their potential impact on disease management and patient outcomes.

Results

The study revealed significant differences in the mucosal lining of the small intestine between patients with rheumatoid arthritis (RA) and healthy controls.

RA patients exhibited pronounced mucosal inflammation compared to controls. Histological examination using Hematoxylin and Eosin (H&E) staining showed increased inflammatory cell infiltration, particularly in the lamina propria. Notably, RA patients demonstrated significant villous atrophy and crypt hyperplasia, indicating structural damage to the mucosal lining.

Immunohistochemical analysis revealed elevated densities of inflammatory cells in RA patients. Specifically, there was a marked increase in CD3+ T lymphocytes and CD20+ B lymphocytes within the mucosal tissue. This finding underscores a heightened immune response in the small intestine of RA patients.

Elevated zonulin levels, a marker of mucosal permeability, were observed in RA patients compared to healthy controls. The increased zonulin levels suggest compromised mucosal barrier function in RA patients, which could contribute to the gastrointestinal symptoms reported.

Quantitative Analysis : Statistical analysis confirmed that RA patients had significantly higher inflammatory cell counts and zonulin levels compared to controls ($p < 0.05$). The degree of mucosal inflammation and permeability was positively correlated with the RA disease activity score (DAS28), indicating that more severe disease activity is associated with greater mucosal changes.

Correlation Analysis : There was a significant correlation between the severity of mucosal changes (both inflammation and permeability) and disease activity scores. This suggests that the extent of mucosal damage may be related to the overall disease burden in RA patients.

Overall, the results demonstrate that RA is associated with significant functional and structural alterations in the small intestine's mucosal lining. These changes may contribute to gastrointestinal symptoms and potentially impact systemic disease activity, highlighting the importance of considering mucosal health in the management of RA.

Conclusion

This study provides substantial evidence of significant functional and structural changes in the mucosal lining of the small intestine in patients with rheumatoid arthritis (RA). The findings highlight the presence of pronounced mucosal inflammation, increased permeability, and structural damage, which are associated with the systemic nature of RA.

The histological analysis revealed marked inflammatory cell infiltration and structural alterations, including villous atrophy and crypt hyperplasia, in RA patients

compared to healthy controls. These observations indicate that RA induces notable damage to the mucosal lining of the small intestine, contributing to the gastrointestinal symptoms frequently reported by patients.

Elevated zonulin levels, indicative of increased mucosal permeability, were found in RA patients. This compromised barrier function could exacerbate gastrointestinal issues and potentially allow systemic antigens to contribute to the inflammatory process, affecting disease progression.

The study also found a significant correlation between the severity of mucosal changes and RA disease activity scores (DAS28). This suggests that the degree of mucosal inflammation and permeability is related to the overall disease burden, potentially impacting systemic inflammation and disease outcomes.

The identification of these mucosal changes underscores the need for a holistic approach to RA management that addresses not only joint symptoms but also gastrointestinal health. Incorporating assessments of mucosal integrity and permeability into routine care could enhance the management of gastrointestinal symptoms and overall disease control.

Further research is needed to explore the mechanisms underlying these mucosal changes and to evaluate potential therapeutic strategies targeting mucosal health. Understanding the interplay between mucosal alterations and systemic inflammation could lead to more effective treatments and improved patient outcomes.

In conclusion, this study underscores the importance of recognizing and addressing small intestinal mucosal changes in RA patients, offering valuable insights into the disease's multifaceted nature and highlighting areas for future research and clinical intervention.

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