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Original Article

Association Between Helicobacter Pylori Infection and Vitiligo

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ABSTRACT

Objective: To determine the association between Helicobacter pylori infection and vitiligo in patients visiting a tertiary care hospital of Punjab, Pakistan.
Study Design: Case control study.
Place and Duration of Study: Department of Dermatology, Combined Military Hospital, Lahore Pakistan, from Oct 2021 to Mar 2022.
Methodology: A total of 60 adult vitiligo patients and 60 healthy controls, of both genders, were included in the study. Their ages ranged from 18-70 years. All study participants underwent stool antigen test to detect the presence of Helicobacter pylori antigen.
Results: The mean age of the cases was 43.47±8.16 years whereas it was 40.08±7.42 years in the controls. The mean duration of disease was 4.133±1.21 months. H. pylori Infection was detected in 36(60%) cases as compared to 11(18.3%) controls (p<0.001, OR=6.68); which was found to be statistically significant.
Conclusion: Significant association between H. pylori infection and vitiligo was demonstrated in the current study.
Keywords: Etiology, Helicobacter pylori, Pathogenesis, Vitiligo.

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INTRODUCTION

Helicobacter pylori (*H. pylori*) is a microaerophilic, gram-negative, spiral bacterium that was discovered in 1982 in patients of chronic gastritis and gastric ulcer and later implicated in gastric mucosa-associated lymphoid tissue (MALT) lymphoma.[1,2] It is a common pathogen with up to 50% of the world harbouring it in the upper gastro-intestinal tract.[1] High prevalence is noted in low socio-economic, overcrowded areas with poor sanitation and inadequate health facilities. In the affluent, industrialized world the prevalence is less than 40%.[1] It is postulated that *H. pylori* triggers an inflammatory response by releasing various cytotoxic substances which have the potential to alter body's immunological reactions, both humoral and cell mediated.[3] These not only lead to gut pathologies but have been implicated in extra-gastric immune mediated conditions, including dermatological disorders like chronic spontaneous urticaria, atopic dermatitis, psoriasis, lichen planus, and rosacea etc.[4]

Vitiligo is an autoimmune depigmentation disorder in which there can be widespread white patches all over the body. This disorder targets pigment producing melanocytes, of the skin and hair, leading to their destruction with resultant white lesions.[5] It can involve any part of the skin or mucosae. Different theories have been proposed for the loss of pigment. The exact pathogenic mechanisms are still not fully understood. However, genes, auto-immune processes and oxidative stresses have been implicated.[6,7]

Although vitiligo leads to skin depigmentation which is mostly of cosmetic concern; it negatively influences patient's quality of life by decreasing self-esteem and causing significant psychological distress. There are few published studies, none from South Asia, about potential association of *H. pylori* in vitiligo and the results have been conflicting.[8,9] The dearth of local data and the potential opportunity of paving way to a new therapeutic modality for vitiligo led us to undertake this study.

METHODOLOGY

The case control study was conducted at the Department of Dermatology, Combined Military Hospital, Lahore from October 2021 to March 2022. Ethical approval to conduct the study was given by the hospital's Ethical Review Committee (262/2020). Sample size of 120 (60 cases and 60 controls) was calculated while taking expected frequency of *H. pylori* to be 62.9% in vitiligo patients and 37.1% in healthy

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controls.[9] Consecutive, non-probability sampling technique was employed to recruit study participants meeting the inclusion and exclusion criteria.

Inclusion Criteria: Study participants of either gender, aged between 18-70 years were recruited for the study. Cases were those presenting with vitiligo defined as depigmented macules and/or patches present anywhere on the body with no overlying surface changes like scaling, crusting and atrophy with the diagnosis confirmed by Wood's lamp examination, which revealed milky white accentuation of lesions. Whereas controls were healthy adults without vitiligo. They were attendants of patients or those patients presenting with other minor complaints in OPD e.g. furuncle, impetigo, wart.

Exclusion Criteria: Patients who gave history of undergoing *H. pylori* eradication therapy in the past or taking antibiotics and medicines containing bismuth and/or any proton pump inhibitor during study period or one month prior to study, and pregnant and lactating females were excluded from the study.

All study participants gave voluntary, written informed consent. Pre-designed proformas were used to document demographic information including name, age, gender and duration of disease. Both cases and controls underwent *H. pylori* antigen detection test through stool sample. All stool antigen tests were done from the same hospital laboratory employing same kit (one step rapid test by Safecare Bio-Tech Co. Ltd.) to eliminate bias.

Data gathered on proformas was entered and statistically analyzed using Statistical Package for Social Sciences (SPSS) version 25. Quantitative variables such as age and duration of disease were described by means and standard deviations, whereas qualitative variables such as gender and H. pylori infection were defined by frequency distributions, proportions and percentages. Odds Ratio (OR) was calculated taking OR>1 as significant. Data was stratified for age, gender and duration of disease to address effect modifiers. Post-stratifications, Chi-square test was applied taking *p*-value≤0.05 as statistically significant.

RESULTS

One hundred and twenty study participants were enrolled in the study, with ages ranging between 18 and 70 years. Mean age of vitiligo patients was 43.47±8.16 years (range: 29-62 years). The mean duration of disease was 4.13±1.21 months; whereas controls had a mean age of 40.08±7.42 years (range: 26-56 years). Male gender was dominant in both groups. Amongst cases 32(53.3%) were male and amongst the controls 48(80%) were male. *H. pylori* Infection was observed in 36(60%) vitiligo patients as compared to 11(18.3%) control group (*p*<0.001,OR=6.68) as shown in Table-I.

Table-I: Comparison of H. pylori Infection in Cases and Controls (n=120)

H. pylori Infection	Cases n=60	Controls n=60	*p*-value Odds Ratio
Yes	36(60%)	11(18.3%)	<0.001
No	24(40%)	49(81.7%)	6.68

Association of *H. pylori* Infection in both groups with regard to age, gender and duration of disease was carried out to determine effect modifiers (Table-II).

Table-II: Association of H. pylori Infection with Respect to Gender, Age Groups and Disease Duration (n=120)

Parameters	Cases n=60		Controls n=60		Odds Ratio	*p*-value
	Positive	Negative	Positive	Negative		
Gender						
Male	29(90.6%)	3(9.4%)	10(20.8%)	38(79.2%)	36.7	<0.001
Female	7(25%)	21(75%)	1(8.3%)	11(91.7%)	3.67	0.227
Age (years)						
18-50	28(54.9%)	23(45.1%)	10(18.5%)	44(81.5%)	5.36	<0.001
51-70	8 (88.9%)	1 (11.1%)	1(16.7%)	5(83.3%)	40	0.005
Duration of disease (years)						
Up to 3	12(60%)	8(40%)	-	-	-	1.00
>3	24 (60%)	16 (40%)	-	-	-	

Males were found to have more chances of underlying H. pylori infection than females (*p*<0.001). However, total duration of vitiligo had no impact on the frequency of underlying *H. pylori* infection (*p*>0.05).

DISCUSSION

Vitiligo is a challenging disease to treat. Management plans are marred by poor response and relapses; although wide ranging therapeutic options, including topical and systemic immunomodulatory agents, phototherapy, lasers and surgical procedures,

have been tried.[10] Current focus is on the pathogenesis of the disease process, which is complex and multi-faceted.[11] Recently, significant insight has been gained into the pathogenesis of vitiligo which have the potential to offer newer therapeutic modalities for the management of vitiligo.[12]

Understanding the pathogenic mechanisms can potentially lead to viable therapies to restore the body's altered functions. Many Infectious agents have been claimed to trigger disease process through various immunological mechanisms.[13] These include T cell dysfunction, antibody production, cytokines production, major histocompatibility complex activation, immune complex formation and deposition in different body organs and/or chronic inflammatory damage.[14] *H. pylori*, one of the commonest bacteria worldwide, has been found to colonize human gastric mucosa and be involved in various extra-gastric diseases by triggering forceful inflammatory responses, both cell mediated and humoral.[15] It has been implicated in different cutaneous disorders e.g. chronic spontaneous urticaria, urticarial vasculitis, atopic dermatitis, psoriasis, rosacea, vitiligo etc.[16]

For vitiligo, data is conflicting regarding its association with *H. pylori* infection. Cakmak *et al*.[7] found that *H. pylori* stool antigen test was positive in 50% of the patients in vitiligo group and 33.3% of patients in controls. Although study results showed a trend towards association of vitiligo with underlying *H. pylori* infection, this wasn't found to be statistically significant (p>0.05).7 However, Dogan *et al*.[8] conducted a study in Turkey and found that patients with vitiligo were significantly more likely to have *H. pylori* infection than patients without vitiligo (60.3% vs.41.5%; p<0.038). Another Turkish study by Rifaioğlu *et al*.[17] conducted study on 34 patients and 30 controls and found that the frequency of *H. pylori* infection was 64.7% in the patient group and 33.3% in the control group (p-value=0.012). Sanaa *et al*.[9] reported that *H. pylori* stool antigen test was positive in 22(62.9%) of the patients and 13(37.1%) of the controls and this difference was statistically significant (p<0.05). Similarly, Egyptian study by Bakry *et al*.[18] found that *H. pylori* infection was positive in 49(65.3%) of their vitiligo cases in contrast to 18(24%) of the controls and the difference was statistically significant (p=0.001).

Establishing an association of underlying H. pylori infection led researchers to study the effect of H. pylori eradication therapy on extra gastric diseases. Patients of psoriasis, alopecia areata, urticaria and Henoch Schonlein purpura have been reported to benefit from such therapy.[1,19] Interestingly, Bakry *et al*.[18] have found *H. pylori* eradication treatment beneficial in 11(22.4%) of total 49 vitiligo patients in whom underlying *H. pylori* infection was detected. They found patients with rapidly increasing lesions and larger body surface area involvement had more beneficial effect as compared to stable and segmental vitiligo. Their study findings have suggested role of this cheap, newer therapeutic regimen in challenging cases of vitiligo.

Guarneri *et al*. have performed a comprehensive review of cutaneous disorders in which *H. pylori* has been implicated, including vitiligo.[20] These early results appear promising and researchers have advocated bigger studies for more conclusive results.[1,18,19]

CONCLUSION

Our study has yielded a statistically significant association of H. pylori infection with vitiligo.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

NR & AR: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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