Case Report

Helicobacter Pylori: Beyond The Gut - Insights Into Its Association With Dermatological Conditions

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Abstract

Introduction: Helicobacter pylori (H. pylori) is a Gram-negative bacterium associated with gastrointestinal diseases and extra-gastrointestinal manifestations, including dermatological conditions. Understanding the precise mechanisms and clinical implications of the H. pylori-skin disorder association is essential.

Materials and methods: A cross-sectional observational study was conducted at a private dermatology centre in Ahmedabad, Gujarat, from January 2021 to August 2023. Patients coming with various dermatological conditions and with suspected H. pylori infection underwent clinical examination, laboratory tests, and skin biopsy to confirm the diagnosis of disease. The statistical analysis assessed associations between demographics, dermatological conditions, and H. pylori antibody test results.

Laboratory Investigation: H. pylori antibody levels were measured using serology by doing H.pylori IgG antibody level testing and cut off values of >0.90 were considered positive. Statistical Analysis: Data entry and analysis involved Microsoft Excel 360, calculating proportions, percentages and drawing appropriate inferences.

Results: Of 1131 enrolled patients (male-female ratio 1:1.43), 22% tested positive for H. pylori, with higher positivity rates in patients aged >60 years and 40-60 years. Analysis revealed varying proportions of H. pylori positivity across dermatological conditions, with alopecia areata and chronic urticaria showing the highest rates.

Conclusions: While studies suggest H. pylori's involvement in dermatological diseases, further research is needed to understand this relationship fully. Systematic investigations into the impact of eradication therapy are essential to inform clinical management strategies and guide future research directions.

Keywords: Helicobacter Pylori; Extra-gastrointestinal Manifestations; Immune Dysregulation; Molecular Mimicry; Eradication Therapy.

Introduction

Helicobacter pylori (H. pylori) is a Gram-negative bacterium known for its intricate relationship with various gastrointestinal diseases, including gastritis, peptic ulcer disease, and gastric malignancies. However, emerging evidence suggests its involvement in extra-gastrointestinal manifestations like hematological, cardiovascular, neurological, metabolic, autoimmune and dermatological conditions.[1]

Several studies have implicated H. pylori in the pathogenesis of various skin disorders, ranging from chronic urticaria and rosacea to autoimmune blistering diseases such as bullous pemphigoid and dermatitis herpetiformis. The association of H, pylori with various disease like psoriasis vulgaris, Behçet's disease, alopecia areata, Henoch-Schoenlein purpura, sweet's syndrome have also been reported. While the precise mechanisms underlying this association remain incompletely understood, proposed mechanisms include molecular mimicry, immune dysregulation, and systemic inflammation induced by H. pylori infection.

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In recent years, accumulating evidence has suggested a bidirectional relationship between H. pylori infection and skin disorders, with some dermatological conditions potentially serving as extragastric manifestations of H. pylori-related systemic inflammation. Conversely, eradication of H. pylori has been reported to ameliorate certain skin disorders in selected patient populations, underscoring the clinical relevance of understanding this intricate interplay.

A comprehensive study was conducted at a private dermatology centre in Ahmedabad, Gujarat from Jan 2021 to Aug 2023 to summarize the existing literature on the association between H. pylori infection and various skin disorders, elucidating the potential mechanisms involved which can help in the further treatment planning of the disease.

Materials and Methods

Study Design

This research employs a cross-sectional observational study design. All the patients visiting a private dermatology centre from Jan 2021 to Aug 2023, with a history of certain signs or symptoms like dyspepsia, abdominal pain, loss of appetite, frequent bloating/burping and stress were enrolled for the study. A thorough clinical examination was done and a final diagnosis was achieved in some patients with the help of laboratory tests and skin biopsy to confirm the diagnosis of the disease.

Inclusion Criteria

Patients who gave consent for complete examination and testing for H.pylori infection were included in the study.

Exclusion Criteria

Patients who did not give consent were excluded from the study.

Consent and Confidentiality

Informed consent was obtained from all participants, and strict confidentiality measures were maintained throughout the study.

Laboratory Investigations

All the patients were advised H Pylori antibody test to detect circulating Ig G antibodies. The cut off values of >0.90 were considered positive. [44]

Statistical Analysis

Data were entered and processed in Microsoft Excel 360 and was analyzed based on age, sex, dermatological conditions and H Pylori antibody test result. Percentages were calculated and appropriate statistical tests were applied to find out the association.

Results

The study enrolled total of 1131 patients with 462 males (41 %) and 669 females (59%). Almost 45% patients belonged to the age group 20-40 years.

The H. Pylori test was positive in 247 patients (22%). Female preponderance was seen. Almost 59% H Pylori positive patients were female while 41% were males. The results were not statistically significant (Table 1). The association was not significant. (Chi-square statistic 0.026, p value 0.88, not significant at $p < 0.05$).

Most of the H. Pylori patients belonged to age group > 60 years (35%) and 40-60 years (28%). The results were statistically significant (Table 2). The association was statistically significant. (Chi-square statistic 35.27, p value < 0.001).

Gender	H Pylori + (>0.90)		H pylori -		Total
	No.	%	No.	%	No.
M	102	41.3	360	40.7	462
F	145	58.7	524	59.3	669
Total	247	100	884	100	1131

Table 1: H.pylori distribution among both the genders

Age group	H Pylori + (>0.90)		H Pylori -		Total
	No.	%	No.	%	No.
0-20	21	11.1	169	88.9	190
20-40	96	18.9	412	81.1	508
40-60	86	27.9	222	72.1	308
>60	44	35.2	81	64.8	125
Total	247	21.8	884	78.2	1131

Table 2: H.pylori distribution among various age groups

When analysing disease-wise, out of 247 H. Pylori positive patients, maximum patients were of Alopecia areata (16.5%) followed by Chronic urticaria (11.7%). Rosacea (10%), Lichen Planus (8.9%) and Vit B12 deficiency (8.9%). (Table 3)

Dermatological condition	Number of patients with H Pylori +	%
Atopic Dermatitis	18	7.2
Aphthous ulcers	15	6
Alopecia Areata	41	16.5
Behcet Disease	2	0.8
Vit B12 deficiency	22	8.9
Chronic Urticaria	29	11.7
Chronic Immune thrombocytopenic Purpura	3	1.2
Hair loss	21	8.5
Henoch Schoelein Purpura	2	0.8
Lichen Planus	22	8.9
Lupus	3	1.2
Lymphoma	1	0.4
Psoriasis	17	6.8
Prurigo Nodularis	12	4.8
Pemphigus	2	0.8
Rosacea	25	10.1
Systemic sclerosis	2	0.8
Sjogren's Syndrome	1	0.4
Vitiligo	8	3.2
Vasculitis	1	0.4
Total	247	

Table 3: H.pylori distribution among various dermatological conditions

Discussion

Helicobacter pylori and Chronic urticaria

Chronic urticaria, characterized by recurrent wheals and angioedema for over six weeks, presents a significant quality of life burden. Recent evidence suggests a potential association between Helicobacter pylori (H. pylori) infection and chronic urticaria. This discussion aims to explore this clinical link [2]. Chronic idiopathic urticaria (CIU), characterized by detectable histamine-releasing autoantibodies, often correlates with autoimmune conditions like thyroiditis, vitiligo, diabetes, rheumatoid arthritis, and pernicious anemia [3].

The pathophysiological mechanisms remain speculative but may involve H. pylori-induced gastric inflammation leading to the release of pro-inflammatory cytokines such as interleukin (IL)-6, IL-8, and tumor necrosis factor-alpha (TNF-α). Molecular mimicry between H. pylori antigens and host tissues may trigger autoimmune responses, exacerbating urticaria symptoms [4], [5], [6].

Screening for H. pylori in refractory or severe chronic urticaria, particularly in high-prevalence regions, is crucial. If detected, eradication therapy with antibiotics like clarithromycin-based triple therapy or bismuth-based quadruple therapy may be considered as adjunctive treatment.

Helicobacter pylori and Psoriasis vulgaris

Psoriasis, an autoimmune skin condition, is characterized by erythematous papules and plaques with silvery micaceous scales. Its development involves intricate cytokine interactions, genetic predisposition, environmental triggers, and immune dysfunction [7]. treatment options encompass traditional agents like methotrexate, cyclosporine, and acitretin, as well as newer biologics targeting tumor necrosis factor alpha, interleukin 17, and interleukin 23 [8].

Helicobacter pylori (HP), a prevalent microorganism, is linked to various extragastric conditions, including autoimmune diseases. It's suggested that HP may worsen psoriasis by affecting immune responses, particularly in genetically susceptible individuals, potentially exacerbating the condition. Studies have shown a higher prevalence of HP infection in psoriasis patients compared to healthy individuals, and improvements in psoriatic lesions and PASI scores have been reported after HP eradication [9]. However, conflicting evidence exists, leading to ongoing debate about HP's exact role in psoriasis pathogenesis.

Helicobacter pylori and Lichen planus

Lichen planus is a chronic inflammatory skin condition characterized by pruritic, polygonal, purple, flat-topped papules and plaques. Lichen planus is considered to have an autoimmune component mediated by T-cells. Lichen planus can manifest on various areas of the skin or mucous membranes, but it is frequently observed on the flexural aspects of the wrists, the back, and the ankles. Additionally, lesions on mucous membranes are highly prevalent. The prevalence of the condition is higher among females compared to males. [10].

The dominant hypothesis suggests that exposure to external factors like viruses, drugs, or contact allergens leads to changes in self-antigens present in the skin's outer layer. The alteration of self-antigens can trigger an immune response in susceptible individuals, characterized by the recruitment and activation of CD8+ T cells. These cytotoxic T cells infiltrate the epidermis and target keratinocytes, leading to their destruction and the characteristic clinical manifestations of lichen planus, such as pruritic papules and plaques [11], [12]. Overall, the prevailing theory underscores the complex interplay between environmental factors, immune dysregulation, and epidermal alterations in the pathogenesis of lichen planus.

The improvement in the disease outcome can be obtained by combining the bacterial eradication

regimen with the treatment of lichen planus.

Helicobacter pylori and Prurigo nodularis

Prurigo nodularis (PN) is a chronic inflammatory condition characterized by intensely pruritic hyperkeratotic nodules or papules which tend to appear more frequently on the extensor surfaces of the limbs and trunk. Prurigo nodularis causes relentless itching initiating the chronic itch-scratch cycle [13]. It can affect any age group. Emerging evidence has pointed towards a possible link between prurigo nodularis and H. pylori infection, prompting an investigation into this association [14]. The bacterium can be considered as a possible trigger factor in provocating the underlying disease leading to gastrointestinal manifestations along with repeated itching.

Significant improvement in skin lesions was noted after giving H. pylori eradication therapy.

Helicobacter pylori and Alopecia areata

Alopecia areata is a chronic autoimmune condition causing non-scarring hair loss in all the age groups affecting both sexes. It can be associated with other autoimmune diseases like lichen planus, autoimmune thyroiditis, psoriasis [15].

The potential mechanisms underlying any association between H. pylori infection and alopecia areata are not fully understood. It has been proposed that chronic H. pylori infection may contribute to systemic inflammation and immune dysregulation, which could in turn trigger or exacerbate autoimmune responses involved in alopecia areata. Additionally, molecular mimicry between H. pylori antigens and host tissues may lead to cross-reactivity and the production of autoantibodies targeting hair follicles [16].

While some studies have suggested a potential role for H. pylori eradication therapy in the management of alopecia areata, further research is needed to validate these findings and elucidate the underlying mechanisms.

Helicobacter pylori and Hair loss

Hair loss, also known as alopecia, encompasses a spectrum of conditions characterized by partial or complete loss of hair from the scalp or other parts of the body. While androgenetic alopecia is the most common form of hair loss, various other factors, including autoimmune processes, nutritional deficiencies, and infectious agents, can contribute to hair loss [17]. Helicobacter pylori, a Gram-negative bacterium, is primarily associated with gastrointestinal disorders such as gastritis and peptic ulcers but has also been linked to extragastric manifestations, including autoimmune diseases and dermatological conditions.

Proposed mechanisms include immune dysregulation induced by H. pylori infection, leading to inflammatory processes that affect hair follicles. Additionally, nutritional deficiencies associated with H. pylori-related gastritis may contribute to hair loss indirectly. However, methodological limitations and heterogeneity among studies warrant cautious interpretation [18].

Helicobacter pylori and Vitamin B12 deficiency

Vitamin B12 (cobalamin) is crucial for hematopoiesis, neurological function, and DNA synthesis, with deficiency leading to megaloblastic anemia, neuropathy, and cognitive impairment [1]. H. pylori-induced gastritis can cause B12 malabsorption, bacterial overgrowth, and interference with intrinsic factor production [5], exacerbating deficiencies. Chronic antral gastritis, often correlated with H. pylori infection, diminishes gastric acid and pepsin secretion, hindering B12 absorption [19]. H. pylori also exacerbates gastritis and peptic ulcers, further impeding B12 uptake by reducing intrinsic factor availability [20]. Treating H. pylori resolves inflammation, normalizes acid secretion, and improves nutrient absorption, offering potential long-term correction of B12 deficiency and gastrointestinal health

restoration [21].

Helicobacter pylori and Atopic dermatitis

Atopic dermatitis (AD) is a common chronic inflammatory skin condition characterized by pruritic and eczematous lesions. Atopic dermatitis is a multifactorial disease influenced by genetic predisposition, immune dysregulation, and environmental factors. While the pathogenesis of atopic dermatitis is complex and not fully understood, recent studies have suggested a possible role of microbial dysbiosis in the gut-skin axis [22].

The dysregulation of gut microbiota can cause immune dysregulation and systemic inflammation, possibly worsening skin inflammation in atopic dermatitis. H. pylori-induced immune responses and molecular mimicry may also contribute to atopic dermatitis pathogenesis. While evidence suggests a potential association between atopic dermatitis and H. pylori infection, exact mechanisms are unclear [23].

Helicobacter pylori and Rosacea

Rosacea is a chronic inflammatory skin disorder marked by facial erythema, papules, pustules, telangiectasia, and sometimes ocular manifestations. While its cause remains partly unclear, emerging evidence suggests a potential link with Helicobacter pylori (H. pylori) infection [24]. Triggers like alcohol, sun exposure, caffeine, and spicy foods can provoke flare-ups. Rosacea has four subtypes: erythematotelangiectatic, papulopustular, phymatous, and ocular [25].

The association between H. pylori and rosacea may involve immunological and inflammatory pathways. H. pylori-induced gastric inflammation can lead to systemic release of pro-inflammatory cytokines, possibly contributing to rosacea symptoms. Molecular mimicry between H. pylori antigens and host tissues may also trigger immune responses [26], [27]. Clinically, screening for H. pylori may be considered in refractory or severe rosacea cases unresponsive to current treatments. Eradication therapy with antibiotics can serve as adjunctive treatment, providing symptomatic relief for both rosacea and gastrointestinal symptoms.

Helicobacter pylori and Vitiligo

Vitiligo is a common autoimmune skin disorder characterized by the destruction of melanocytes, resulting in depigmented patches on the skin. Despite numerous studies, its exact etiology remains elusive, with a complex interplay of genetic, autoimmune, environmental, and biochemical factors implicated [28]. Helicobacter pylori, a Gram-negative bacterium, has been extensively studied for its role in gastritis, peptic ulcers, and gastric cancer. However, recent research suggests a potential association between H. pylori infection and various extragastric manifestations, including autoimmune diseases [29].

Accumulating evidence suggests a potential association between Vitiligo and H. pylori infection, although the exact underlying mechanisms remain to be elucidated. The possible association of H. pylori in Vitiligo patients warrants screening of vitiligo patients with H. pylori test particularly those with gastrointestinal symptoms or refractory disease [30].

Helicobacter pylori and Pemphigus

Pemphigus encompasses a spectrum of autoimmune blistering diseases characterized by autoantibodies targeting desmosomal proteins desmoglein 1 and 3, leading to intraepithelial blister formation and mucocutaneous erosions [31]. While the exact etiology of pemphigus remains incompletely understood, both genetic predisposition and environmental triggers, including infections, have been implicated [32]. Helicobacter pylori, a Gram-negative bacterium, is well-known for its role in gastrointestinal disorders but has also been associated with various extragastric manifestations, including autoimmune diseases [33].

Helicobacter pylori and Behcet's disease

Behçet's disease is a chronic inflammatory condition affecting multiple organs, with gastrointestinal involvement known as Entero-Behçet disease [34]. While its exact cause is unclear, genetic and environmental factors contribute to its development. Recent studies suggest a potential role of infectious agents like H. pylori in triggering or worsening immune dysregulation in Behçet's disease [35]. The mechanisms linking H. pylori and Behçet's disease are not fully understood but may involve immune dysregulation, systemic inflammation, and molecular mimicry between H. pylori antigens and host tissues. If a causal relationship is established, targeted eradication of H. pylori could be a therapeutic intervention for Behçet's disease, potentially improving genital and oral ulceration [36], [37].

Helicobacter pylori and Henoch Schonlein purpura

Henoch-Schönlein purpura (HSP) is a systemic vasculitis characterized by IgA immune complex deposition, primarily affecting small blood vessels. It typically presents with palpable purpura, arthritis or arthralgia, abdominal pain, and gastrointestinal bleeding. While its exact cause is unclear, bacterial, viral, drug-induced, or environmental factors may contribute to its progression. There's growing interest in the potential association between H. pylori infection and HSP, possibly triggering immune dysregulation and vasculitis development. Significant improvement in gastrointestinal symptoms and purpura was observed with bacterial eradication treatment [38-40].

The potential association between pemphigus and H. pylori infection suggests possible mechanisms like molecular mimicry and systemic immune dysregulation. Further research is needed to understand these mechanisms and assess the therapeutic potential of H. pylori eradication in pemphigus management [41].

Helicobacter pylori and Systemic sclerosis

Systemic sclerosis (SSc) is a complex autoimmune disorder characterized by connective tissue fibrosis affecting the skin and internal organs [42]. Immune dysregulation, vasculopathy, and tissue fibrosis affect multiple organs, including the skin, lungs, heart, and gastrointestinal tract. While its exact cause is unclear, genetic and environmental factors, including infectious agents, are implicated [43]. Bacterial, viral, and parasitic infections, like H. pylori, may trigger autoimmune responses through molecular mimicry and exacerbate inflammation and fibrosis in SSc. H. pylori infection is suggested to contribute to SSc progression, particularly in skin manifestations, with eradication potentially reducing disease activity and improving skin involvement [42].

Conclusion

The mystery of H. pylori (HP) beyond the gastrointestinal apparatus and related diseases remains unsolved and fascinating for researchers. Particularly, the link between HP and skin has been largely evoked, even in common cutaneous conditions. Although some studies have shown that HP has a role in the pathogenesis of some dermatological diseases, it is not known whether HP is a trigger or the causative agent for the disease. The results of studies investigating HP seropositivity in skin diseases and the effect of eradication are conflicting. For this reason, systematic studies examining the relationship between dermatological entities and infection with HP, and documentation of the effect of HP eradication are needed to further our understanding on this topic.

Such studies will also help us uncover the possible role of H Pylori in many more dermatological conditions, which are not previously studied.

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