

# *Helicobacter pylori* and rosacea

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## جراثيم الملوئية البوابية والعدو الوردي

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**الخلاصة:** تشير تقارير نشرت مؤخراً إلى ازدياد معدلات انتشار العدوى بجراثيم الملوئية البوابية بين المصابين بالعدو الوردي، مع بعض البيئات على تحسن في العلامات الجلدية لدى المرضى الذين عولجوا بالمضادات الحيوية لتلك العدوى. وتستقصي دراستنا معدلات انتشار العدوى بالملوئية البوابية بين المصابين بالعدو الوردي في كرمان. وقد أجري اختبار مصلي (سيرولوجي) على 29 مريضاً شُخصت لديهم إصابة كلاسيكية بالعدو الوردي، وذلك باستخدام طريقة معايرة الغلوبولين المناعي جي بمقاييس المتمز المناعي المرتبط بالإنزيم (إليزا). ولدى مقارنة مستويات الأضداد مع مجموعة الشواهد تبين أن معدل انتشار الاختبارات المصلية الإيجابية للملوئية البوابية كان مرتفعاً لدى المجموعة المنحوصة. وهذا يدعم ما سبق أن أُشير إليه من أن هناك شكلاً من العلاقة بين العدو الوردي وبين العدوى بالملوئية البوابية، إلا أن المزيد من الاستقصاءات ومقادير أكبر من العينات ضروريان للحصول على نتائج حاسمة.

**ABSTRACT** Recent reports have suggested an increased prevalence of *Helicobacter pylori* infection in patients with rosacea, with some evidence of dermatological improvement in patients treated with antibiotics for this infection. Our study investigates the prevalence of *H. pylori* infection in rosacea patients in Kerman. Serological examination was done for 29 patients with classical identification of rosacea using the enzyme-linked immunosorbent assay IgG antibody method. Comparison of antibody titres with those of a control group revealed that the prevalence of positive serological tests for *H. pylori* was significantly higher in the test group. This supports the suggestion of some form of relationship between rosacea and *H. pylori* infection, though further investigations with larger sample sizes are required for a definite conclusion.

### Rosacée et *Helicobacter pylori*

**RESUME** Des rapports récents semblent indiquer une augmentation de la prévalence de l'infection à *Helicobacter pylori* chez les patients atteints de rosacée, avec certaines preuves montrant une amélioration dermatologique chez les patients traités par antibiotiques pour cette infection. Notre étude examine la prévalence de l'infection à *H. pylori* chez des patients atteints de rosacée à Kerman. Un examen sérologique a été effectué chez 29 patients avec identification classique de rosacée, à l'aide de la méthode de dosage des anticorps IgG par épreuve immuno-enzymatique. La comparaison des titres d'anticorps avec ceux d'un groupe témoin a révélé que la prévalence de tests sérologiques positifs pour *H. pylori* était significativement plus élevée dans le groupe testé. Ceci vient étayer la suggestion d'une certaine forme de relation entre la rosacée et l'infection à *H. pylori*, bien qu'il soit nécessaire d'effectuer des études plus poussées avec des échantillons de plus grande taille pour arriver à une conclusion définitive.

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## Introduction

Rosacea is a chronic skin disorder preferentially affecting the convexities of the face, and which is characterized by redness and telangiectasia punctuated by episodes of inflammation [1,2]. During the attacks of inflammation, the affected skin typically develops papules, pustules and swelling [3].

Although rosacea is commonest in the third to fourth decades of life, it also occurs in both the elderly and the adolescent [1]. It seems most common in individuals who have their roots in north-west Europe and least common in the heavily pigmented groups from Africa. A Celtic origin may predispose strongly to the disease; less heavily pigmented Caucasians from Asia certainly do suffer from rosacea but do so less frequently than those with light complexions and blue eyes [1,2].

The cardinal physical signs are as follows:

- erythema
- telangiectasia
- papules
- swelling
- pustules.

The persistent erythema and telangiectasia of rosacea are two of its most typical features and remain between acute episodes of inflammation. The papules are rose-red in colour, hemispherical and not usually tender [1]. The swelling in rosacea is of two kinds, one, associated with acute episodes, subsides between attacks; there is also a localized persistent swelling.

Rhinophyma is a bulbous and craggy swelling of the nose that is more commonly found in men. The tissue overgrowth begins at the tip of nose and progresses to involve the alae nasi and the columella. Rarely, other areas, such as the tip of the

chin or the lobes of the ears, may be similarly affected.

Some kind of ocular complication, the commonest of which is conjunctivitis, may occur in 50% of patients with rosacea but in the majority this is of minor importance. Other common benign eye complications include blepharitis, trichiasis, episcleritis, chalazion and hordeolum. More serious for the patient is rosacea keratitis (burning and grittiness of the eyes), a condition which, if untreated, can result in inflammation of the cornea and impaired vision. Uncommonly, persistent lymphoedema develops in one or more areas of the face in patients with rosacea [1,2]. The clinical stages of rosacea are illustrated in Table 1.

Although the precise aetiology remains a mystery, various factors have been suspected of contributing to this condition. These include genetic predisposition, gastrointestinal disturbances (including dyspepsia with gastric hypochlorhydria and infection by the microaerophilic Gram-negative bacterium *Helicobacter pylori*), and infestation with the mite *Demodex folliculorum*, as well as psychogenic factors [1,2], but none has been definitely confirmed.

Recent reports have not only suggested an increased prevalence of *H. pylori* in pa-

Table 1 Clinical progression

Early	Progressive	Late
Episodic flashing	Papules	Induration
Mild telangiectasia	Pustules	Rhinophyma
Transient oedema	Sustained oedema	
	Extensive telangiectasia	

tients with rosacea, but have commented on improvement in the dermatologic condition following the administration of antimicrobial therapy to eliminate *H. pylori* [4-7]. There are also some contradictory reports, which deny the role of the bacterium in rosacea [8-11]. Race and genetic factors may play a significant role in the etiology or background of disease. Therefore, despite the low frequency of rosacea in the Islamic Republic of Iran, we conducted this study to determine whether there is any significant link between this disorder and *H. pylori* infection.

## Methods

A total of 29 patients with clinical diagnosis of rosacea were seen consecutively between May 1999 and April 2001 in dermatology clinics in Kerman. Age of the patients (10 males, 19 females) ranged from 24 to 78 years. All patients were offered serological testing for *H. pylori* using an enzyme-linked immunosorbent assay (ELISA) IgG antibody assay. The control group consisted of 29 age- and sex-matched volunteers recruited from people referred to the laboratories for routine checkups, but who had no indications of rosacea. Statistical analysis was carried out using chi-squared analysis and  $P < 0.05$  was considered significant.

## Results

Infection with *H. pylori* was diagnosed in 24 of 29 patients with rosacea (82.6%) who had positive circulating specific IgG antibodies compared with 17 out of 29 in the control group (58.6%) (Table 2). These groups were statistically different using  $\chi^2$  analysis.

Table 2 Serological test results in patients and control groups

Group	No. positive	No. negative	Total
Patients	24	5	29
Controls	17	12	29
Total	41	17	58

$$\chi^2 = 4.01, P = 0.045.$$

We divided patients and controls into three groups with respect to age. No statistical difference was found between these groups (Table 3). We also compared results in the two sex groups (males and females) in both patients and controls: no statistical difference was found (Table 3).

As indicated by the clinical examinations, patients were divided into three groups according to their clinical stage of rosacea as follows:

- early phase (episodic flushing, mild telangiectasia and transient oedema)

Table 3 Serological test results by age group and sex in both patients and controls

Variable	No. positive	No. negative	Total
<i>Age group (years)<sup>a</sup></i>			
≤ 40	17	6	23
41-55	18	9	27
> 55	6	2	8
<i>Sex<sup>b</sup></i>			
Male	15	5	20
Female	26	12	38
Total	41	17	58

$$^a \chi^2 = 0.8, P = 0.8.$$

$$^b \chi^2 = 0.27, P = 0.6.$$

- progressive phase (papules, pustules, sustained oedema and extensive telangiectasia)
- late phase (induration and rhinophyma)

Comparison of the results is shown in Table 4.

## Discussion

Comparison of antibody titres in the two groups revealed that the prevalence of antibodies for *H. pylori* in patients with rosacea was higher than in the control group (82.6% versus 58.6%). This evidence supports the suggestion of an etiological relationship between *H. pylori* and rosacea.

When the frequencies of positive serological tests were compared according to sex, age group and clinical stage of rosacea, no significant statistical correlation was observed. There are other reports that support the increased prevalence of *H. pylori* infection in patients with rosacea [4–7], but this finding remains controversial because other workers have found no relation between *H. pylori* and rosacea [8–11].

Rebora et al. found histological examination of stomach mucosa gave a positive result for *H. pylori* in 84% of patients with rosacea and a serological test was positive

in 80% [5]. All 20 of their patients were found to be *H. pylori*-positive in one or the other test. They suggested that the consistency between clinical success with metronidazole for rosacea and abatement of *H. pylori* isolates and serology after treatment was additional evidence suggesting an etiological relationship between rosacea and *H. pylori* infection.

Szlachcic et al. studied 60 patients and 60 controls matched for age and sex [6]. The control group comprised patients without any skin disease, with gastrointestinal symptoms similar to those found in rosacea patients but without any endoscopic changes in the gastroduodenal mucosa. The prevalence of *H. pylori* in rosacea patients was about 88% compared with 65% in controls. One week anti-*H. pylori* therapy was carried out and within 2–4 weeks the symptoms of rosacea disappeared in 51 patients, markedly declined in 1 and remained unchanged in another. They suggested that eradication of *H. pylori* leads to dramatic improvement of symptoms of rosacea and reduction in related gastrointestinal symptoms and rosacea could be considered one of the major extragastric symptoms of *H. pylori* infection, probably mediated by *H. pylori*-related cytotoxins and cytokines.

On the other hand, Herr and You suggested no significant difference in *H. pylori* prevalence between patients with rosacea and a control group and no significant lessening of rosacea lesions by treating *H. pylori* infection [8].

Rosacea has often been linked with gastrointestinal disturbances [1,2]. The typical worsening in spring of peptic ulcers is commonly found in rosacea sufferers. Metronidazole was used to treat peptic ulcers long before its activity on *H. pylori* was discovered [5].

Table 4 Serological test results of the patients in different stages of rosacea

Clinical stage	No. positive	No. negative	Total
Early	11	3	14
Progressive	12	1	13
Late	1	1	2
Total	24	5	29

$\chi^2 = 2.5$ ,  $P = 0.28$ .

On the other hand, rosacea has a multifactorial etiopathogenesis, and metronidazole does have effects other than simple antibacterial activity [5].

Due to the difficulty in finding control patients to cooperate using invasive techniques and the fact that rosacea is uncommon in the Islamic Republic of Iran, large case-control studies are difficult to conduct, but necessary before an etiological

relationship between rosacea *H. pylori* is firmly established.

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## References

1. Marks R. Rosacea. flushing and perioral dermatitis. In: Champion, RH, Burton, JL, Ebling FJG, eds. *Textbook of dermatology*, 6th ed., vol. 3. Oxford, Blackwell Scientific Publications, 1992:1851-63.
2. Plewig G, Jansen T. Rosacea. In: Freedburg I, ed. *Fitzpatrick's dermatology in general medicine*, 5th ed., vol. 1. New York, McGraw-Hill Publications, 1999:785-93.
3. Greaves MW. Flushing and perioral dermatitis. In: Champion, RH, Burton, JL, Ebling FJG, eds. *Textbook of dermatology*, 6th ed., vol. 3. Oxford, Blackwell Scientific Publications, 1992:2099-112.
4. Wolf R. Acne rosacea and *Helicobacter pylori* betrothed. *International journal of dermatology*, 1996, 35:302-3.
5. Rebora A, Dargo F, Parodi A. May *Helicobacter pylori* be important for dermatologists? *Dermatology*, 1995, 191:6-8.
6. Szlachcic A et al. *Helicobacter pylori* and its eradication in rosacea. *Journal of physiology and pharmacology*, 1999, 50(5):777-86.
7. Wedi B, Kapp A. *Helicobacter pylori* infection and skin disease. *Journal of physiology and pharmacology*, 1999, 50(5):753-76.
8. Herr H, You CH. Relationship between *Helicobacter pylori* and rosacea: it may be a myth. *Journal of Korean medical science*, 2000, 15(5):551-4.
9. Jones MP et al. *Helicobacter pylori* in rosacea: lack of an association. *Archives of dermatology*, 1998, 134:511.
10. Schneider MA et al. Serologic determination of *Helicobacter pylori* in rosacea patients and controls. *Clinical research*, 1992, 40:831.
11. Sharma VK et al. A study of the prevalence of *Helicobacter pylori* infection and other markers of upper gastrointestinal tract disease in patients with rosacea. *American journal of gastroenterology*, 1998, 93:220-2.