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The role of *Helicobacter pylori* infection in skin disorders

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Abstract

This study was aimed to determine the relationship between *Helicobacter pylori* infection and skin disorders, sixty six patients who suffering from skin diseases (Urticaria and atopic dermatitis) who attended at Dermatological Clinic Al-Numan Teaching Hospital. Aged (6--62) years have been investigated and compared to Twenty two samples of apparently healthy individual's were studied as control group . All the studied groups were subjected to measurement of anti- *Helicobacter pylori* antibodies IgA by Enzyme linked immunosorbent assay (ELISA). The results of current study revealed that there were a significant elevation ($P<0.05$) in the concentration of *H. pylori* IgA antibodies in sera of patients with chronic urticaria and atopic dermatitis compared to control group, and there were non significant differences ($P>0.05$) in the concentration of *H. pylori* IgA Ab in sera of patients according to the ages and gender. **Conclusion**, *Helicobacter pylori* may have a role in the pathogenesis of chronic urticaria and atopic dermatitis, and the results of present study suggest that *H.pylori* infection should be included in diagnostic workup of patients with skin disorders.

Key words: Skin diseases, *Anti-Helicobacter pylori* IgA Abs, Urticaria and atopic dermatitis.

دور الخمج بالبكتريا الملثوية البوابية في المتلازمات الجلدية

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الخلاصة

هدف الدراسة لتحديد العلاقة بين الخمج بالبكتريا الملثوية البوابية والمتلازمات الجلدية تم التحري عن (66) مريض يعانون من الامراض الجلدية (الشري والتهاب الجلد التأتبي) من الذين يقصدون قسم الامراض الجلدية في مستشفى النعمان التعليمي وكانت متوسط أعمارهم (6-62 سنة) وتمت المقارنة مع (22) من الأشخاص الأصحاء ظاهريا وعدت مجاميع سيطرة. خضعت جميع عينات الدراسة لقياس تركيز اعداد IgA للبكتريا الملثوية البوابية بواسطة تقنية الامتزاز المناعي المرتبط بالانظيم. أظهرت نتائج الدراسة ارتفاعا معنويا ($P<0.05$) في التركيز أعداد IgA للبكتريا الملثوية البوابية في مصول المرضى المصابين بالشري والتهاب

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الجلد الناتبي مقارنة مع مجاميع السيطرة ولم يلاحظ ارتفاعا معنويا ($P>0.05$) في تركيز اعداد IgA للبكتريا الملتوية البوابية في مصول المرضى وفقا للعمر والجنس. الاستنتاج: يمكن أن تلعب البكتريا الملتوية البوابية دورا في امراضية الشري والتهاب الجلد الناتبي وتقتصر نتائج الدراسة الحالية بان يكون التحري عن البكتريا الملتوية البوابية متضمنا في الفحوصات الروتينية للمتلازمات الجلدية.

Introduction

Helicobacter pylori (HP) is a frequent gastrointestinal infectious agent having worldwide distribution. It is a Gram-negative, microaerophilic, spiral bacterium that shows particular tropism for the gastric mucosa, and induces a strong inflammatory response with release of various bacterial and host dependent cytotoxic substances [1]. Most infections are probably acquired in childhood, but geographic area, age, race, socioeconomic status, and hygiene seem to play roles in the prevalence of *Helicobacter pylori*. Higher rates of infection tend to occur at a younger age in developing countries compared to developed countries and in regions characterized by lower socioeconomic status and higher density living [2]. Some authors have suggested a potential role of HP infection in several extra-intestinal pathologies including haematological, cardiovascular, neurological, metabolic, autoimmune, and skin diseases [3, 4]. The postulate role of HP in the pathogenesis of extra-intestinal manifestation is based on the fact that local inflammation has systemic effects. The bacterium colonizes gastric mucosa and induces strong inflammatory responses with release of various bacterial and host-dependent cytotoxic substances. Gastric HP infection is a chronic process lasting for decades, and persistent infection induces a chronic inflammatory and immune response able to induce lesions both locally and remote to the primary site of infection. The systemic effects may involve increased mucosal permeability to alimentary antigens, immunomodulation, an autoimmune mechanism or the impairment of vascular integrity. The various immunopathogenesis during the HP –caused disease might be due to an unbalanced Th1 or Th2 mediated response post infection [5]. Among skin disease that H.P has been related to is chronic urticaria, and the authors proposed that some mechanisms such as an increase in gastrointestinal mucosal permeability for antigens, immunomodulation, autoimmunity or vascular wall dysfunction might be involved in this association [6, 7]. The diagnosis of *H. pylori* infection is an important issue. Recently, there are at least seven diagnostic assays for *H. pylori*: bacterial culture, urease test, urea breath test, histology, PCR, serology, and a stool antigen test [8, 9]. The aim of this study is to determine the relationship between *Helicobacter pylori* infection and skin disorders.

Patients and methods

The present study included of sixty six patients who suffering from skin diseases (Urticaria and atopic dermatitis) who attended at Dermatological Clinic/ Al-Numan Teaching Hospital. The samples were collected from the beginning of October 2015 to the end of January 2016. The ages of the total patients ranged from 6-62 years. Twenty two samples of apparently healthy individual's including 16 males and 6 females were studied as control group. All the samples were marked by number of samples, name of patient and a day of sample collection.

Blood samples collection:

Five milliliter of blood sample was collected from patients clinically diagnosed with Urticaria and Atopic dermatitis and apparently healthy individuals then the blood sample was put into plan tube which let stand at room temperature until the coagulant was form for immunological tests, then the samples were centrifuged at 3000 rpm for 5 minutes and the serum samples were collected in eppendroff tubes. All samples stored at -20 until use in immunological tests.

Immunological examination

All the studied groups were carried out to measure anti-*Helicobacter pyloi* IgA by ELISA test (Certified/Germany) according to the leaflet of kit [10].

Statistical Analysis

The Statistical Analysis System –SAS-program was used to effect of different factors in study parameters. T-test was used to significant compare between means, and Chi-square test was used to significant compare between percentages of this study [11].

Results and Discussion:

The results of current study revealed that there were a significant elevation ($P < 0.05$) in the concentration of *H. pylori* IgA antibodies in sera of patients with chronic urticaria and atopic dermatitis (16.74 ± 0.51) U/ml compared to control group (14.04 ± 1.35) U/ml, as shown in Figure-1

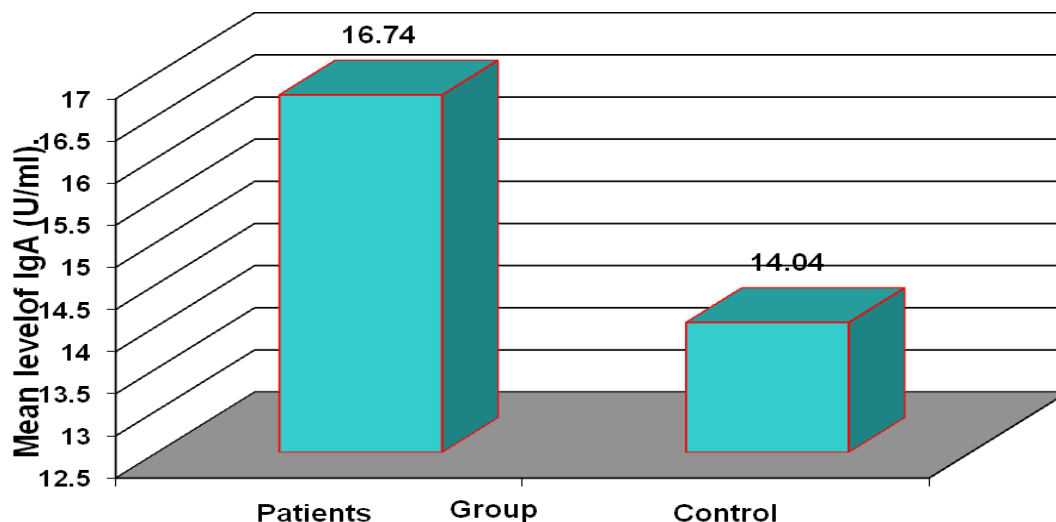


Figure 1. Mean level of anti-*Helicobacter pylori* IgA concentration (U/ml) in sera of urticaria and atopic dermatitis patients and control group.

Also, the results of this study revealed that there were non significant elevation ($P > 0.05$) in the concentration of *H. pylori* IgA Ab in sera of CU patients (17.37 ± 0.79) U/ml and sera of AD (16.26 ± 0.67) compared to control group (14.04 ± 1.35) U/ml as shown in Figure-2 and 3;

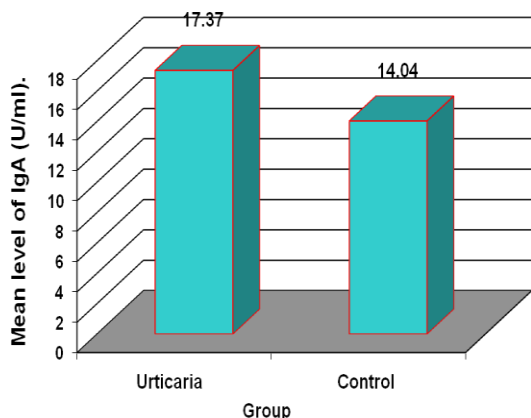


Figure 2. Mean level of anti *Helicobacter pylori* IgA concentration (U/ml) in srea of urticaria patients and contro groups.

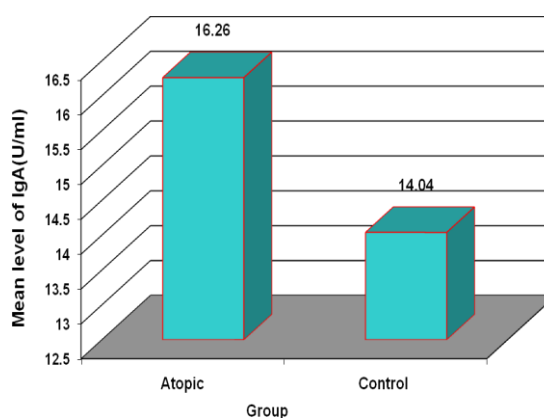


Figure 3. Mean level of anti *Helicobacter pylori* IgA concentration (U/ml) in atopic dermatitis patients and control groups.

While there were non significant differences ($P > 0.05$) in the concentration of *H. pylori* IgA Ab in sera of patients according to the ages and gender. The total concentration of IgA were (15.96 ± 0.81) U/ml in sera of patients within age group less than 40 years compared to (17.69 ± 0.76) in sera of patients within age group more than 40 years as shown in Table- 1.

Table 1- Effect of gender and age in IgA concentration in Level of anti *Helicobacter pylori* IgA

The factors	No	Mean \pm SE of IgA concentration
Gender		
Male	11	17.08 \pm 0.92
Female	19	16.54 \pm 0.62
LSD value	---	2.174 NS
P-value	---	0.620
Age group		
Less than 40	18	15.96 \pm 0.81
More than 40	12	17.69 \pm 0.76
LSD value	---	2.138 NS
P-value	---	0.138
NS: Non-significant.		

This study analyzes the association between *Helicobacter pylori* infection and skin disease. The results of the present study were agreement with other studies. Positive anti-*H.pylori* antibodies were detected in 102 out of 198 in study conducted in Japan by sakurane [12] of patients with refractory skin disease including AD for HP infection. Other study show the prevalence of anti-HP IgA Abs was 51 out of 69 (73.9%) of patients with skin manifestations [13]. While other study found the IgA anti-HP antibodies were present in 62% of patients with skin disorders [14]. Another study shows that the increased titer of IgA against *H pylori* didn't show statistical differences [15]. A potential association between chronic spontaneous urticaria and HP infection of the upper gastrointestinal tract has been proposed [16,17]]. Numerous publication have been appeared HP as a causative in chronic urticaria, and HP may have an indirect role in urticaria, there is a positive correlation between a positive autologous test and HP suggesting its role in autoimmune pathogenesis [18,19]].

It is thought that infection with HP increase the permeability of the stomach lining and thus increases the exposure to allergen in the gastro-intestinal tract. Also, the immune response to HP produces antibodies that may encourage release of histamine in the skin. IgE- containing cells in gastric and duodenal mucosa seem to be the culprits, the possibility that patients with urticaria develop specific IgE against HP is an attractive pathogenic explanation that unfortunately has not been confirmed. The immunomodulatory role of HP infection in CU is a subject of intensive debate. This immunomodulation is not only dependent on the virulence of HP but also on host and environmental factors. The immunological stimulation of chronic infection may produce mediators that non specific increase in sensitivity of the coetaneous vasculature to agents that enhance vascular permeability. Also, IgG and IgA antibodies to 19-KDa HP- associated lipoprotein were found to play a role in the pathogenesis of CU [20, 21]. ELISA technique, fast, easy, and relatively in expensive could identify patients who have been infected with the organism, and it is the third method used as a non invasive method to diagnosis HP infection and it is the only test which is not affected by local changes in the stomach that could lead to a low bacterial load and false-negative results of the other tests [22, 24].

Conclusion

Helicobacter pylori may have a role in the pathogenesis of chronic urticaria and atopic dematiteis, and the results of present study suggest that *H.pylori* infection should be included in diagnostic workup of patients with skin disorders.

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