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Severe Acne Vulgaris is Associated with *Helicobacter pylori* Infection: First Report in the Literature

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Both Acne vulgaris and infection with *Helicobacter pylori* (HP) are very prevalent all over the world. The objective of this study was to examine possible association between HP infection and various severities of Acne vulgaris. In this case-control study, 100 adolescents and young adults were recruited from two educational dermatological centers in Tabriz over a one-year period (2012-2013), including 25 normal subjects (controls) and 75 patients with Acne vulgaris (mild = 25, moderate = 25, severe = 25). Infection with HP was investigated using ¹³C-urea Breath Test (UBT). Serum level of immunoglobulin G (IgG) against HP was also measured in all the participants. All the groups were matched for their participants' age and sex. The rate of HP infection was 56% in the control group, 60% in the cases with mild Acne vulgaris, 72% in the cases with moderate Acne vulgaris and 88% in the cases with severe Acne vulgaris. In terms of the rate of HP infection, there was no significant difference between the controls and the cases with mild Acne vulgaris ($p = 0.77$), nor between the controls and the patients with moderate Acne vulgaris ($p = 0.24$). The rate of HP infection, however, was significantly higher in the cases with severe Acne vulgaris comparing with the controls ($p = 0.01$). Mean serum level of IgG was also significantly higher in the same group (1.87 ± 1.62 U vs. 2.98 ± 1.29 U, $p = 0.05$). Based on the findings of the present study, a significant association was present between severe Acne vulgaris and HP infection. Further studies with larger sample sizes are recommended.

Key words: *Helicobacter pylori*, acne vulgaris, urea breath test

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INTRODUCTION

Helicobacter Pylori (HP) is a ubiquitous bacterium. It is estimated that over half of the world population carry this gram-negative, microaerophilic microorganism in their gastrointestinal tract (Somi *et al.*, 2008; Mahmood and Hamid, 2010; Suhaila *et al.*, 2010; Fakhrjou *et al.*, 2011; Sheikhan *et al.*, 2011). The role of this bacterium is almost confirmed in the pathogenesis of peptic ulcer, gastric cancer and mucosa-associated lymphoid tissue lymphoma (Umehara *et al.*, 2003). However, its role is not limited to these conditions and various reports have suggested HP as a major contributor to a large number of extra gastric conditions such as cardiovascular and dermatological diseases (Savarino *et al.*, 2000; Ortiz *et al.*, 2001; Gasbarrini *et al.*, 2003; Migneco *et al.*, 2003).

Like HP infection, Acne vulgaris is one the most frequent skin diseases all over the world. Adolescents and young adults are frequently involved but older individuals are not spared (Dawson and Dellavalle, 2013; Feinberg and Shwayder, 2013). Due to its high frequency, many studies are trying to define the exact mechanism of Acne vulgaris and develop efficient treatments (Babaeinejad *et al.*, 2011; Fouladi, 2012; Khodaeianiet *al.*, 2012; Babaeinejad and Fouladi, 2013; Goforoushan *et al.*, 2013; Khodaeiani *et al.*, 2013; Kapoor and Saraf, 2011). The pilosebaceous unit (Fouladi, 2013), microbial agents and hormonal factors (Navali *et al.*, 2011; Deepika *et al.*, 2012) have been proposed as major elements in the pathogenesis of acne vulgaris.

Apparently no other study has ever tried to examine the contributing role of HP in the pathogenesis of Acne vulgaris. Common features in pathogenesis of the two entities such as the role of inflammatory cytokines and superoxide, seborrhea and shared mechanisms between HP and extradigestive antigens, however, put forward a possible connection between HP infection and Acne vulgaris (Charlett *et al.*, 1999; Szlachcic, 2002; Amedei *et al.*, 2003; Gupta *et al.*, 2003). Thus, this study aimed to investigate a possible association between HP infection and various severities of Acne vulgaris in a case-control setting for the first time.

MATERIALS AND METHODS

One hundred adolescents and young adults were enrolled into a case-control study that was conducted in two dermatological clinics in Tabriz from January 2012 to January 2013. The subjects were categorized into four groups: Control: 25 individuals without current or

previous Acne vulgaris; 25 patients with mild Acne vulgaris according to the Evaluator Global Severity Score (EGSS) (Eichenfield *et al.*, 2010); 25 patients with moderate Acne vulgaris according to the EGSS and 25 patients with severe Acne vulgaris according to the EGSS.

Subjects with previous gastrointestinal symptoms and those with a positive history of steroid/antibiotic use were not included. To detect HP infection, all the participants underwent ¹³C-urea Breath Test (UBT) which has been shown highly sensitive and specific in this regard (Sacca *et al.*, 2006). In addition, blood samples were collected from all the participants and the serum level of immunoglobulin G (IgG) antibody against HP was detected by Enzyme-Linked Immunosorbent Assay (ELISA) method, using Biotech Trinity (Trinity Biotech PLC, Bray, Ireland) kits. Frequency of HP infection according to the results of UBT was compared between the controls and the groups of the patients with *Acne vulgaris*.

Sample size calculation and statistical analysis:

According to our pilot study, the prevalence of HP infection was 60% in normal Iranian young adults. Assuming HP infection in all patients with Acne vulgaris (at a significance level of 5%, with a power of 80%), 16 cases were required in each group which was augmented to 25 (total = 100). Data were shown as mean±standard deviation and frequency (%). The SPSS software for Windows (ver.16) was used. Independent samples t test (for age and serum level of IgG) and the Chi-square test (for sex and the frequency of HP infection) were employed for analyzing. p = 0.05 was considered statistically significant.

RESULTS

Demographics: Subjects without Acne vulgaris (controls) were 14 males (56%) and 11 females (44%) with a mean age of 22.80±3.50 years (range: 18-30). In the group with mild Acne vulgaris, there were 17 males (68%) and 8 females (32%) with a mean age of 23.04±3.99 years (range: 18-30). In the group with moderate Acne vulgaris, there were 14 males (56%) and 11 females (44%) with a mean age of 24.16±4.01 years (range: 18-30). In the group with severe Acne vulgaris, there were 16 males (64%) and 9 females (36%) with a mean age of 24.12±3.98 years (range: 18-30). There was no significant difference between the studied groups regarding their sex (Chi-square test p = 0.77) and age (One-way ANOVA p = 0.48). Age and sex of the studied population are summarized in Table 1.

Table 1: Demographics of the studied population including patients with mild, moderate and severe Acne vulgaris and their normal counterparts (controls)

Variable	Mild acne (n = 25)	Moderate acne (n = 25)	Severe acne (n = 25)	Control (n = 25)	p-value
Sex					
Male	17.00 (68)	14.0 (56)	16.0 (64)	14 (56)	0.77
Female	08.00 (32)	11.0 (44)	09.0 (36)	11 (44)	
Age (year)	23.04±3.99	24.16±4.01	24.12±3.98	22.80±3.50	0.48

Data are presented as mean±standard deviation and frequency (%)

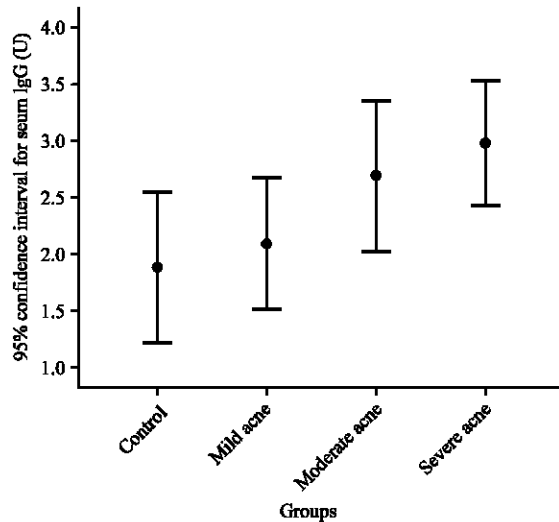
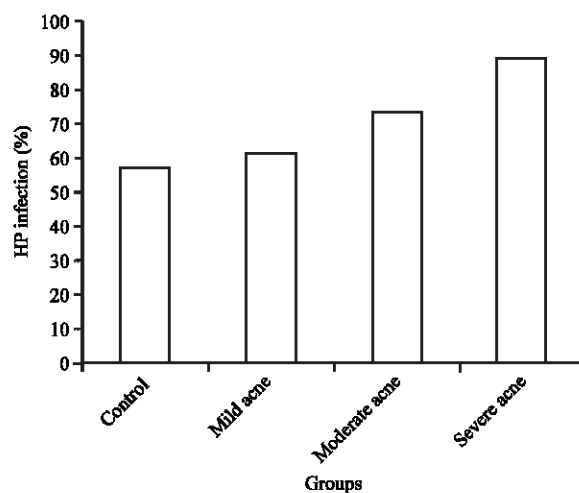


Fig. 1: Error bars of the mean serum levels of immunoglobulin G (IgG) in the studied population including patients with mild, moderate and severe Acne vulgaris and their normal counterparts (controls)

Fig. 2: Percentage of *Helicobacter pylori* (HP) infection in the studied population including patients with mild, moderate and severe Acne vulgaris and their normal counterparts (control)

Serum IgG level: Mean level of serum IgG was 1.87 ± 1.62 U in the control group, 2.09 ± 1.40 U in the cases with mild Acne vulgaris, 2.70 ± 1.61 U in the cases with moderate Acne vulgaris and 2.98 ± 1.29 U in the cases with severe Acne vulgaris. Based on the result of One-way ANOVA, there was a significant difference between the four groups in terms of the mean serum level of IgG ($p = 0.04$). Based on the *post hoc* analysis, this difference was significant only between the controls and the cases with severe Acne vulgaris (Tukey test $p = 0.05$); indicating that the mean serum level of IgG was significantly higher in the cases with severe Acne vulgaris than in the controls. Error bars of the mean levels of serum IgG in the four studied groups are shown in Fig. 1.

HP infection: HP infection was positive in 14 subjects (56%) in the control group, 15 cases (60%) in the patients with mild Acne vulgaris, 18 cases (72%) in the patients with moderate Acne vulgaris and 22 cases (88%) in the patients with severe Acne vulgaris. According to the results of the Chi-square test, there was no significant difference between the controls and the patients with mild ($p = 0.77$) or moderate ($p = 0.24$) Acne vulgaris in this regard. Comparing the controls and the cases with severe Acne vulgaris, however, the rate of HP infection was significantly higher in the later group (Chi-square test $p = 0.01$). Percentages of HP infection in the four groups are depicted in Fig. 2.

DISCUSSION

The major role of HP has been delineated in development of peptic ulcer (Umehara *et al.*, 2003). However, this microorganism has been implicated in the pathogenesis of other nondigestive conditions, too (Gasbarrini *et al.*, 2003; Migneco *et al.*, 2003; Savarino *et al.*, 2000; Ortiz *et al.*, 2001; Diaz *et al.*, 2003; Zandi *et al.*, 2003; Mini *et al.*, 2005; Boixeda de Miquel *et al.*, 2006).

In the present study, for the first time in the literature, it was shown that the rate of HP infection was significantly higher in subjects with severe Acne vulgaris, comparing with that in their uninvolved sex and age-matched counterparts (88% vs. 56%, $p = 0.01$). Due to its novelty, the exact physiopathology underlying this association between HP and severe Acne vulgaris cannot be determined. However, according to previous findings, some mechanisms could be suggested in this regard.

For example, it has been shown that HP induces and augments the synthesis of toxic oxygen metabolites

such as inflammatory cytokines and superoxide (Szlachet, 2002). These products, on the other hand, can promote inflammation of the gastric mucosa and pathologic changes of the skin (Franco *et al.*, 1999) which are the characteristics of Acne vulgaris (Fivenson, 2006), as well. Another justification for this association between Acne vulgaris and HP infection is a shared point between the two entities; seborrhea. It has been shown that there might be a significant association between HP infection and seborrhea (Charlett *et al.*, 1999). On the other hand, a coexistence of seborrheic dermatitis and other skin diseases particularly Acne vulgaris has been suggested (Gupta *et al.*, 2003). Therefore, a connection between Acne vulgaris and HP infection can be hypothesized on the basis of seborrheic mechanism. This association needs to be confirmed in further studies.

The third possible mechanism is the role of HP itself. According to available data, cross-mimicry mechanisms between HP and extradigestive antigens have been proposed (Amedei *et al.*, 2003). This similarity can describe the connection between this bacterial infection and Acne vulgaris.

The forth mechanism is the ability of HP to produce lipase enzyme. In a study on association between blepharitis and HP infection the role of this enzyme has been emphasized. The same mechanism also exists in the pathogenesis of Acne vulgaris which clearly corroborates the hypothesis of "lipase activity" of HP (Sacca *et al.*, 2006). Last but not least, many antibiotics effective against Acne vulgaris, such as metronidazole, tetracycline, doxycycline, etc., are also effective against HP infection. This similarity may also indicate a possible role of this bacterium in pathogenesis of Acne vulgaris (Sacca *et al.*, 2006). Although, the findings of the present work are quite novel and with great clinical importance in terms of the treatment of Acne vulgaris, further studies with larger sample sizes are required to definitely clarify this association.

CONCLUSION

According to the findings of the present study, a significant association exists between severe Acne vulgaris and HP infection.

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