Ann Med Res 2021;28(5):1054-8

Annals of Medical Research

DOI: 10.5455/annalsmedres.2021.02.135

Original Article

Relationship between *Helicobacter Pylori* and Parapsoriasis

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Abstract

Aim: Parapsoriasis is a rare skin disorder characterized by erythematous, squamous, atrophic patchy lesions. Its etiopathogenesis and trigger factors still remain unclear. Parapsoriasis cases carry an increased risk of transformation into cutaneous T cell lymphoma. In the literature, there is no data about *Helicobacter pylori* (*H. pylori*) frequency in parapsoriasis. This study aims to evaluate the relationship between *H. pylori* infection and parapsoriasis.

Materials and Methods: The study included thirty patients with parapsoriasis who had no dispeptic complaint and thirty healthy individuals. The patient group was divided into two groups as patients with small plaque parapsoriasis (SPP) and those with large plaque parapsoriasis (LPP) based on clinical examination. Carbon 14 urea breath test was performed to evaluate presence of *H. pylori* in both patient and control groups.

Results: Parapsoriasis cases had a significantly higher rate (18/30, 60.0%) of *H. pylori* positivity than controls (9/30, 30.0%) (p=0.020). Whereas patients with SPP and patients with LPP had similar rates of *H. pylori* positivity (55.6% vs 44.4%, p=0.279). Comparison of *H. pylori* status according to gender it was found that majority of *H. pylori* positive individuals were men, indicating a significant difference (p=0.014).

Conclusion: Our results revealed that *H. pylori* infection is increased in patients with parapsoriasis. Therefore, it was thought that *H. pylori* may be associated with parapsoriasis and this agent may play a role in the etiopathogenesis of the disease.

Keywords: Carbon 14 urea breath test; etiopathogenesis; *Helicobacter pylori*; Parapsoriasis

INTRODUCTION

Parapsoriasis is a rarely seen group of dermatoses with chronic course and resistance, which is characterized by erythematous, squamous and atrophic patchy lesions with variable sizes. There are two main form of disease including small plaque parapsoriasis (SPP) and large plaque parapsoriasis (LPP). The SPP is characterized by round/oval erythematous patches or digitate lesions with diameter <5cm. The LPP is characterized by amorphous, atrophic in general or poikilodermatous, erythematous lesions with diameter >5cm. The lesions are mainly localized at lateral aspect of trunk and proximal parts of extremities. In both forms, lesions are typically asymptomatic with mild itching. The most important issue is that parapsoriasis carries a risk for progression to Mycosis Fungoides (MF), the most common form of Cutaneous T cell Lymphoma (CTCL). The SPP is generally considered as a chronic, benign condition; however, there are some cases with initial diagnosis of SPP which subsequently developed MF. The LPP is regarded as a premalignant dermatosis that is associated with risk for progression to MF. The transformation rate for LPP to CTCL is 10% per year (1,2).

In parapsoriasis, etiopathogenesis and triggering factors are not known. The diagnosis is made based on clinical findings as well as histopathological examination. In histopathological examination, focal, single cell epidemotrophism of small lymphocytes with cerebriform nuclei, superficial dermal infiltration of CD4+ T cells and T cell clonality are observed (1,2).

Helicobacter pylori is a microaerophilic, Gram-negative, spiral bacterium that colonizes gastric mucosa and trigger a potent inflammatory response through release of several cytotoxic substances. It has been shown that

Received: 07.02.2021 **Accepted:** 30.04.2021 **Available online:** 25.05.2021
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H. pylori is associated with chronic atrophic gastritis, peptic ulcer, primary low-grade B cell gastric mucosa-associated lymphoid tissue (MALT) lymphoma and gastric adenocarcinoma (3-5). *H. pylori* produces many toxins including urease, phospholipase, alcohol dehydrogenase, vacuolating cytotoxin, hemolysin, platelet activating factor and mucolytic factor. These toxins cause damage to stomach and duodenum preferentially but they also interact with other tissues (3).

It is known that *H. pylori* is associated with major gastroduodenal diseases. *H. pylori* seroprevalence was investigated in other disorders. Previous studies showed that *H. pylori* seropositivity could be associated with several diseases such as cardiovascular, respiratory, neurological, dermatologic and autoimmune disorders (3,4). The association of *H. pylori* infection with autoimmune dermatologic disorders has been reported in the literature (6,7). However, there is no data about *H. pylori* frequency in parapsoriasis in the literature.

Carbon 14 (14C) urea breath test, Carbon 13 (13C) urea breath test, stool antigen and *H. pylori* serology (ELISA-IgG test kit) are non-invasive methods that determine presence of *H. pylori* infection. The 14C urea breath test is an easy-to-use, safe and sensitive test that can be used in children to detect urease-positive *H. pylori* infection in the stomach (8). This study aims to evaluate the relationship between *H. pylori* infection and parapsoriasis.

MATERIALS and METHODS

This prospective, case-control study was conducted at Hatay Mustafa Kemal University, Faculty of Medicine, between September 2018 and January 2020. The study included 30 patients who attended Dermatology outpatient clinic and diagnosed with parapsoriasis by the clinic and histopathological examination and 30 age- and gender-matched, healthy controls without dyspeptic complaints. The patient group was further divided into two subgroups of SPP and LPP based on clinical examination. The study was approved by the local Ethics Committee and all participants gave written informed consent before the study.

A 14C-urea breath test was performed to assess the status of *H. pylori* infection (9) in the parapsoriasis patients and controls. The individuals younger than 18 years, pregnant or breastfeeding women, those with comorbid diseases, those treated with antibiotics and bismuth within 1 month prior to sampling and those receiving H2 receptor antagonists, proton-pump inhibitors or sucralfate were excluded. The 14C urea breath test was performed at Nuclear Medicine Department, Faculty of Medicine, Hatay Mustafa Kemal University Hospital. After 6-hours fasting, all participants were asked to intake one 14C capsule with a glass of water. The 14C capsule (HeliCap, Kibion, Uppsala, Sweden) contains 37kBq (1μCi) 14C-labeled urea. The participants asked to blow test card (Heliprobe BreathCard, Kibion, Uppsala, Sweden) 10 minutes after ingestion of capsule. The participants asked to continue blowing test card until yellow indicator turns orange over 5 minutes. Then, the test cards were quantitatively measured using the heliprobe analyzer (Heliprobe-analyzer, Kibion, Uppsala, Sweden). Results were calculated at 250 seconds and recorded as counts per minute (cpm). The cpm>50 value was considered as infected (*H. pylori* positive).

Statistical analysis

The descriptive statistics are shown as mean and standard deviation for continuous variables whereas count and percent for categorical variables. Cross-tabs for categorical variables were analyzed using Pearson Chi-square test. Continuous variables were compared using independent groups Student's t Test. Data were analyzed using R programming version 4.0.2. P value ≤0.05 was considered as statistically significant.

Sample size: According to the literature (10), the rate of *H. pylori* antibody positive among the individuals included in the study was reported as 71%. When the expected rate was taken as 90%, it was calculated that at least 60 patients (in both groups) should be included in the R program according to 90% power.

RESULTS

There were 30 individuals, 17 (56.7%) males and 13 females (43.3%) in parapsoriasis group as well as in the control group. Out of 30 enrolled patients with parapsoriasis, 63.3% (n=19) of the patients had SPP while 36.7% (n=11) had LPP. No statistically significant difference was found between the parapsoriasis group and control group in mean age (mean±SD) (45.63±13.75 years vs 45.90±13.72 years; p=0.940).

Parapsoriasis cases had a significantly higher rate (18/30, 60.0%) of *H. pylori* positivity than controls (9/30, 30.0%) (p=0.020) (Table 1). Whereas patients with SPP and patients with LPP had similar rates of *H. pylori* positivity (55.6% vs 44.4%, p=0.279) (Table 2).

Male gender predominance was found in patients with *H. pylori* positivity (p=0.014) (Table 3). No significant difference was detected between cases with and without *H. pylori* positivity in terms of mean age (mean±SD) (48.74±12.40 years vs 43.33±14.26 years; p=0.127).

Table 1. Distribution and comparison of the patient with parapsoriasis and control groups status of H. pylori infection.

Group		Helicobacter pylori infection	
		Positive	Negative
Control	n (%)	9 (30.0)	21 (70.0)
Parapsoriasis	n (%)	18 (60.0)	12 (40.0)

$\chi 2 = 5.455$ p=0.020
Pearson's Chi-square test was used to analyze whether there was a difference in H. pylori status between patient and control groups. The test indicated a significant difference (p=0.020).

Table 2. Distribution and comparison of lesion type according to gender and H. pylori status in the patient group

		Lesion type		χ^2	p
		Small Plaque Parapsoriasis n=19	Large Plaque Parapsoriasis n=11		
Gender	Female n (%)	7 (53.8)	6 (46.2)	0.889	0.346
	Male n (%)	12 (70.6)	5 (29.4)		
Helicobacter pylori	Positive n (%)	10 (55.6)	8 (44.4)	1.172	0.279
	Negative n (%)	9 (75.0)	3 (25.0)		

Pearson's Chi-square test was used to analyze statistically. The test indicated no significant difference in lesion type according to gender and H. pylori status (p>0.05)

Table 3. Comparison of *H. pylori* infection status according to gender.

Gender	*Helicobacter pylori*	
	Positive	Negative
Female n (%)	7 (26.9)	19 (73.1)
Male n (%)	20 (58.8)	14 (41.2)

$\chi 2 = 6.058$ p=0.014
Pearson's Chi-square test was used to analyze whether there was difference between male and female genders according to *H. pylori* status. The test indicated a significant difference (p=0.014).

DISCUSSION

Parapsoriasis is an inflammatory skin disease with symptoms similar to clinical and histopathological findings of early-stage Mycosis fungoides. The etiopathogenesis and triggering factors have not been clarified in parapsoriasis yet. In parapsoriasis, no consistent relationship has been found in studies investigating presence of Epstein-Barr virus, cytomegalovirus and human herpes viruses (HHV6 and HHV8) (11).

H. pylori is microaerophilic, Gram-negative, spiral bacterium that colonizes gastric mucosa and affects 40-60% of world population. Although toxins released by *H. pylori* primarily cause damage in stomach and duodenum, they also interact with other tissues. It has been suggested that, in addition to gastric diseases, *H. pylori* can play a role in several immune-mediated diseases and skin disorders (6).

14C-urea breath test is a non-invasive, easy to use and highly specific test used to detect urease-positive *H. pylori*. 14C-urea breath test has a diagnostic sensitivity of 0.96 (9%% CI: 0.95-0.96) and specificity of 0.93 (95% CI: 0.91-0.94) (12). Although 14C capsule stays in mouth for a short period of time, the sensitivity may be decreased due to oral urease-positive bacteria (9).

The association between *H. pylori* infection and skin disorders is still a research subject. Chronic urticaria is a skin disorder with best-defined relationship with *H. pylori*. In addition, although it has not been proven, skin disorders, in which *H. pylori* is implied in the etiopathogenesis, include cutaneous pruritus, nodular prurigo, Behçet's disease, lichen planus, rosacea, aphthous stomatitis, atopic dermatitis, alopecia areata and psoriasis among others (13).

Mogaddam et al. (7) found that there was a significant difference in *H. pylori* prevalence in the chronic idiopathic urticaria patient group and that remission was achieved in 72.7% of cases with urticaria when *H. pylori* was treated in patients with H .pylori infection. In another study, patients with urticaria or history of food allergy were compared with healthy individuals by stool test for *H. pylori* antigen. It was reported that *H. pylori* is a risk factor for chronic urticaria and food allergy and suggested that stool test for *H. pylori* antigen should be performed in patients with urticaria or food allergy (14). In a meta-analysis assessing correlation between *H. pylori* and rosacea, it was found that *H. pylori* infection play role in the development of rosacea. In the study, it was reported that patients with rosacea should be screened for *H. pylori* infection. It was also reported that treatment for *H. pylori* eradication should be given to enhance therapeutic effectiveness in *H. pylori* positive patients with rosacea. In addition, authors reported that *H. pylori* can cause onset or aggravation of rosacea-related inflammation by stimulating immune system via many inflammatory mediators (15). In a study investigating relationship between *H. pylori* seroprevalence and psoriasis onset and severity, it was reported that *H. pylori* infection affected development and disease severity of psoriasis (16). In a meta-analysis evaluating the relationship between *H. pylori* and psoriasis, nine studies were examined. The urea breath test was used in three of these studies, the *H. pylori* ELISA test in five, and the *H. pylori* stool antigen test in one. It has been reported as a result of meta-analysis that *H. pylori* infection plays a role in the development of psoriasis (17). In a study, it was found that psoriasis area severity index scores were significantly higher in psoriasis patients with *H. pylori* infection. It was reported that treatment of *H. pylori* infection improved effectiveness of treatment and shortened the time that is necessary to obtain the response in the psoriasis (18). In a multi-center study including several European countries, it was

concluded that *H. pylori* infection triggered episodes and that *H. pylori* eradication could markedly decrease disease severity in patients with hereditary angioedema (19). In a study investigating relationship between *H. pylori* infection and vitiligo, *H. pylori* prevalence was evaluated in 34 patients with vitiligo and 30 healthy individuals using 14C urea breath test. Authors found that *H. pylori* prevalence was significantly higher in patients with vitiligo (20). *H. pylori* positivity was investigated using endoscopy in a study including 48 patients with Behçet's disease and 40 healthy individuals. It was found that *H. pylori* prevalence and eradication rate were comparable in patients with Behçet's disease and controls with no significant differences between groups (21).

The gastric MALT lymphoma, one of the extra-nodal non-Hodgkin lymphomas, is a tumor related with chronic bacterial infection. *H. pylori* is implied as an etiological agent in the development of gastric MALT lymphoma and there is a relationship between increased risk for gastric MALT lymphoma and *H. pylori*. The *H. pylori* leads to clonal proliferation in MALT lymphoma, a low-grade B cell lymphoma, through continuous antigenic stimulation (22). There is evidence suggesting the relationship between *H. pylori* and T lymphocytes in gastric MALT lymphoma. *H. pylori* may induce antigen-specific T cell response in gastric region and drive long-term Th1 response through development of specific T cells that lead to onset of low-grade gastric MALT lymphoma. It was reported that lymphocytes migrate and infiltrate gastric MALT area as a result of stimulation of T lymphocytes and cytokines in gastric mucosa by *H. pylori*, inducing gastric MALT lymphoma development and lymphomagenesis (23, 24). In a study on relationship between *H. pylori* and T lymphocytes, it was found that marked proportion of T cells underwent proliferation as a response to HP1454 protein localized in outer membrane of *H. pylori* in chronic gastritis and gastric adenocarcinoma patients with *H. pylori*. It was also reported that the protein promoted Th1/Th17 inflammatory response in vivo and exerted pro-inflammatory activity by modulating T cell response (25). Albeit rare, there are cases with association of cutaneous T cell lymphoma with MALT lymphoma (26).

There is limited number of studies about parapsoriasis in the literature. The relationship between parapsoriasis and *H. pylori* has not been investigated so far. The fact that parapsoriasis may progress to mycosis fungoides (a kind of CTCL) suggests that the studies should be screened in the perspective of mycosis fungoides. The CTCL arises from malignant transformation of T cells which are localized in the skin and harbor cutaneous lymphocyte antigen receptor on cell surface. However, the mechanism underlying indeterminate clonal T cell proliferation has not been fully elucidated. It has been accepted that MF develops due to multi-stage pathogenesis as a result of chronic antigenic stimulation and gene mutation (27, 28).

In the literature, there are two studies investigated relationship between MF and *H. pylori*. Daye et al. used *H. pylori* stool antigen to detect *H. pylori* in 50 patients with MF and 50 healthy individuals. Authors detected positive *H. pylori* stool antigen test in 12 of patients with MF and reported that there was no significant difference in *H. pylori* stool antigen positivity between MF and control groups. In addition, there was no significant difference between *H. pylori* positivity and gender, MF stage and disease duration (29). In the thesis, Bulut evaluated 31 patients with MF and 31 healthy individuals and studied *H. pylori* IgG antibody in blood samples and *H. pylori* antigen in stool samples in all subjects. Bulut reported no significant difference between MF and control groups (10). However, both studies were limited by small sample size.

In our study, we compared patients with parapsoriasis, which is known to be precursor of MF, and healthy individuals and found that *H. pylori* positivity was significantly higher in parapsoriasis group. It was concluded that there may be a potential relationship between *H. pylori* and parapsoriasis and that *H. pylori* may be one of the microorganisms that may trigger parapsoriasis. It was found that parapsoriasis patients with *H. pylori* positivity were mostly men, indicating statistically significant difference. This finding suggested that *H. pylori* infection may be associated with male gender. It is known that parapsoriasis and MF are more prevalent among men (11, 27). It was also reported that *H. pylori* infection was more frequently seen among men (30).

This study has some limitations including small sample size due to fact that parapsoriasis is a rare disease, the use of single method for detection of *H. pylori* and lack of re-assessment of disease activity following eradication treatment in patients with *H. pylori*.

CONCLUSION

In conclusion, it was determined that there was a significant difference in *H. pylori* prevalence in the parapsoriasis patients group compared with healty group. The data obtained in this study revealed that increased *H. pylori* frequency in parasoriasis patients may evidence of the relationship between the disease and *H. pylori* infection. So, *H. pylori* may play a role in the etiopathogenesis of parapsoriasis and, it may be one of the microorganisms may triggering the disease. Since parapsoriasis is a rare disease, it may be helpful to conduct prospective, multi-center studies to investigate the relationship between *H. pylori* and parapsoriasis, MF.

Competing interests: The authors declare that they have no conflict of interest.

Financial Disclosure: This study was supported by the Scientific Research Project Support Scholarship (2018) of the Turkish Dermatology Association, Turkey.

Ethical approval: Ethical approval was obtained for the study from Hatay Mustafa Kemal University, Faculty of Medicine (22/03/2018-2). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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