DOI: 10.15171/mejdd.2017.59

Association between *Helicobacter Pylori* Infection and Alopecia Areata: A Study in Iranian Population

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Received: 29 Nov. 2016
Accepted: 28 Feb. 2017

ABSTRACT

BACKGROUND

Alopecia areata is an immune mediated inflammatory hair loss, which occurs in all ethnic and age groups, and both sexes. However no significant etiology has been known for this disease. *Helicobacter pylori (H. pylori)*, is an organism colonized in gastric mucosa. This bacterium has been associated with certain extra-digestive dermatological conditions. The causal relationship between alopecia areata and *H. pylori* infection has been discussed in literature. Therefore, we conducted this study to evaluate the prevalence of *H. pylori* infection in patients with alopecia areata and assess the risk of this infection in patients with this disease in order to determine its potential roles in the physiopathology of this disease.

METHODS

Between 2014 and 2015, we prospectively studied 81 patients with alopecia areata and 81 healthy volunteers with similar age and sex. Patients without any history of *H. pylori* infection were included in the study and underwent urease breath test. All results were analyzed using SPSS software (version 21.0) and *p* value<0.05 was considered as statistically significant.

RESULTS

81 patients and 81 controls with the mean age of 34.9±11.6 and 38.2±13.4 years were studied (p=0.097). 48 (59.3%) and 45 (55.6%) individuals were male, in cases and control groups respectively (p =0.634). The result of urea breath test (UBT) was positive in 43 (53.1%) patients in cases and 27 (33.3%) individuals in control group, which was significantly different (p =0.011). The risk of *H. pylori* infection in alopecia areata was 2.263 (95% CI: 1.199-4.273).

CONCLUSION

The results of our study showed significant difference between *H. pylori* infection in individuals with and without alopecia areata, which shows that *H. pylori* contamination may be effective in physiopathology of alopecia areata. Therefore these results should be tested in large multivariable cohorts and controlled trials to reach more accurate evidence in the future and to generalize this idea to larger population.

KEYWORDS:
Helicobacter pylori; Alopecia areata; Urease breath test

Please cite this paper as:
Behrangi E, Mansouri P, Agah S, Ebrahimi Daryani N, Mokhtare M,Azizi Z,Ramezani GhamsariM, Rohani Nasab M, Azizian Z. Association between *Helicobacter Pylori* Infection and Alopecia Areata: A Study in Iranian Population. *Middle East J Dig Dis* 2017:9:107-110. DOI: 10.15171/mejdd.2017.59.

INTRODUCTION

Alopecia areata is a chronic inflammatory disease leading to non-scar forming hair shedding. Except the head, as the most common site of involvement, other hairy locations may be affected and in severe cases all parts of the body would develop alopecia.[1] Alopecia areata has a prevalence rate of 1 per 100,000

subjects and a risk coefficient of 2%.[1] Until now definite etiology is not known but some evidence have shown autoimmune underlying mechanisms of this disease.[2] Histological findings are the most important documents that show the presence of T-lymphocyte infiltration around the terminal hair follicles.[1] T-cell mediated perifolliculitis leading to normal cell cycle disruption is one of the proposed etiologies.[1] *Helicobacter pylori (H. pylori)* is a microaerophilic gram negative bacteria colonized in the stomach [3] leading to contamination of 50% of worldwide population.[4] Currently it has been shown that *H. pylori* may be related to various non-gastrointestinal disorders including chronic urticaria [5-7], roseace [5-8], psoriasis [8,9], Schönlein-Henoch purpura [10], Behçet disease [11,12], chronic itching [13], progressive systemic sclerosis [14,15], Sjögren syndrome [16,17], and sweet syndrome .[18] Most of these diseases have shown partial or complete improvement after *H. pylori* eradication.[7,9,19-21] Different mechanisms have been proposed including; formation of antigen-antibody complexes and cross-reactive antibodies with molecular behavior pattern.[21-23] *H. pylori* would promote local inflammatory and chronic immune responses [24-26] leading to release of inflammatory mediators including interleukin-1, tumor necrosis factor alpha (TNF-α), interferon (INF) gamma, leukotriene (LT) C4, and platelet-activating factors (PAF). These mediators may be involved in the pathogenesis of skin diseases .[27,28] Since there are few studies [29-31] on the correlation between *H. pylori* and alopecia areata and considering the importance of this issue and undetermined role of *H. pylori* in alopecia areata, this study was performed to determine the possible association between *H. pylori* infection and alopecia areata in Iranian population.

MATERIALS AND METHODS

In this case-control study, of the subjects attending to dermatology clinic of Rasool-Akram Hospital, Tehran, Iran between 2014 and 2015, 81 patients with alopecia areata and 81 patients without alopecia areata were enrolled as case and control groups, respectively. The subjects who had positive history of treatment for *H. pylori* were excluded. The status for *H. pylori* was checked by urea breath test (UBT) in Sara Nuclear Medicine Center. The subjects with positive UBT test were treated in Gastroenterology Clinic by standard regimen for eradication of *H. pylori* including amoxicillin (500 mg, 2 per12 hours), clarithromycin (500mg, 1 per 12 hours) and pantoprazole (1 per 12 hours) for a two-week period. The results were presented as mean±standard deviation for continuous variables and as percent for categorical variables. The statistical analysis was performed by SPSS software (version 21.0) utilizing independent sample t, Chi-Square, and logistic regression tests. The significance level was considered as 0.05.

This study was approved by Ethics Committee of Iran University of Medical Sciences. The Helsinki Declaration was respected during the study.

RESULTS

Patients' characteristics:

Total of 81 cases and 81 controls with mean age of 34.9±11.6 and 38.2±13.4 years were studied (p=0.097). Amongst all, 48 (59.3%) and 45 (55.6%) patients were male, in cases and control groups, respectively (p =0.634).

UBT results:

The result of UBT was positive in 43 (53.1%) patients in the cases and 27 (33.3%) subjects in the control groups, respectively which was significantly different (p =0.011).

Risk of *H. pylori* infection in alopecia areata:

By risk analysis, the risk of *H. pylori* infection in alopecia areata was 2.263 (95% CI: 1.199-4.273). Multivariate logistic regression analysis of two treatment groups with adjusting the effect of sex and age as confounding variables also showed significant risk of *H. pylori* infection in alopecia areata with odds ratio of 2.090 ±(1.090-4.009).

However, sex had no significant relationship with the results (p =0.794). Among 93 men, 41 (44.1 %) had positive UBT results. This is while among 69 women, 29 (42%) had positive *H. pylori* test (p =0.79). This result showed that sex had no significant effect on the risk of *H. pylori* infection in alopecia areata. Moreover age of the patients had significant effect on the risk of *H. pylori* infection in alopecia areata. However the results showed the lower age (33.2 vs 39.1 years) was significantly related to positive response (p =0.003).

DISCUSSION

Alopecia areata is a chronic inflammatory disease seen in both sexes and all ages. In severe cases all parts of the

body would develop alopecia.[1] Despite importance of this disease, definite etiology is not yet illuminated. *H. pylori* has been shown to have an association with skin diseases as a super-antigen .[5,6,9,11,12,15,32-34] However, this study was performed to demonstrate the association between alopecia areata and *H. pylori* infection as a possible etiology of alopecia areata. In this case-control study, 81 patients with alopecia areata and 81 subjects without the disease were enrolled as case and control groups, respectively. Mean age was 34.9 years in the cases and 38.1 years in the control group, respectively. 48 (59.3%) and 45 (55.6%) patients were men, in the cases and the control groups, respectively. Both age and sex were matched in the two groups. UBT showed positive result in 53.1% (43) patients in the cases and 33.3% (27) in the controls, which was significantly different (p=0.011), showing two fold higher risk of alopecia areata in subjects with *H. pylori* contamination. Among 93 male subjects, 41 patients (44.1%) had positive test result for *H. pylori* while 29 women (42%) had positive results showing no statistically significant difference. The mean age was 33.2 years in those with positive results and 39 years in those with negative results showing higher *H. pylori* infection rate in younger subjects. A case report by Campuzano-Mayag 30 described a 43-year-old man who had history of alopecia areata for 8 months and had no improvement during treatment. His disease remitted after *H. pylori* eradication. This is while in a study by HZ Abdel-Hafez and colleagues, on 31 patients with alopecia areata and 24 healthy volunteers for the presence of *H. pylori* surface antigen (HPS Ag), despite higher HPS Ag in patients with alopecia areata, it was not statistically significant.29 Moreover, in a study by Rigopoulos and co-workers 31 on 30 patients with alopecia areata and 30 healthy controls who were matched by age and sex, IgG antibodies of *H. pylori* were tested. However, the results showed no statistical difference in seropositivity of the two groups (p=0.3). But in our study there was significant difference between *H. pylori* infection in patients with and without alopecia areata and it was found that *H. pylori* infection would increase the chance of alopecia areata more than two times. In our study, it seems that *H. pylori* contamination may be effective in the physiopathology of alopecia areata. Hence these results can propose a hypothesis of probable correlation between these two diseases and the possible need for including this test for the assessment of this bacterium in the list of diagnostic approaches for patients with alopecia areata. However due to the limitation of our study including the type of our study (since a case control study is a preliminary study with lower costs to find out a correlation among possible factors and diseases) and its weakness in controlling confounding variables and other possible factors that may be responsible for positive results, other studies with high rank of evidence should be performed to express more certain results. Another limitation of our study was the lack of multiple laboratory tests for better identifying *H. pylori* infection. Therefore, our positive results should be tested in larger multivariable cohorts and controlled trials to reach more accurate evidence in the future and to generalize this idea to larger population.

ACKNOWLEDGEMENTS

This study was supported by a grant from Iran University of Medical Sciences.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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