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Research Article

The frequency of Helicobacter pylori stool antigen in patients with different types of vitiligo in Iraqi Patients

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ABSTRACT

Background A potential role of H. pylori infection in several extra-intestinal diseases including autoimmune and inflammatory skin diseases such as chronic urticaria, alopecia areata, psoriasis, and rosacea have been reported. Vitiligo is a common depigmenting skin disorder and autoimmunity has been suggested in the pathogenesis of vitiligo. There are few reports of association of H. pylori infection and vitiligo.

Aim of study The aim of our study is to evaluate the relationship between H. pylori infection and vitiligo.

Patients and methods The study group included 40 patients with vitiligo, and the control group included 40 age- and gender-matched individuals. H. pylori stool antigen test was performed in the patient and control groups to detect the presence of H. pylori infection.

Results H. pylori stool antigen test was positive in 22 (62.9%) of the patients and 13 (37.1%) of the controls. Statistically significant difference was found in H. pylori stool antigen test positivity between the patient and the control groups ($P < 0.05$). No significant relationship was found between H. pylori stool antigen test positivity and activity of vitiligo, family history, type, duration, and associated gastrointestinal symptoms of vitiligo.

Conclusion The results indicate that H. pylori infection is increased in vitiligo patients, and may be necessary to screen vitiligo patients for H. pylori infection.

Keywords: Health; patients; infections; vitiligo

INTRODUCTION:

Vitiligo is an acquired disorder characterized by white macules due to progressive destruction of melanocytes[(1).] Globally, it affects nearly 0.5–2% of the general people, start any time from shortly after birth to late adulthood[(2).] Although its exact pathogenesis is not obvious, autoimmunity is strongly involved in the development of the disease [(1)]. Experimental and epidemiological studies have indicated to a close relationship between HP infection and evolution of some skin diseases and other diseases such as cardiovascular and immunologic [(3).] An infection with HP has been implicated in several autoimmune and inflammatory skin diseases such as chronic urticaria, Behcet's disease, psoriasis, alopecia areata and rosacea [(1).]

HP infection causes a considerable immunomodulation, that are triggered by chronic inflammatory process and resultant Th1 response with production IL-2 and IFN-gamma [(4)].

A potential role with tolerogenic effects induced by T regulatory cells(Tregs) and dendritic cells (DCs) have also been implicated [(4)]. So, there is initiation and maintainance of immune tolerance by inducible Tregs, which are generated in the periphery. Based upon these findings, it is currently agreed that infection with HP may affect the risk of developing of several autoimmune skin conditions [(4)].

HP infection can be diagnosed serologically by detecting IgG antibodies with 85% and 79%, sensitivity and specificity, respectively[(5).] Also, Urea breath test: 95% sensitivity and a specificity, done by drinking 13C- or 14C-labeled urea[(6)] and HP stool antigen test: 95% specificity and a sensitivity[(7)]. In this study, we used the HP stool antigen test to detect the frequency of HP infection in patients with vitiligo.

AIM OF STUDY

To investigate the frequency of Helicobacter pylori stool antigen in patients with different types of vitiligo.

PATIENTS AND METHODS

Patients and methods

This a case control study, performed in dermatology and venereology out- patient clinic of Al-Sader Medical City in the central-south Iraq during the period between January 2019 to January2020.

Patients

A number of 40 patients with vitiligo and 40 healthy controls, were included in the study. The age and gender matched controls were taken from patients admitted to the dermatology clinic for other dermatological conditions, such as skin warts, nevi, fungal infection…etc, the patients were diagnosed clinically by the dermatologist as having vitiligo at any body site and any clinical types except, the segmental one. Each patient informed that he or she is a part of scientific study and a written informed consent obtained from each of them.

The participants were divided into two groups:

-Group 1: (The cases) which consisted of 40 patients in whom a diagnosis of vitiligo was made on basis of typical clinical features and Wood"s light examination. All patients were interviewed and a detailed history was taken in form of patient age, gender, duration of illness, family history, any history of illnesses such as autoimmune diseases, associated gastrointestinal symptoms like nausea, dyspepsia, epigastric pain, heartburn, hunger in the morning and any history of gastritis or peptic ulcer. Vitiligo was considered as an active disease in patients who had an extension of the lesions or appearance of new lesions in the last six weeks (VIDA score +4). Clinical examination was focused on type of vitiligo. Patients were classified as having either:

1-Localized vitiligo: focal, and mucosal types.

2-Generalized vitiligo: vulgaris, acro-facial, universal and mixed vitiligo.

-Group 2: (The controls) consisted of 40 apparently healthy persons matched cases according to both, age and sex. They were assessed for any gastrointestinal symptoms related to HP infection.

The main exclusion criteria for these groups are:

1- Patients and controls with a history of previous HP eradication therapy.

2- Patients and controls taking antibiotics and proton pump inhibitors for 2 weeks before the test, also medicines containing bismuth during one month previously.

3- Pregnant and lactating females.

4- Patients younger than 16 years.

Helicobacter pylori stool antigen test:

All subjects were required to submit a fresh stool samples in the lab of Gastroenterology unit, which were checked for evidence of HP infection by stool antigen with immunoassay – based H. pylori Antigen Rapid Test Cassette according to manufacturer's instructions (BIOZEK), that involve a lateral flow chromatographic immunoassay, as in the following:

1. Collect 1-2 ml or 1-2 g of stool in a dry, clean container. The test should be performed within six hours from collection for better outcome.
2. Aspirate stool specimens, and transfer few drops into the specimen collection tube with the extraction buffer.
3. Admix the specimen and the extraction buffer by forcible shaking. Leave the tube for two minutes.
4. Transfer two drops of the extracted specimen to the test cassette specimen well.
5. Read results at 10 minutes later.

Helicobacter pylori stool antigen test (HpSA) was used because it is a rapid and noninvasive method with sensitivity of (95%) and specificity (95%) and it is potentially very helpful in diagnosing active and repeated HP infection[8].

The positivity rates of HpSA were then compared between the two groups and any correlation of positivity for HpSA test with vitiligo or with the presence of gastric symptoms was also noted.

Analysis of data

Data were processed in Microsoft Access Software and analyzed by SPSS version 20. Mean, standard deviation, number, and percentage as descriptive statistics. The characteristics of subjects were analyzed by chi-squared test or student test used accordingly and P value equal or less than 0.05 regardedassignificant.

RESULTS

Patients data

A total of 80 subjects had been included in this study. The participants were divided into two groups, the first group (n=40) were patients with vitiligo, 23 males (57.5%) and 17 females (42.5%) with a male to female ratio of (1.3: 1); their age ranged from 16-63 years with a mean age of (28.2±13.3 SD) and a mean duration of vitiligo was (69.8 ±95.5 months) (1 month-480 month).

The second group (n=40) were healthy controls, there was 23 males (57.5%) and 17 female (42.5%) with a mean age of (30.03±13.9 S.D). There was no statistically significant difference between females and males in both patients and control groups. **Table 1 and 2**.

Table (1) Distribution of the cases and controls according to the age groups

Age group	Cases N(%)	Controls N(%)	Total
<20 years	20(50.0)	20(50.0)	40
20-40 years	13(32.5)	13(32.5)	26
> 40 years	7(17.5)	7(17.5)	14
Total	40	40	80

P=1.00(χ2=0.00 df =2)

Table (2) Distribution of the cases and controls according to the gender:

Gender	Cases N(%)	Controls N(%)	Total
Male	23(57.5)	23(57.5)	46
Female	17(42.5)	17(42.5)	34
Total	40(50.0)	40(50.0)	80

P=1.00(χ2=0.00 df =1) OR (95%C.I) = 1.00(0.41-2.43)

About 50% of patients with vitiligo belong to less than 20 years of age, those associated with positive HpSA was most frequently (51.4%) recorded in this age group while the least presentation was noted in those patients more than the age of 40 years (14.3%), **Table (3)**.

Table (3) Association between H.pylori infection and age groups among cases and controls

Age group	H.pylori antigen		Total
	Positive N(%)	Negative N(%)	
<20 years	18(51.4)	22(48.9)	40
20-40 years	12(34.3)	14(31.1)	26
> 40 years	5(14.3)	9(20.0)	14
Total	35(100)	45(100)	80

P=0.80(χ2=0.45 df =2)

H.pylori stool antigen test (HpSA) positivity in cases and controls:

H.pylori stool antigen test was positive in 35 (43.75 %) subjects of the studied population, 22 (62.9%) patients of group 1 (cases) and 13 (37.1%) subjects of group 2. The prevalence of HpSA positivity was found to be statistically higher in cases group than in control group (p value 0.04) (Odds Ratio =2.53),

Table (4).

Table (4) Comparison between cases of vitiligo and controls according to the result of H. pylori stool antigen test:

H.pylori antigen	Cases N(%)	Controls N(%)	Total
Positive	22(62.9)	13(37.1)	35
Negative	18(40)	27(60)	45
Total	40(50.0)	40(50.0)	80

P=0.04(χ2=4.11 df =1) OR (95% C.I) = 2.53(1.02-6.30)

Types of vitiligo in patients with positive HpSA:

Twenty seven patients had generalized vitiligo (17 males and 10 females) and 13 patients had localized vitiligo (6 males and 7 females). **Figure (1)**

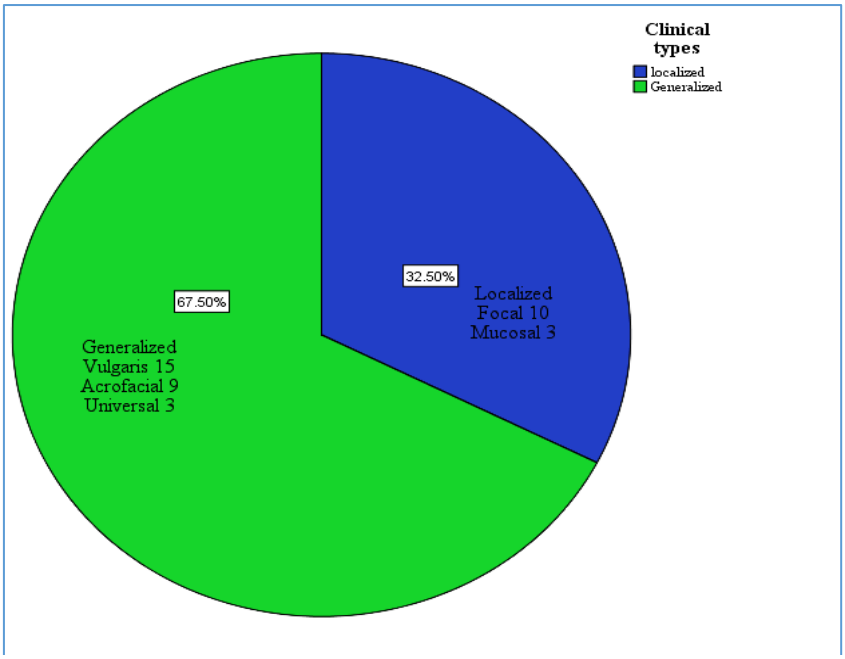

Fig.1:Distribution of vitiligo cases according to their clinical types.

Studied parameters:

There was no significant relationship between HpSA test positivity and the presence\absence of associated gastrointestinal symptoms, the family history, type, duration, and activity of vitiligo except associated autoimmune skin diseases; Positive HpSA value was correlated with the presence\absence of associated autoimmune skin diseases, it was observed in 10 (83.3%) out of 12 subjects with autoimmune skin diseases(AID) had actually positive HP infection according to HpSA. On the other hand, of the 28 subjects with no history of any autoimmune skin diseases, positive stool antigen test was demonstrated in 12 (42.9%) individuals this

difference was found to be statistically significant (p 0.02), **table (5a nd 6) , figure (2)**.

Table (5) Types of skin autoimmune diseases among vitiligo cases.

Autoimmune disease	Frequency	Percentage
Alopecia areata	7	58.3
Chronic urticarial	2	16.6
Behçet's disease	1	8.3
Psoriasis	2	16.6

Table (6) Association between H. pylori infection and different clinical variables among cases of vitiligo.

Clinical variable	H. pylori test		Test	P value
	Positive	Negative		
1.Associated AID				
Yes	10(83.3%)	2(16.7%)	$\chi2=5.56$ OR(95%C.I)=6.67(1.23-36.23)	0.02
No	12(42.9%)	16(57.1%)		
2.Family history				
Positive	7(50.0%)	7(50.0%)	$\chi2=0.22$ OR(95%C.I)=0.73(0.20-2.70)	0.64
Negative	15(55.6%)	12(44.4%)		
3.GIT symptoms				
Positive	12(70.6%)	5(29.4%)	$\chi2=2.90$ OR(95%C.I)=3.12(0.83-11.79)	0.09
Negative	10(43.5%)	13(56.5%)		
4.Disease activity				
Stable	12(54.5%)	10(45.5%)	$\chi2=0.04$ OR(95%C.I)=1.04(0.30-3.65)	0.95
Progressive	10(55.6%)	8(44.4%)		
5.Duration of disease in months				
Mean±SD	73.2±79.7	65.6±114.1	t(95%C.I)=0.25(-54.54-69.80)	0.52

*P<0.05

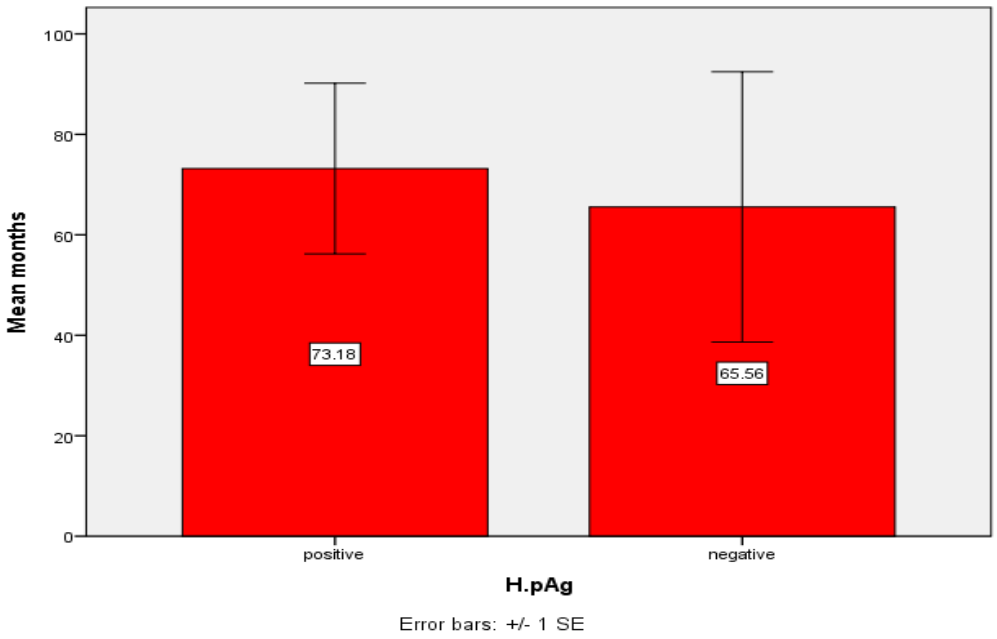

Fig.2: Mean duration of vitiligo in months according to the result of HP antigen testing.

DISCUSSION

Vitiligo is a multifactorial disease with a combined interaction between genetic, environmental, biochemical and immunological factors. The exact etiopathogenesis of vitiligo is not clear; however, several findings suggest that autoimmunity is strongly linked to vitiligo etiology [(1)].

Helicobacter pylori is one of the common infectious agents globally. In addition to causing local tissue damage in the gastric mucosa, HP has also been shown to be involved in various

diseases that are not directly related to the gastrointestinal system.

Several major dermatological conditions have been reported to be associated with HP infection. In terms of dermatological diseases, HP has been reported to be associated with Behcet's disease, recurrent aphthous stomatitis, pruritus, pruritus , psoriasis, lichen planus, Henoch-Schönlein purpura [9]. The results of these reports vary, and the role of HP in autoimmune diseases is inconclusive[1].

Testing for HP is usually performed with non-invasive methods such as serological tests, 13 or 14C-UBT and stool antigen tests. Histological examination and the urease test are invasive techniques but have a higher diagnostic value[9].

The inflammatory response to HP is believed to result in the emergence of cross-reactive antibodies producing autoimmunity [1]. Reports have suggested that HP may trigger lesions in chronic skin diseases, also may be a cause of deterioration and/or may lead to increased resistance and chronic manifestation.

In the current study, HP infection was positive in 22 (62.9%) vitiligo cases compared with 13 (37.1%) in the control group ($p = 0.04$) (OR = 2.53). This indicates that those people with positive HP have 2.5 times more likelihood to have vitiligo, in comparison with those who are free from HP.

The relation between HP infection and vitiligo has been discussed in Turkey by Rifaioglu et al., which investigated 34 patients with vitiligo and 30 healthy controls, matched with regard to age and sex, using UBT for detection of HP infection and reported significantly higher frequency of HP infection in patients with vitiligo than the control group ($P = 0.012$) [10].

In the present study, among the different variables, Positive HpSA value was correlated with the presence \ absence of associated autoimmune skin diseases, the result was statistically significant ($p=0.02$).

The link between HP infection and autoimmune diseases has been looked in different studies:

1- Sadighha et al., found that patients with chronic urticaria had significantly higher IgG antibodies against HP [11].
2- Hafez et al., found that patients with alopecia areata had statistically significant difference between patients and a control group in terms of the prevalence of HP infection [10].

In the present study, no significant correlation was found between HP stool antigen positivity and the presence of family history, type, duration, activity of vitiligo and associated GIT complaints.

About HpSA test accuracy, negative and positive predictive values, were 93.8%, 92.3%, 95.1% respectively. So, for diagnostic and screening purposes, the new stool antigen test was approximate to that of other methods [12].

Weingart et al., utilized fecal antigen test. This supports the present study to diagnose HP and to monitor the success of eradication therapy in adults and adolescents.

However, the reasons for false negative results as the following:

1- Discontinous shedding of the bacterial antigen in the stool may account for the false negative results [13].
2- Using antimicrobials as frequently prescribed by the general practioners. It was not possible to exclude such cases without previous knowledge [13].

The argument in the results above could have many reasons. One of them is the sort of diagnosis of HP infection (methods); The financial and invasive properties (along with sensitivity and specificity) play important role for the differences between various methods, therefore every investigator may select a sort depended on the circumstances, while unknowingly making a bias. Another factor extending such argument is the people picking; location and race account for a large disparity in HP spread, people with HP infection are mostly asymptomatic, thus people are chosen in a way that selection bias happens when including patients visiting outpatient clinic [14].

CONCLUSION AND RECOMMENDATION

Conclusion

This study suggests that infection with HP may act as a trigger for vitiligo and plays a role in the etiopathogenesis of the disease.

In patients with positive HP stool antigen test, there was a higher prevalence of autoimmune skin disease, suggesting that these appreciably increase the chance of HP being the incriminating factor for patients with vitiligo.

Recommendation

1. Limitations of this study include a relatively small number of patients and controls.
2. For better results, using more than one method to detect HP infection.
3. The remission rates of vitiligo should be assessed after HP eradication therapy.
4. We wish that this study encourages studies regarding the association between vitiligo versus psoriasis versus pityriasis alba and HP infection because of the similarity in etiopathogenesis.

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