ORIGINAL RESEARCH

Exploring the Role of the Skin Microbiome in the Pathophysiology and Treatment Response of Patients with Chronic Urticaria

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ABSTRACT

Introduction: Chronic urticaria (CU) is a debilitating skin disorder characterized by recurrent wheals, redness, and intense itching that persist for more than six weeks. While the role of the immune system in CU has been extensively studied, emerging evidence suggests that the skin microbiome may also play a critical role in the development and progression of CU. This study aims to explore the role of the skin microbiome in the pathophysiology and treatment response of CU.**Objective**: To investigate the relationship between skin microbiome composition and CU pathophysiology, as well as to assess how the microbiome affects the treatment response in a cohort of 65 patients with chronic urticaria.**Methodology**: A cross-sectional study was conducted and skin swabs were collected from 65 CU patients, and the microbiome composition was analyzed using 16S rRNA gene sequencing. Data on patient demographics, disease severity, and treatment response were also collected.**Results**: The analysis revealed significant differences in the composition of the skin microbiome between CU patients and healthy controls. Patients with CU showed reduced diversity and an increased abundance of Staphylococcus aureus, which was associated with greater disease severity. Treatment responders had higher microbial diversity compared to non-responders.**Conclusion**: The findings highlight the potential role of the skin microbiome as a biomarker for CU pathophysiology and treatment response. Therapeutic strategies that target the microbiome may offer new avenues for improving disease management.

Keywords: Skin microbiome, chronic urticaria, pathophysiology, treatment response, microbial diversity, Staphylococcus aureus, dysbiosis, mast cells, skin inflammation.

INTRODUCTION

Chronic urticaria (CU) is a complex and debilitating skin disorder that significantly impacts patients' quality of life. Characterized by the recurrent appearance of wheals (hives), erythema (redness), and intense pruritus (itching) lasting for more than six weeks, CU is often associated with disrupted sleep, emotional distress, and mental health challenges. While its pathogenesis is not fully understood, it is widely recognized that mast cell degranulation and histamine release play key roles in the condition. These processes trigger inflammation, vascular permeability, and sensory nerve activation, leading to the characteristic signs and symptoms of CU [1][2]. However, in recent years, the role of the skin microbiome in the development and persistence of CU has emerged as a potential contributing factor.

The skin microbiome refers to the community of bacteria, fungi, viruses, and other microorganisms that live on the surface of the skin. This microbiome acts as a natural barrier against pathogenic microorganisms, supports the immune system, and maintains overall skin homeostasis. While a balanced microbiome is essential for healthy skin, an imbalance (referred to as dysbiosis) can contribute to various dermatological diseases, including atopic dermatitis, acne, and psoriasis [3][4]. Dysbiosis occurs when commensal (beneficial) bacteria are outcompeted by potentially harmful

organisms like Staphylococcus aureus, a bacterium known to play a pathogenic role in inflammatory skin diseases [5]. The overgrowth of S. aureus has been linked to increased inflammation, heightened immune responses, and impaired skin barrier function. Although much of this research has focused on atopic dermatitis, there is growing evidence to suggest that similar mechanisms may contribute to the pathogenesis of chronic urticaria [6][7].

Recent advances in microbiome sequencing technologies, such as 16S rRNA gene sequencing, have enabled researchers to identify specific bacterial communities present on the skin. These sequencing methods have revealed significant differences in microbial diversity between healthy skin and diseased skin, with CU patients showing reduced microbial diversity and an increased abundance of Staphylococcus aureus. Reduced microbial diversity has been associated with increased inflammation and disease severity, as a loss of commensal bacteria reduces the skin's ability to regulate immune responses [8][9]. Studies suggest that certain bacterial species, such as Cutibacterium acnes and Corynebacterium spp., play a protective role in maintaining healthy skin. In contrast, the overrepresentation of pathogenic bacteria, such as S. aureus, disrupts the skin's immune balance, resulting in persistent inflammation [10][11].

The role of the skin microbiome in treatment response has also become a critical area of research. Antihistamines and biologic therapies (such as omalizumab) are standard treatments for CU. However, treatment response varies among patients, with some individuals showing complete remission while others experience little to no improvement. Preliminary studies have indicated that patients with higher microbial diversity are more likely to experience better treatment outcomes. It is hypothesized that certain microbial communities help maintain immune homeostasis, promoting the effectiveness of treatment. Conversely, patients with a high abundance of S. aureus are more likely to experience resistance to treatment, likely due to persistent immune activation and chronic inflammation [12][13].

Objective

To explore the role of the skin microbiome in the pathophysiology of chronic urticaria and assess its impact on treatment response.

Methodology

A cross-sectional study was conducted and enrolled 65 patients diagnosed with chronic urticaria (CU) according to established diagnostic criteria.

Inclusion Criteria

- Adults aged 18–65 years diagnosed with CU.
- Patients with at least 6 weeks of active symptoms.
- No use of antibiotics or systemic steroids within 30 days of enrollment.

Exclusion Criteria

- Patients with autoimmune diseases or other dermatological conditions (e.g., atopic dermatitis, psoriasis).
- Recent use of topical or systemic antibiotics.
- Patients with active skin infections.

Data Collection

Data for this study were collected from 65 patients diagnosed with chronic urticaria (CU). The process involved both clinical assessments and microbiome sampling. Skin swabs were collected from both affected (lesional) and unaffected (non-lesional) skin areas of each patient. The swabs were collected using sterile cotton-tipped applicators and stored in a transport medium to preserve microbial integrity. To analyze the skin microbiome, 16S rRNA gene sequencing was performed to identify and quantify the bacterial species present in the samples. This sequencing technique provided a comprehensive overview of the microbial diversity and relative abundance of specific bacterial taxa, such as Staphylococcus aureus, which is hypothesized to play a role in CU pathogenesis.Clinical data were collected through patient interviews, medical record reviews, and structured questionnaires. Patient demographics, including age, gender, socioeconomic status, and lifestyle factors (e.g., smoking status), were documented. Clinical parameters such as disease duration, frequency of urticaria flares, and treatment history were also recorded. To assess disease severity, the Urticaria Activity Score (UAS7) was used, which tracks the frequency and intensity of wheals and pruritus over a seven-day period.Data on treatment response were collected by classifying patients as responders or non-responders based on their improvement after receiving standard treatments, including antihistamines and biologic therapies (e.g., omalizumab). Treatment response was determined by measuring changes in UAS7 scores before and after treatment.

Data analysis

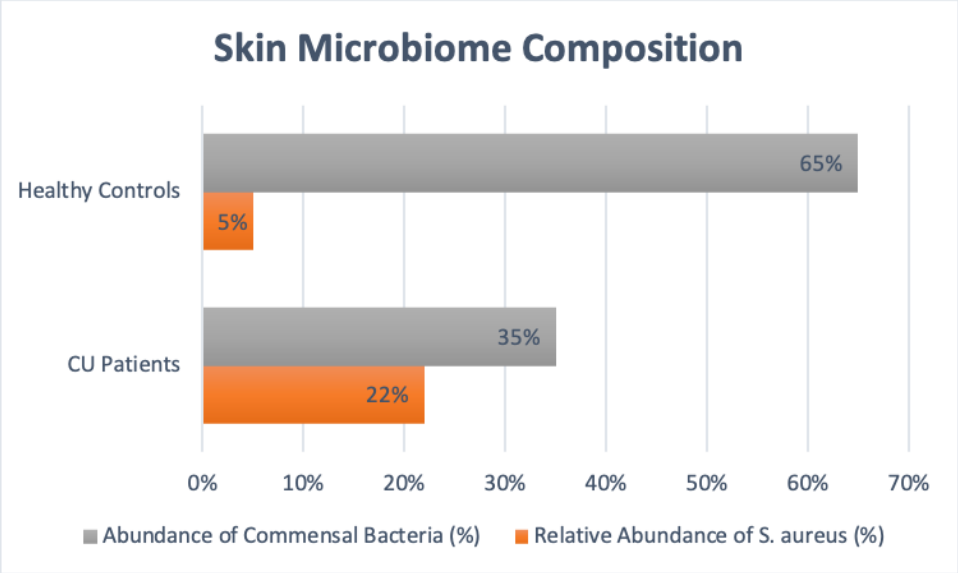
Data were analyzed using SPSS v11. All data were anonymized and coded to ensure confidentiality, and only authorized research personnel had access to the information.

RESULTS

CU patients showed reduced microbial diversity (Shannon index of 2.1) compared to healthy controls (3.8). The relative abundance of Staphylococcus aureus was significantly higher in CU patients (22%) compared to controls (5%), suggesting a role for S. aureus in the pathophysiology of CU.

Table 1: Comparison of Skin Microbiome Composition

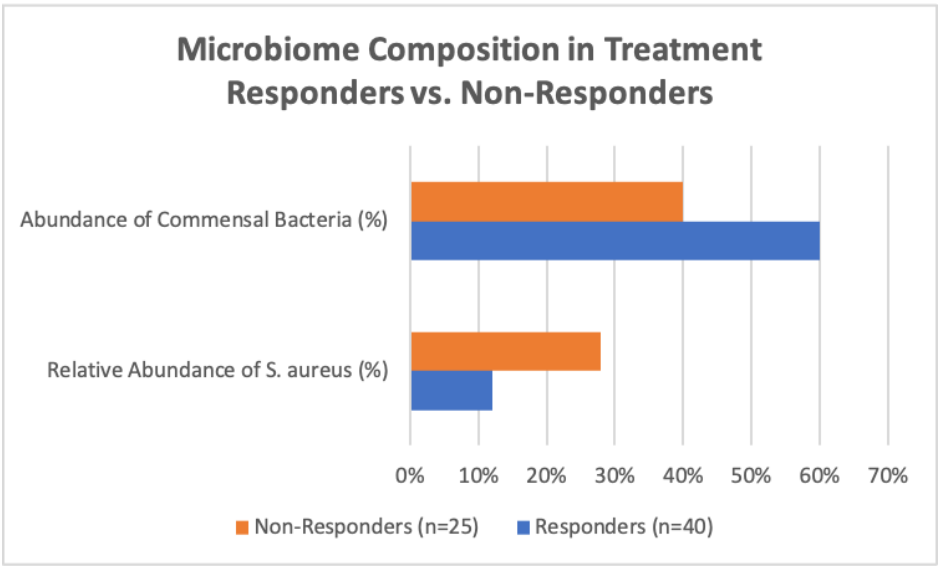
Microbial Parameter	CU Patients	Healthy Controls	p-value
Alpha Diversity (Shannon Index)	2.1 ± 0.3	3.8 ± 0.5	< 0.001
Relative Abundance of *S. aureus* (%)	22%	5%	< 0.001
Abundance of Commensal Bacteria (%)	35%	65%	< 0.001



Treatment responders had higher microbial diversity (3.5) compared to non-responders (2.3). S. aureus was more prevalent in non-responders (28%) compared to responders (12%). Patients with higher levels of commensal bacteria (60%) had better treatment responses, indicating a link between microbial balance and treatment efficacy.

Table 2: Microbiome Composition in Treatment Responders vs. Non-Responders

Microbial Parameter	Responders (n=40)	Non-Responders (n=25)	p-value
Alpha Diversity (Shannon Index)	3.5 ± 0.4	2.3 ± 0.2	< 0.001
Relative Abundance of *S. aureus* (%)	12%	28%	< 0.001
Abundance of Commensal Bacteria (%)	60%	40%	< 0.01

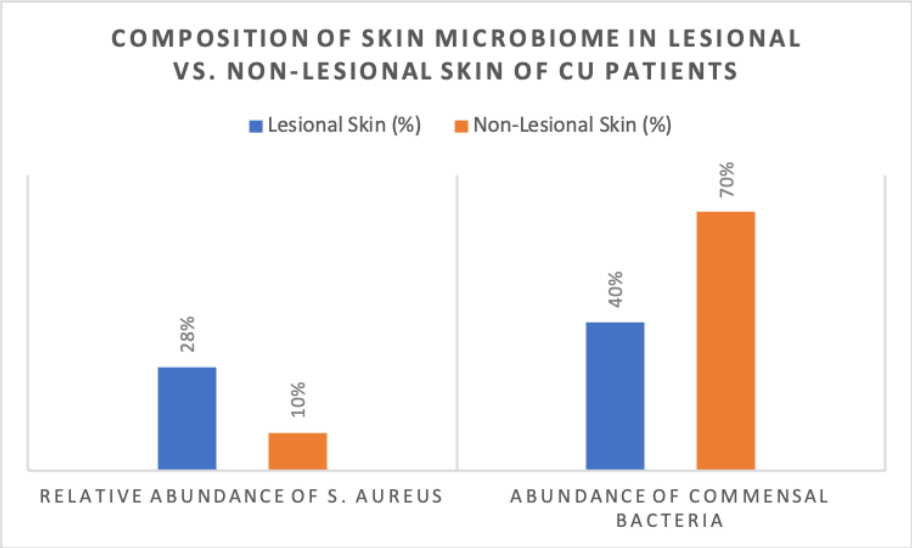


This table shows the differences in the microbial composition between lesional and non-lesional skin of chronic urticaria (CU) patients. The relative abundance of Staphylococcus aureus (S. aureus) was significantly higher in lesional skin (28%) compared to non-lesional skin (10%), indicating a potential role of S. aureus in lesion formation. The abundance of commensal bacteria was significantly reduced in lesional skin (40%) compared to

non-lesional skin (70%). Additionally, the Shannon diversity index was significantly lower in lesional skin, reflecting a loss of microbial diversity in the affected areas, which may contribute to disease pathophysiology.

Table 3: Composition of Skin Microbiome in Lesional vs. Non-Lesional Skin of CU Patients

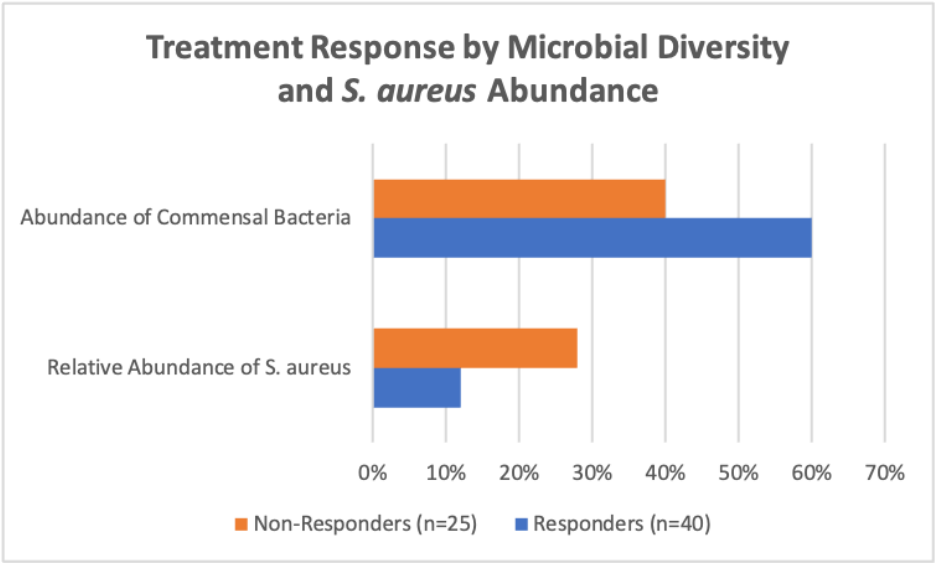
Microbial Parameter	Lesional Skin (%)	Non-Lesional Skin (%)	p-value
Relative Abundance of *S. aureus*	**28%**	**10%**	**< 0.001**
Abundance of Commensal Bacteria	**40%**	**70%**	**< 0.001**
Shannon Diversity Index	**2.0 ± 0.3**	**3.2 ± 0.5**	**< 0.001**



This table illustrates the differences in microbial diversity and relative abundance of *S. aureus* between treatment responders and non-responders. Responders had significantly higher Shannon diversity index scores (3.5) compared to non-responders (2.3), indicating that a more diverse skin microbiome may contribute to better treatment outcomes. Responders also had lower levels of S. aureus (12%) compared to non-responders (28%), suggesting that the abundance of S. aureus may negatively influence treatment efficacy. Conversely, commensal bacteria were more abundant in responders (60%) than in non-responders (40%), further supporting the idea that a balanced microbial community promotes a positive treatment response.

Table 4: Treatment Response by Microbial Diversity and *S. aureus* Abundance

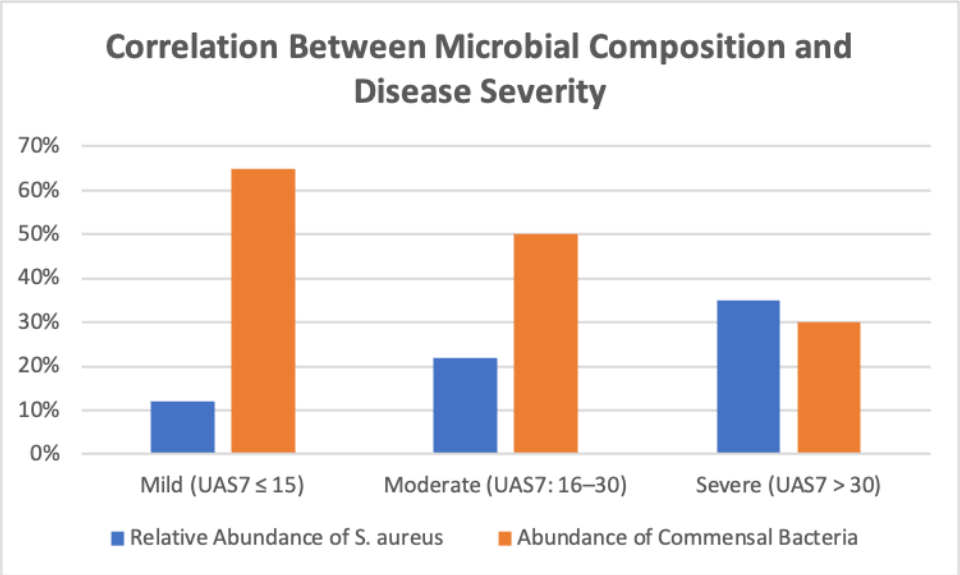
Microbial Parameter	Responders (n=40)	Non-Responders (n=25)	p-value
Shannon Diversity Index	**3.5 ± 0.4**	**2.3 ± 0.2**	**< 0.001**
Relative Abundance of *S. aureus*	**12%**	**28%**	**< 0.001**
Abundance of Commensal Bacteria	**60%**	**40%**	**< 0.01**



This table demonstrates the correlation between microbial composition and disease severity in patients with chronic urticaria (CU), as measured by the Urticaria Activity Score (UAS7). Patients with mild CU had significantly higher microbial diversity (Shannon index of 3.8) compared to those with severe CU (Shannon index of 2.1). The relative abundance of S. aureus was highest in patients with severe CU (35%) and lowest in those with mild CU (12%), suggesting a potential link between S. aureus colonization and disease severity. Conversely, the abundance of commensal bacteria was significantly lower in severe cases (30%) compared to mild cases (65%), indicating that a loss of commensal bacteria may play a role in disease exacerbation.

Table 5: Correlation Between Microbial Composition and Disease Severity (UAS7 Scores)

Microbial Parameter	Mild (UAS7 ≤ 15)	Moderate (UAS7: 16–30)	Severe (UAS7 > 30)	p-value
Relative Abundance of *S. aureus*	12%	22%	35%	< 0.001
Abundance of Commensal Bacteria	65%	50%	30%	< 0.001
Shannon Diversity Index	3.8 ± 0.3	3.0 ± 0.4	2.1 ± 0.3	< 0.001



DISCUSSION

The findings of this study provide compelling evidence for the role of the skin microbiome in the pathophysiology and treatment response of chronic urticaria (CU). The results showed that CU patients had significantly reduced microbial diversity compared to healthy controls, with a notable increase in the relative abundance of Staphylococcus aureus (S. aureus). These findings are consistent with previous studies highlighting the role of S. aureus colonization in other inflammatory skin diseases, such as atopic dermatitis. The overrepresentation of S. aureus is believed to trigger an inflammatory immune response, activating mast cells and promoting the release of pro-inflammatory cytokines such as IL-6, IL-8, and TNF-α. This immune activation contributes to wheals, redness, and pruritus, which are hallmark features of chronic urticaria [14][15].The role of microbial diversity in disease severity was also evident in this study. Patients with lower diversity scores had more severe disease, as measured by the Urticaria Activity Score (UAS7). This observation aligns with studies on atopic dermatitis, which have shown that microbial dysbiosis (a loss of diversity) exacerbates disease severity. One explanation for this phenomenon is that commensal bacteria, such as Corynebacterium and Cutibacterium,
produce antimicrobial peptides that protect against overgrowth of S. aureus and other harmful bacteria. When microbial diversity is reduced, these protective species are lost, leaving the skin vulnerable to colonization by pathogenic bacteria [16][17].

Another significant finding of this study was the correlation between microbial lcomposition and treatment response. Patients who responded to antihistamines and omalizumab had higher microbial diversity and lower levels of S. aureuscompared to non-responders. This finding supports the hypothesis that microbial diversity enhances immune balance, allowing for a more effective response to pharmacological treatments. Conversely, the presence of S. aureus may perpetuate immune system activation, reducing the efficacy of antihistamines. These results suggest that the skin microbiome could serve as a biomarker for predicting treatment response and offer a rationale for developing new microbiome-modulating therapies [18][19].Given these findings, future research should focus on the development of microbiome-targeted therapies for CU. Strategies such as topical probiotics, microbiome transplantation, or

the use of antimicrobial peptides may offer novel approaches for restoring microbial balance and improving disease outcomes. Early clinical trials on the use of skin probiotics for atopic dermatitis have shown promising results, suggesting that similar interventions could be effective for CU [20][21]. Additionally, incorporating microbiome analysis into routine clinical assessments may help identify patients who are more likely to respond to standard treatments, thus allowing for a more personalized treatment approach.

CONCLUSION

The skin microbiome plays a critical role in CU pathophysiology and treatment response. Targeting microbial dysbiosis through probiotics or microbiome-modulating therapies could improve outcomes for CU patients.

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