TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2014) 44: 1051-1054
© TÜBİTAK
doi:10.3906/sag-1309-87

Investigation into the frequency of *Helicobacter pylori* infection with carbon 14 urea breath test in patients with vitiligo

Emine Nur RİFAİOĞLU[1,*], Füsun AYDOĞAN[2], Bilge BÜLBÜL ŞEN[1], Tuğba ŞEN[1], Özlem EKİZ[1]
[1]Department of Dermatology, Faculty of Medicine, Mustafa Kemal University, Hatay, Turkey
[2]Department of Nuclear Medicine, Faculty of Medicine, Mustafa Kemal University, Hatay, Turkey

Received: 20.09.2013 • **Accepted:** 19.02.2014 • **Published Online:** 24.10.2014 • **Printed:** 21.11.2014

Background/aim: Vitiligo is a common, acquired depigmenting skin disorder. The relationship between *Helicobacter pylori* (HP) infection and autoimmune dermatological disease has been previously reported. However, the frequency of HP infection in patients with vitiligo has not been reported. In this study, we aimed to investigate the frequency of HP infection with the carbon 14 (C14) urea breath test (UBT) in patients with vitiligo.

Materials and methods: This study included 34 patients (18 males and 16 females) with vitiligo and 30 age- and sex-matched healthy controls. HP infection was diagnosed using the C14 UBT (Heliprobe). Statistical analysis was performed using SPSS 19.

Results: The frequency of HP infection was 64.7% in the patient group and 33.3% in the control group according to the C14 UBT (chi-square test, P = 0.012). HP infection frequency is statistically significantly higher in patients with vitiligo.

Conclusion: To the best of our knowledge, this is the first investigation of the frequency of HP positivity in patients with vitiligo. To better understand the role of HP in vitiligo as an etiological or initiating factor, further experimental and clinical studies with a greater number of patients are needed.

Key words: Helicobacter pylori, carbon 14, urea breath test, vitiligo

1. Introduction

Vitiligo is an acquired depigmenting skin disorder. It occurs clinically by the appearance of well-circumscribed, asymptomatic, white macules following the loss of functional melanocytes in the epidermis (1). The prevalence rate of vitiligo ranges from 0.06% to 2.28% in the population (2). The main etiopathogenesis of vitiligo is multifactorial. According to various pathophysiological theories, it may be associated with autoimmunity, neurogenic dysregulation, autocytotoxicity, biochemical dysregulation, oxidative stress, and weak melanocyte viability (1,3–6). Several potentially environmental factors such as infectious agents appear to be related with vitiligo (7–9).

Helicobacter pylori (HP) is a major health problem affecting about 50% of the world population (10). Gastric ulceration and carcinogenesis are associated with HP infection (11). HP infection has been linked to various autoimmune dermatological diseases, such as alopecia areata, Behçet's disease, chronic urticaria, pruritus, psoriasis, and rosacea (12–17). The frequency of HP has not been studied in patients with vitiligo. Noninvasive tests such as the carbon 13 or carbon 14 (C14) urea breath test (UBT), stool antigen tests, and serology are used to detect HP infection (18). In this study, we used the C14 UBT to detect the frequency of HP infection in patients with vitiligo.

2. Materials and methods

2.1. Patient and control groups

With the approval of the local ethics committee, a prospective study was conducted in our dermatology department clinic. The study comprised 34 patients with vitiligo and 30 age- and sex-matched healthy controls. The patients with vitiligo were newly diagnosed and older than 16 years. The patients with gastrointestinal symptoms or those who had received eradication therapy for HP earlier were excluded from the study. Other exclusion criteria were age under 16 years, pregnancy or lactation, and the use of antibiotics, proton pump inhibitors, or H2 blockers in the 40, 7, and 14 days, respectively, leading up to sample collection. According to the working clinical classification, vitiligo was classified as vitiligo vulgaris, acrofacial, focal, segmental, universal, or mucosal (16).

* Correspondence: eminenurrifai@gmail.com

2.2. C14 UBT

HP infection was diagnosed using the C14 UBT (Heliprobe Breath Card TM, Kibion, Uppsala, Sweden). Before the test, the patients were asked to eat or drink nothing for 6 h. Antacids and H2 receptor antagonists were discontinued 24 h before the test. One week prior to the test, proton pump inhibitors and sucralfate were stopped (17). Antibiotics were discontinued over a month before the test. Capsules containing 37 kBq (1 μCi) C14 with urea/citric acid (Helicap, Kibion) were swallowed by the patients with 25 mL of water. Breath specimens were obtained from the subjects with Heliprobe breath cards (Heliprobe Breath Card TM, Kibion) 10 min after the patient swallowed the capsule. Patients insufflated onto the breath card. When its color indicator changed from orange to yellow, insufflation was stopped. The breath card was placed into a Geiger Müller counter (Heliprobe TM analyzer, Kibion). The C14 activity was counted for 250 s. Results were specified as counts per minute (cpm). Counts of ≤25 cpm were described as Heliprobe 0 = not infected, counts of 25–50 cpm were defined as Heliprobe 1 = equivocal, and counts of ≥50 cpm were classed as Heliprobe 2 = infected. The thyroid autoantibodies, thyroid stimulating hormone, and vitamin B12 levels of the patients with vitiligo were also measured.

2.3. Statistical analyses

All statistical analyses were performed using SPSS 19. Data were expressed as mean ± standard deviation. Pearson's chi-square nonparametric test was used for comparisons between the groups. $P < 0.05$ was considered as significant. Pearson's correlation and Fisher's exact test were used to assess the association between HP and the clinical type of vitiligo and between HP and autoimmune disease.

3. Results

Eighteen men and 16 women with vitiligo were included in this study, in addition to 18 male and 12 female controls. There was no significant difference between the ages of the patients and the controls (Table 1). The frequency of HP infection was 64.7% in the patient group and 33.3% in the control group with the C14 UBT (Pearson's chi-square test, $P = 0.012$) (Figure). According to the working clinical classification, the clinical types of vitiligo are shown in Table 2. The association between autoimmune disease and vitiligo is described in Table 3. There was no positive correlation between the presence of autoimmune disease and HP infection.

Table 1. Demographic features and C14 UBT positivity rates of patients and controls.

	Vitiligo	Control	P
Age (years)	48.5 ± 1.9	44.2 ± 2.7	>0.05
Sex (M/F)	18/16	18/12	>0.05
C14 UBT (+/-)	22/12	10/20	<0.05

M = Male, F = female, UBT = urea breath test.

4. Discussion

HP is a gram-negative bacterium that colonizes the gastric mucosa of more than half of the world's population (10). HP infection is seen more frequently in developing countries than in developed countries, perhaps because of poor health status (21). As a result of gastric colonization by HP, most infected individuals show histological signs of chronic gastritis (22). Several studies have reported a link between HP and systemic diseases (13–17). The incidence of HP in patients with vitiligo has not been previously studied. In this study, we found the prevalence of HP to be 64.7% in the vitiligo group, whereas it was 33.3% in the control group. The prevalence of HP is significantly higher in individuals with vitiligo than in their healthy counterparts in our study. C14 UBT is a reliable and noninvasive technique for the diagnosis of HP infection. The sensitivity of the UBT was 96.6%–100% and its specificity was 76%–100% in different studies (20,23). However in a study from Turkey, the prevalence of HP infection was detected as 68% using the C14 UBT in 1680 patients with variable gastrointestinal complaints (24). In the current study, the prevalence of HP in the control

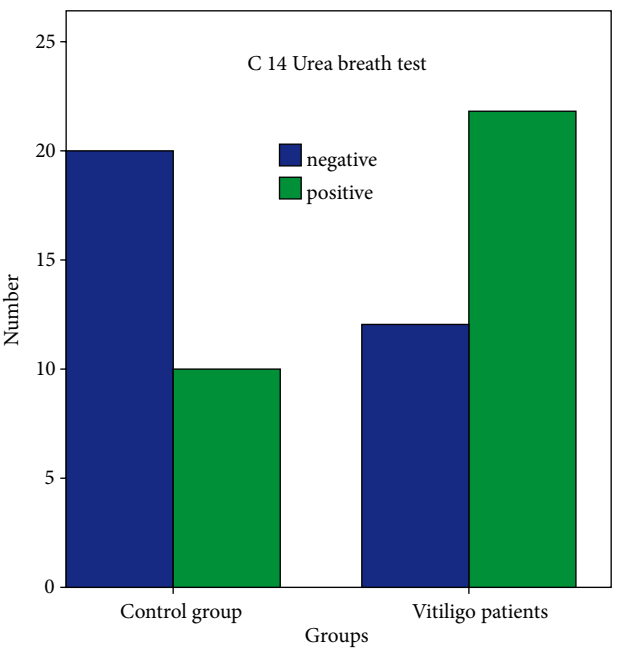

Figure. C14 UBT positivity in patients and controls.

Table 2. Clinical types of vitiligo seen in this study.

	Number of patients	%
Vulgaris	12	35.3
Segmentalis	4	11.8
Acrofacialis	10	29.4
Focalis	3	8.8
Universalis	2	5.9
Mucosal	3	8.8
Total	34	100

Table 3. Related autoimmune diseases of vitiligo and family history.

	Number of patients	%
Related autoimmune disease	9	26.5
Thyroid autoantibody positivity	7	20.5
Autoimmune chronic urticaria	1	2.9
Alopecia areata	2	5.9
Family history	3	8.8

group was lower compared to the aforementioned studies. In our study, all patients and controls were asymptomatic for gastritis. This may explain the lower incidence of HP in the control group.

The relationship between HP infection and autoimmune disease has been discussed in many studies. Chronic urticaria provides the best evidence for a link between HP infection and autoimmune disease. For example, Magen et al. divided their patients with urticaria into 2 groups depending on their resistance and responsiveness to antihistamines and compared the incidence of HP positivity with C13 UBT. They found no statistically significant improvement after eradication therapy in the 2 groups (25). However, in another study, IgG antibodies against HP were found to be significantly higher in patients with urticaria (26). Additionally, Hafez et al. found a statistically significant difference between patients with alopecia areata and a control group in terms of the prevalence of HP infection (27). Meanwhile, Onsun et al. detected HP infection rates of 59.3% and 61.3%, respectively, in patients with psoriasis and controls (16). Although they found that HP positivity was not significantly different between the psoriasis patients and the controls, they detected a significant correlation between the severity of psoriasis and HP positivity (16).

The pathogenesis of vitiligo has not been well documented. However, there is extensive evidence to support the autoimmune theory. One study reported that 19.4% of vitiligo patients have a previous history of autoimmune thyroid disease compared to 2.4% in the general population (28). In our study, the positivity of thyroid autoantibody was detected in 20.6% of the vitiligo group, similar to the literature. In another study from Turkey, the incidences of alopecia areata and chronic urticaria in patients with vitiligo were 12.5% and 2.5%, respectively, and family history was found in 27.5% (29). In our study, the rates of alopecia areata and chronic urticaria were found to be 2.7% and 5.5%, respectively.

Infections are responsible for the development of autoimmunity (30). Microbial agents are involved in the development of autoimmunity because of their communication with the environment and the immune system of the human organism (7). The most commonly accused infection agents in the etiopathogenesis of vitiligo are human immunodeficiency virus, hepatitis C virus (HCV), and cytomegalovirus (CMV) (8,9). However, in a study by Akbayir et al., HCV RNA was isolated from only 1 patient among 102 subjects with vitiligo (8). Additionally, Grimes et al. isolated CMV DNA at rates of 31% and 15%, respectively, from involved and noninvolved skin biopsies, while the control samples were negative (9).

In conclusion, the limitation of our study was the small number of patients and controls and the absence of patient follow-up data after the eradication therapy.

This is the first investigation of the frequency of HP positivity in patients with vitiligo. Although our study suggests that HP infection may have a role in the pathogenesis of vitiligo or may act as a triggering factor, future studies with larger patient groups are needed to understand the role of HP in vitiligo as an etiological or initiating factor. In future studies, the remission rates of vitiligo should be assessed after HP eradication therapy. We hope that our study encourages future studies of the association between vitiligo and HP infection.

References

1. Lee BW, Schwartz RA, Hercogova J, Valle Y, Lotti TM. Vitiligo road map. Dermatol Ther 2012; 25: S44–S56.

2. Kruger C, Schallreuter KU. A review of the worldwide prevalence of vitiligo in children/adolescents and adults. Int J Dermatol 2012; 51: 1206–1212.

3. Wu J, Zhou M, Wan Y, Xu A. CD8+ T cells from vitiligo perilesional margins induce autologous melanocyte apoptosis. Mol Med Rep 2013; 7: 237–241.
4. Namazi MR. Neurogenic dysregulation, oxidative stress, autoimmunity, and melanocytorrhagy in vitiligo: can they be interconnected? Pigment Cell Res 2007; 20: 360–363.
5. Lin X, Tian H, Xianmin M. Possible roles of B lymphocyte activating factor of the tumour necrosis factor family in vitiligo autoimmunity. Med Hypotheses 2011; 76: 339–342.
6. Westerhof W, Manini P, Napolitano A, d'Ischia M. The haptenation theory of vitiligo and melanoma rejection: a close-up. Exp Dermatol 2011; 20: 92–96.
7. Metwalley KA, Farghaly HS. Hepatitis C virus infection in a child with autoimmune polyendocrine syndrome type 2: a case report. J Med Case Rep 2012; 6: 221.
8. Akbayir N, Gökdemir G, Mansur T, Sökmen M, Gündüz S, Alkim C, Barutcuoglu B, Erdem L. Is there any relationship between hepatitis C virus and vitiligo? J Clin Gastroenterol 2004; 38: 815–817.
9. Grimes PE, Sevall JS, Vojdani A. Cytomegalovirus DNA identified in skin biopsy specimens of patients with vitiligo. J Am Acad Dermatol 1996; 35: 21–26.
10. Porras C, Nodora J, Sexton R, Ferreccio C, Jimenez S, Dominguez RL, Cook P, Anderson G, Morgan DR, Baker LH et al. Epidemiology of *Helicobacter pylori* infection in six Latin American countries (SWOG Trial S0701). Cancer Causes Control 2013; 24: 209–215.
11. Mhaskar RS, Ricardo I, Azliyati A, Laxminarayan R, Amol B, Santosh W, Boo K. Assessment of risk factors of *Helicobacter pylori* infection and peptic ulcer disease. J Glob Infect Dis 2013; 5: 60–67.
12. Campuzano-Maya G. Cure of alopecia areata after eradication of *Helicobacter pylori*: a new association? World J Gastroenterol 2011; 17: 3165–3170.
13. Ersoy O, Ersoy R, Yayar O, Demirci H, Tatlican S. *H pylori* infection in patients with Behcet's disease. World J Gastroenterol 2007; 13: 2983–2985.
14. Ben Mahmoud L, Ghozzi H, Hakim A, Sahnoun Z, Zeghal K. *Helicobacter pylori* associated with chronic urticaria. J Infect Dev Ctries 2011; 5: 596–598.
15. Neri S, Ierna D, D'Amico RA, Giarratano G, Leotta C. *Helicobacter pylori* and prurigo nodularis. Hepatogastroenterology 1999; 46: 2269–2272.
16. Onsun N, Arda Ulusal H, Su O, Beycan I, Biyik Ozkaya D, Senocak M. Impact of *Helicobacter pylori* infection on severity of psoriasis and response to treatment. Eur J Dermatol 2012; 22: 117–120.
17. El-Khalawany M, Mahmoud A, Mosbeh AS, Abd Alsalam F, Ghonaim N, Abou-Bakr A. Role of *Helicobacter pylori* in common rosacea subtypes: a genotypic comparative study of Egyptian patients. J Dermatol 2012; 39: 989–995.
18. Hernando-Harder AC, Booken N, Goerdt S, Singer MV, Harder H. *Helicobacter pylori* infection and dermatologic diseases. Eur J Dermatol 2009; 19: 431–444.
19. Hercogova J, Schwartz RA, Lotti TM. Classification of vitiligo: a challenging endeavor. Dermatol Ther 2012; 25: S10–S16.
20. Özdemir E, Karabacak NI, Değertekin B, Cırak M, Dursun A, Engin D, Ünal S, Ünlü M. Could the simplified (14)C urea breath test be a new standard in noninvasive diagnosis of *Helicobacter pylori* infection? Ann Nuc Med 2008; 22: 611–616.
21. Mishra S. Is *Helicobacter pylori* good or bad? Eur J Clin Microbiol Infect Dis 2013; 32: 301–304.
22. Suzuki H, Franceschi F, Nishizawa T, Gasbarrini A. Extragastric manifestations of *Helicobacter pylori* infection. Helicobacter 2011; 16: S65–S69.
23. Oztürk E, Yeşilova Z, Ilgan S, Arslan N, Erdil A, Celasun B, Ozgüven M, Dağalp K, Ovali O, Bayhan H. A new, practical, low-dose 14C-urea breath test for the diagnosis of *Helicobacter pylori* infection: clinical validation and comparison with the standard method. Eur J Nucl Med Mol Imaging 2003; 30: 1457–1462.
24. Türkölmez S, Cayir D, Aydoğan F, Korkmaz M. The relationship of *Helicobacter pylori* positivity with age, sex, and ABO/Rhesus blood groups in patients with gastrointestinal complaints in Turkey. Helicobacter 2007; 12: 244–250.
25. Magen E, Mishal J. Possible benefit from treatment of *Helicobacter pylori* in antihistamine-resistant chronic urticaria. Clin Exp Dermatol 2013; 38: 7–12.
26. Sadighha A, Shirali R, Zahed GM. Relationship between *Helicobacter pylori* and chronic urticaria. J Eur Acad Dermatol Venereol 2009; 23: 198–199.
27. Abdel-Hafez HZ, Mahran AM, Hofny ER, Attallah DA, Sayed DS, Rashed HA. Is *Helicobacter pylori* infection associated with alopecia areata? J Cosmet Dermatol 2009; 8: 52–55.
28. Alkhateeb A, Fain PR, Thody A, Bennett DC, Spritz RA. Epidemiology of vitiligo and associated autoimmune diseases in Caucasian probands and their families. Pigment Cell Res 2003; 16: 208–214.
29. Akay BN, Bozkir M, Anadolu Y, Gullu S. Epidemiology of vitiligo, associated autoimmune diseases and audiological abnormalities: Ankara study of 80 patients in Turkey. J Eur Acad Dermatol Venereol 2010; 24: 1144–1150.
30. van Eden W, Koets A, van Kooten P, Prakken B, van der Zee R. Immunopotentiating heat shock proteins: negotiators between innate danger and control of autoimmunity. Vaccine 2003; 21: 897–901.