

The Prevalence of Vitiligo Variants in Association with *Helicobacter pylori* Infection

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Abstract *Background:* More than 50% of the world's population is infected with *H. pylori* (*Helicobacter pylori*). Its prevalence continues to increase and is more prevalent in developing countries and those living in unsanitary conditions. On the other hand; Vitiligo is a progressive disease of unknown etiology, poorly responding to treatment and has a severe impact on patient's lives. *Objectives:* This study is aimed to determine the prevalence of vitiligo variants and to detect whether or not there is an association between vitiligo and *H. pylori* infection. *Patients and Methods:* An observational case finding hospital-based study was carried out over a period of 3 months from October 2011-December 2011. A total of 64 vitiligo patients attended the clinic in Al Jawda Medical Centre in Khartoum; the patients had a thorough medical history taken from them and underwent a complete physical examination, and were tested for *H. pylori* using different laboratory methods. Questionnaires with relevant information have been completed. *Results:* *H. pylori* showed 53 positive cases out of the total number of 64 vitiligo cases which revealed an *H. pylori* prevalence of (82.8 %) which is considered as very high incidence rate. However, statistically, a p-value of more than 0.05 (p-value 0.729) renders it statistically insignificant and therefore an association between vitiligo and *H. pylori* is unlikely. The commonest vitiligo variant diagnosed in those with a positive *H. pylori* infection was Vitiligo vulgaris which constituted 64.2% of the total number of cases. *Conclusion:* There was a very high prevalence rate of *H. pylori* among vitiligo patients, and this should urge further larger scale research specifically well-designed case controls or cohorts regarding the association between vitiligo and *H. pylori* infection.

Keywords Vitiligo, *Helicobacter pylori*, Sudan

1. Background

Helicobacter pylori, previously named *Campylobacter pyloridis*, is a Gram-negative, microaerophilic bacterium found in the human stomach. It was first identified and isolated in 1982 by Barry Marshall and Robin Warren, who concluded that it was present in patients with chronic gastritis and gastric ulcers. Colonization of the stomach with *H. pylori* leads to a variety of upper gastrointestinal disorders, such as chronic gastritis, peptic ulcer disease, gastric mucosa-associated lymphoid tissue (MALT) lymphoma. It is the first formally recognized bacterial carcinogen and is linked to the development of gastric cancer. [1].

2. Introduction

More than 50% of the world's population harbor *H. pylori* in their upper gastrointestinal tract. [2] The prevalence of *H. pylori* in industrialized countries is relatively constant and remains under 40% and is lower in children/adolescents than in adults/senior citizens. Within geographical regions, the prevalence of *H. pylori* inversely correlates with socioeconomic status and in relation to living conditions during childhood. [1] Infections are usually acquired in early childhood, and if left untreated may persist throughout a person's lifetime. *H. pylori* are contagious, although the exact route of transmission is not known, direct person-to-person transmission via the oral-oral or fecal-oral or gastro-oral route is most likely. [3] Food prepared in less than ideal conditions or exposed to contaminated water or soil may increase the risk of transmission of *H. pylori*. Lack of hygiene, low social class, and high-density living conditions seem to be related to a higher prevalence of *H. pylori* infection as transmission of *H. pylori* is facilitated. Accurate and simple tests for the detection of *H. pylori* infection are available. They include serologic tests, urea breath tests, stool antigen tests, and endoscopic biopsies

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which are available in hospital or clinic settings. [4]

On the other hand, Vitiligo is an acquired pigmentary disorder of the skin and mucous membranes, and it is characterized by circumscribed depigmented macules and patches. Vitiligo is a progressive depigmentation disorder resulting from an autoimmune response targeting epidermal melanocytes. Vitiligo affects 0.5-2% of the world population, and the average age of onset is 20 years. [5]

Vitiligo is a multifactorial polygenic disorder with a complex pathogenesis. Although several theories have been proposed about the pathogenesis of vitiligo, the exact cause is unknown. Generally agreed upon principles are an absence of functional melanocytes in vitiligo skin and a loss of histochemically recognized melanocytes, owing to their destruction. Current complex theories regarding the destruction of melanocytes include autoimmune mechanisms, cytotoxic mechanisms, and an intrinsic defect of melanocytes, oxidant-antioxidant mechanisms, and neural mechanisms. [5, 6] The most accepted hypothesis is the autoimmune theory which is based on the presence of melanocyte-specific antibodies that can initiate necrosis of cultured human melanocytes. [7]

The most widely used classification of vitiligo is localized (Focal, Segmental, Mucosal), generalized (Acrofacial, Vulgaris, Mixed) and universal types and is based on the distribution.

When progression, prognosis, and treatment are considered, vitiligo can be classified into two major clinical types: segmental and non-segmental.

Rationale

This study was raised as a proposal trying to correlate between Vitiligo and *H. pylori* infection as highly antigenic bacterium.

Vitiligo is well known as one of the autoimmune diseases and *H. pylori* is also known as highly antigenic bacterium, and then proposed as possible underlying cause for Vitiligo.

3. Purpose of the Study

H. pylori have been reported to affect approximately 50 percent of the world's population [8], and recent evidence suggests that *H. pylori* infection plays a role in the pathogenesis of a variety of skin diseases. The eradication of *H. pylori* has been shown to be effective in a number of patients with chronic autoimmune urticaria, psoriasis, alopecia areata and Schönlein-Henoch purpura. Conflicting data exists regarding the association of *H. pylori* infection with Behçet's disease, scleroderma, and autoimmune bullous diseases. [9]

Despite the magnitude and high incidence of *H. pylori*, no research has been conducted to determine if an association between vitiligo and *H. pylori* infection is present.

In recent literature, an association between *H. pylori* and extra-digestive manifestations has been proposed. One large

clinico-epidemiological study carried out by Bashir et al 2011 [10] on 3,723 Sudanese patients, to detect the prevalence of extra-digestive (extra-gastric) *H. pylori* skin manifestations, and to determine the influence of *H. pylori* eradication through triple therapy. The study was conducted on patients with the clinical prognosis of patients with chronic idiopathic urticaria (CIU), Urticarial vasculitis, Atopic dermatitis and some other skin conditions. This study revealed that 20.6% (746/3723) of the skin cases examined have extra-digestive *H. pylori* skin manifestations. Authors of this study highly recommended performing *H. pylori* test is in suspected skin cases; skin diseases associated with gastric, respiratory and joint manifestations, as well as diabetes mellitus and vascular manifestations. Since *H. Pylori* positive cases (37.0%) dramatically responded to *H. pylori* eradication therapy and 60.8% showed a good clinical response, authors also recommended commencing 12 weeks of eradication antimicrobial triple therapy. [10]

H. pylori is a very common bacterium that has become a burden to many communities, health systems and those it manifests on whether financially, socially or psychologically. On the other hand, vitiligo is a deforming disease with an increasing incidence. This study is aimed to determine the prevalence of vitiligo variants and to detect whether or not there is an association between vitiligo and *H. pylori* infection.

4. Patients and Methods

An Observational case-finding hospital based study was conducted at the Dermatology clinic at the Al Jawda Medical Centre JMC, Khartoum, Sudan. The study duration was a total of 6 months, from September 2011 till February 2012.

The study subjects were patients attending the dermatology outpatient clinic in the specified period. Those clinically diagnosed with vitiligo underwent an *H. pylori* test through either *H. pylori* ICT, ELISA, or a Stool Antigen test. All vitiligo variants have been included in the study. In total 64 patients attended the dermatology clinic during the specified period. A detailed history was obtained from patients, and then a thorough physical examination was performed by the consultant dermatologist. A clinical diagnosis of vitiligo according to the distribution of lesions was made by the dermatologist. The skin lesions were reported and documented considering the distribution, configuration, morphology and colour of the lesions. All patients diagnosed with vitiligo underwent a set of *H. pylori* confirmatory investigations.

5. Results and Discussion

Data was entered from the questionnaires and later analyzed by the Statistical Package for the Social Sciences (SPSS) version 20. The significance of testing was conducted using a Chi-square test and a p-value of 0.05 or

less was considered significant.

Background characteristics of those diagnosed with vitiligo

A total of sixty-four patients were diagnosed with vitiligo and were included in this study. Of those, 36 (56.3%) of them were females, and 28 (43.8%) were males. When the respondents were classified according to their different ages, it was found that 25 (39.1%) fell within the (20 – 39 years) age group. Whereas 19 (29.7%) were between the ages of (40 – 64), with an average age of 26 years among those included in the study. Upon classification of the study subjects according to marital status, 36 (56.3%) were found to be single whereas 23 (35.9%) were married and a minority were divorced or widowed, two and three patients, respectively. Since the clinic is located in the capital, Khartoum, naturally most patients (96.9%) were from urban regions whereas two patients traveled from rural areas. Forty-nine (76.6%) patients were originally from the North of Sudan, whereas only 6 (9.4%) originated from the West. Five patients (7.8%) were from East Sudan, and four patients (6.3%) were originally from central Sudan. When patients were classified according to their level of education, 20 (31.3%) patients were found to have received primary level education, whereas 43 (67.2%) were found to have either secondary or university education.

The most notable symptom patients presented with was hypopigmentation in 38 (59.4%) patients. A minority complained of additional symptoms such as pruritus and dryness of the skin accompanying the skin hypopigmentation. A total of 60 (93.8%) patients were found to have a history of disease duration lasting years except for 4 (6.3%) patients who noted a history of days or months. When physically examined, the majority of patients (76.6%) had widespread, scattered, bilateral and symmetrical cutaneous lesions, while only a minority had localized single or clustered lesions. The morphology of individual lesions among the study subjects was documented and showed that 55 (85.9%) of them were found to have both macules and

patches, whereas 6 (9.4%) were found to have macules or patches (3.7%) only. When the color of lesions among study subjects was examined, it was noted that 35 (54.7%) of the patients were found to have milky white lesions, whereas 13 (20.3%) were found to have porcelain white lesions. Eleven (17.2%) had trichrome vitiliginous lesions, and only one patient had erythematous lesions.

After a clinical diagnosis of vitiligo was made, vitiligo cases were classified according to the distribution of lesions as presented in the figure 1 below. The majority of patients, 40 (62.5%) were found to have Vitiligo vulgaris.

Vitiligo in association with *H. pylori*

H. pylori were detected in the majority of vitiligo patients, 37 (57.8%) by *H. pylori* ICT, whereas 25 (39.1%) were confirmed by *H. pylori* ELISA.

Confirmatory investigations for *H. pylori* showed that 53 (82.8%) patients were *H. pylori* positive and 11 (17.2%) patients were negative out of all 64 as shown in Table (1).

Table (1). Showed the results of confirmatory investigations for *H. pylori*

All cases	Prevalence	Percent
Positive	53	82.8
Negative	11	17.2
Total	64	100

When the test of association (Chi-Square test) was applied to the different variables handled in this study, it was found that the types of vitiligo were not found to be associated with gender (p-value: 0.346). Tests of association did not show any association between diagnoses of vitiligo and age (p-value: 0.346) or occupational background (p-value: 0.557) or residence (p-value: 0.880) or origin (p-value: 0.831). There was, however, an association between vitiligo and marital status (p-value: 0.000) as well as educational level (p-value: 0.015).

Tests of Association showed no relationship between vitiligo and *H. pylori* as shown in Figure (2) below.

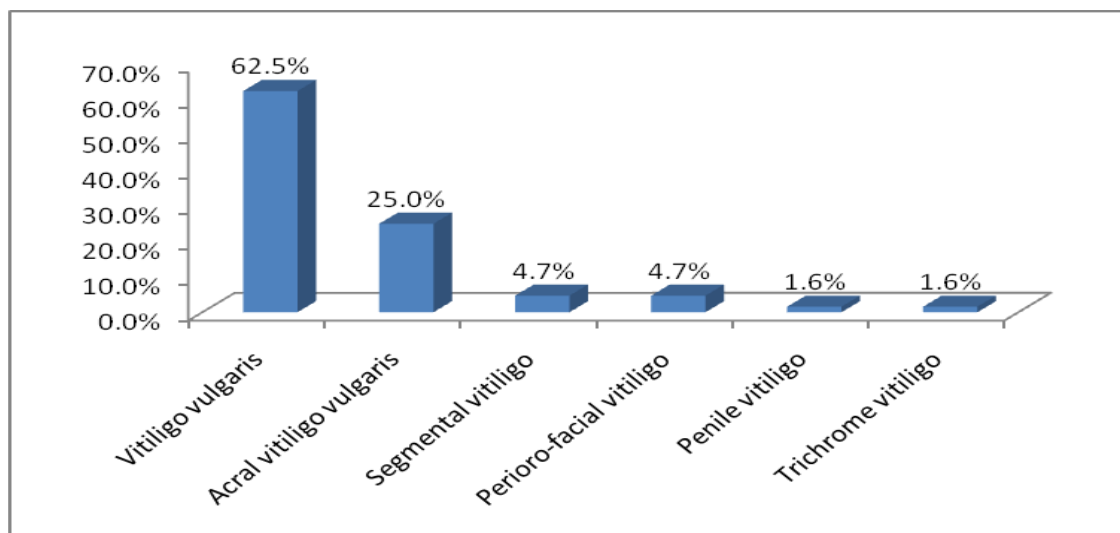
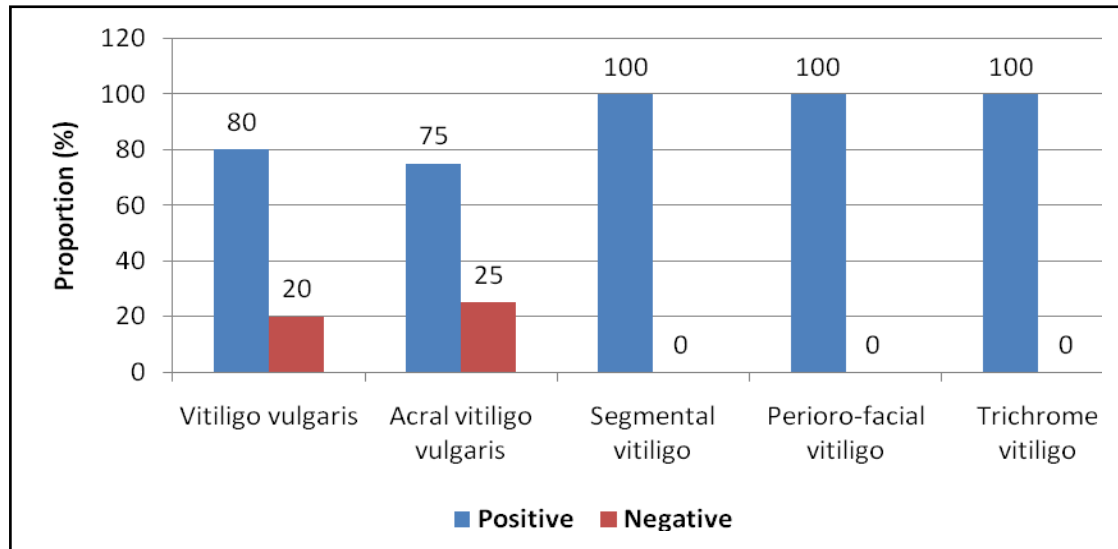


Figure (1). Showed the Diagnoses of Vitiligo variants (n=64)



P value: 0.729

Figure (2). Showed the relationship between vitiligo and *H. pylori* (n=63)

Background characteristics of vitiligo patients with positive *H. pylori* results

When vitiligo patients with a positive *H. pylori* test were classified according to gender, it was reported that 22 (41.5%) were males while 31 (58.5%) were females. Vitiligo patients with positive an *H. pylori* test were mostly between the ages 20-39 years old (41.5%), while 28.3% were between the age 40-64 years. 22.6% were below the age of 20, and only 7.5% were above the age of 65. When vitiligo patients with a positive *H. pylori* test were classified according to marital status, it was noticed that 31 (58.5%) were single while 17 (32.1%) were married. Almost all patients (98.1%) were from urban areas, and the majority 40 (75.5%) were originally from Northern Sudan. Close to half of most vitiligo patients with *H. pylori* infection (47.2%) were university graduates and 15 (28.3%) had completed primary schooling and 22.6% completed secondary level school.

Table (2). Showed the nature of vitiligo among study subjects with positive result for *H. pylori* (n=53)

Positive Vitiligo Cases	Prevalence	Percentage
Vitiligo vulgaris	34	64.2
Acral Vitiligo vulgaris	12	22.6
Segmental vitiligo	3	5.7
Perioro-facial vitiligo	3	5.7
Trichrome vitiligo	1	1.9
Total	53	100

The nature of vitiligo among study subjects with positive results for *H. pylori* are illustrated in Table (2). Thirty-four (64.2%) of the *H. pylori* positive cases were noted to have Vitiligo vulgaris, whereas 12 (22.6%) had acral vitiligo

vulgaris and only 2% were diagnosed with trichrome vitiligo rendering it the least type of vitiligo amongst those with a positive *H. pylori* test.

6. Conclusions and Recommendations

This study revealed that 53 *H. pylori* positive cases out of the total number of 64 vitiligo cases, which resulted in an *H. pylori* prevalence of 82.8%. This prevalence rate, though considered high, showed a p-value of more than 0.05 (p-value: 0.729) which rendered it statistically insignificant in spite of the high association between Vitiligo and *H. pylori* positive cases. This should call for further controlled study.

- 1) Although *H. pylori* infection is primarily confined to the gastric mucosa, evidence in the current literature suggested its association with various several extra digestive diseases [10].
- 2) Eradication of *H. pylori* has proven to be effective in some cases of autoimmune urticaria, psoriasis, alopecia areata and Schönlein-Henoch purpura [10]. The evidence is marginal regarding the association of *H. pylori* infection with Behçet's disease, scleroderma, and autoimmune bullous diseases and currently, few researches has been conducted on the association of *H. pylori* infection with other skin autoimmune diseases, such as vitiligo.
- 3) This should urge larger scale systematic studies evaluating the relationship between *H. pylori* and dermatologic diseases as well as documentation of the effect of *H. pylori* eradication therapy on these different diseases.

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