

ORIGINAL ARTICLE

Association of Acne Vulgaris and *Helicobacter pylori* Infection: A Case-control Study

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ABSTRACT

Key words:

Fluorescent Immunoassay, Global Acne Grading System, *Helicobacter Pylori*, and Acne Vulgaris.

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Background: Acne Vulgaris (AV) is a common skin condition that affects people of all ages. Dermatologic disorders such as Behcet's disease (BD), Henoch-Schoenlein purpura, and psoriasis vulgaris (PV) have been linked to *Helicobacter pylori* (*H.pylori*). There is debate regarding the relationship between *H. pylori* infection and other dermatological conditions including AV. **Objective:** To evaluate the levels of *H.pylori* antigen (Ag) in cases with AV, to find out possible association of *H. pylori* with AV and its severity. **Methodology:** The sixty participants in this prospective case control study were divided into two groups: the case group, which consisted of 30 AV patients, and the control group, which also comprised 30 healthy controls (HC) of similar age and sex. Determination of acne severity was done using "global acne grading system". Fresh stool samples from each subject were sent to the laboratory for detection of *H. pylori* Ag by using rapid quantitative method which depends on FIA (Fluorescent Immunoassay) using automated analyzer Gotten device. **Results:** Half (50%) of the studied acne cases had severe degree acne, 30% had moderate degree acne and 20% mild degree acne. There was a statistically significant positive correlation between *H. pylori* antigen and either of acne severity and Global score. The *H. pylori* antigen did not significantly correlate with sex, domicile, occupation, or marital status in either of the two cases. The amount and expression of *H. pylori* antigen were statistically significantly correlated with acne severity. The *H.pylori* Ag expression showed a significantly higher expression in severe acne group (100%) compared to mild acne group (16.7%) and moderate group (11.1%). **Conclusion:** The results of this investigation showed a favorable correlation between *H. pylori* infection and both AV severity and global score. The *H. pylori* antigen has a modest sensitivity and specificity, making it capable of distinguishing between cases and control groups.

INTRODUCTION

Acne Vulgaris (AV) is a worldwide ailment affecting sebaceous glands and the hair follicles that surround them, influenced by a multitude of genetic and environmental variables¹. The incidence of AV is directly correlated with an individual's age. It is highest in teenagers, decreases as an adult, and becomes extremely uncommon after menopause². Furthermore, there are other factors that influence the prevalence of AV, such as race, lifestyle, stress levels, and tobacco use³. Notably, AV pathogenesis is caused by the interaction of eight different types of bacteria growing too quickly and becoming inflamed. As a result, hyperkeratotic plugs, sometimes referred to as microcomedones, form, which gradually expand into closed or open comedones inside the pilosebaceous unit.

This illness typically manifests at the pubertal transition, when the hormonal environment affects the pilosebaceous glands' activity^{2,4}.

H. pylori is a spiral-shaped, microaerophilic Gram negative, flagellated microbe that is roughly three μm long and 0.5–1 μm in diameter. It is found in the human stomach epithelium's mucous layer and is 50% more common worldwide than in industrialized countries. This difference has been attributed to changes in living conditions and inadequate hygiene in developing countries⁵⁻⁷.

The majority of *H. pylori* infections often arise in families during a child's early years of life.⁸⁻⁹ It has been shown that the primary routes of infection are oral-oral and/or fecal-oral, while contaminated food and water may also be involved¹⁰. Notably, *H pylori* may play a part in the pathophysiology of a number of

extraintestinal illnesses, including pulmonary, cardiac, biliary, hepatic, and dermatological conditions. Essentially, chronic urticaria, PV, and rosacea have been considered the most frequent forms of dermatologic disease-related *H. pylori*¹⁰. The aim of the work is to measure the *H. pylori* antigen levels in AV patients and determine whether there may be a relationship between *H. pylori* and AV, as well as the strength of that relationship.

METHODOLOGY

Patients:

Over the course of a year, sixty individuals from Mansoura University Hospitals' Out-patient Clinics of Dermatology, Andrology, and STDs took part in this prospective case control study, from August 2022 to August 2023. They were split into two groups: a control group with 30 healthy, matched-sex, and age- and gender-matched controls, and a cases group with 30 AV patients.

Inclusion criteria

- All five of the study's subjects had classic acne vulgaris lesions of varying degrees.

Exclusion criteria

- Cases having a history of drug intake which interferes with *H. pylori* within the preceding 28 days before participation in the study, which include proton-pump inhibitors, tetracyclines, clarithromycin, amoxicillin and metronidazole.
- Cases with a history suggestive of gut diseases other than *H. pylori*.
- Cases with a history suggestive of other dermatological disorders.
- Cases with a history suggestive of chronic medical diseases.

Methods:

Entire participants were subjected to full history taking which included age, duration of disease, previous family history of similar condition, smoking and previous medical history. The complete general examination comprised weight, Height, body mass index (BMI) was conducted. Examination of AV was done to detect types of lesions and their distribution. Assessment of AV severity was conducted based on "global acne grading system"¹².

Investigations

Fresh stool samples were taken from both groups in sterile containers. Each sample was rapidly sent to laboratory for detection of *H. pylori* Ag. We used rapid quantitative method which depend on FIA (Fluorescent Immunoassay) using automated analyzer Gotten device. The assay range below 10 ng/ml was considered negative and assay range above 10 ng/ml was considered positive.

Ethical Consideration

The study design was approved by Mansoura Faculty of Medicine IRB (code: MS.22.06.2047). The approval of the managers of the healthcare facilities (where the study was conducted) was obtained. Written informed consent was acquired from every individual involved. Confidentiality was respected. Collected data was used for scientific purposes only.

Statistical analysis

The collected data were analyzed by SPSS software, version 25 (PASW statistics for windows). Qualitative data were defined using number and percent. Quantitative data were defined using median for non-normally distributed data and mean±SD for normally distributed data following assessing normality using Kolmogorov-Smirnov test. Chi-Square and Fisher exact test were used to compare qualitative data between groups as appropriate. Mann Whitney U and Kruskal Wallis test were utilized to compare between 2 studied groups and more than 2 studied groups, correspondingly. The student-t test was used to compare 2 independent groups. The Spearman's correlation is utilized to detect the strength and direction of a linear correlation between two non-normally distributed continuous variables and/or ordinal variables. With regard to all the previously used testes, p is considered significant when its value was less than 0.05.

RESULTS

Table (1) shows non statistically significant differences between cases and controls regarding all the studied sociodemographic characteristics, except for the BMI which was statistically significant ($P < 0.05$). There were variations between the case and control groups that were not statistically significant. Expression and amount of the *H. pylori* antigen ($p > 0.05$). There was a non statistically significant difference between studied groups regarding past drug history for previous *H. pylori* & past history of chronic illness ($P > 0.05$). Table (2) illustrates that 50% of the studied acne cases had severe degree acne, 30% had moderate degree acne and 20% had mild degree acne. Table (3) illustrates that the area under ROC curve in differentiating cases from control groups is poor (0.569) with the best detected cut off point is 8.45 yielding 63.3% sensitivity & 56.7% specificity. Table (4) illustrates statistically significant positive correlations between *Helicobacter pylori* antigen & either of acne severity and Global score ($P < 0.05$, each). Table (5) shows a non statistically significant correlations between *Helicobacter pylori* antigen and the following, sex, residence, occupation and marital status ($p > 0.05$ each). A strong and statistically significant correlation had been seen between the amount and expression of *H. pylori* antigen and the severity of acne, as shown in table (6). A striking observation is the considerable increase in the

mean quantity of *H. pylori* antigen (measured in ng/ml) alongside the severity of acne, with mean \pm SD values escalating from 7.68 ± 5.19 in the mild group to 25.52 ± 14.17 in the severe group. This trend is supported by a very strong statistical significance ($p < 0.001$). Pairwise comparisons showed a significant difference between mild and moderate groups as well as mild and severe groups ($p < 0.001^*$). The antigen expression showed a

significantly higher expression in severe (100%) acne group compared to mild (16.7%) and moderate acne groups (11.1%). There was a statistically significant difference between mild and moderate groups as well as mild and severe groups ($p < 0.001^*$). Figure (1) illustrate that 50% of the studied acne cases had severe degree acne, 30% had moderate degree acne and 20% had mild degree acne.

Table 1: Comparison of sociodemographic characteristics, Helicobacter pylori antigen, past drug history for treatment of previous H. pylori and past history of chronic illness of the studied groups

	Cases N=30	Control N=30	Test of significance
Age/years mean \pm SD	25.47 \pm 8.12	26.20 \pm 10.02	t=0.311 P=0.757
Sex [n(%)]			
Males	10(33.3)	15(50.0)	$\chi^2=1.71$
Females	20(66.7)	15(50.0)	P=0.190
Residence [n(%)]			
Rural	21(70.0)	16(53.3)	$\chi^2=1.76$
Urban	9(30.0)	14(46.7)	P=0.184
Occupation [n(%)]			
Housewife	3(10.0)	2(6.7)	MC=4.45
Manual worker	5(16.7)	10(33.3)	P=0.217
Employee	3(10.0)	6(20.0)	
Not working	19(63.3)	12(40.0)	
Marital status [n(%)]			
Single	19(63.3)	14(46.7)	$\chi^2=1.68$
Married	11(36.7)	16(53.3)	P=0.194
BMI (kg/m²) mean \pm SD	24.10 \pm 4.07	26.09 \pm 3.36	t=2.06 p=0.04*
Helicobacter pylori antigen quantity (ng/ml) Median (min-max)	14(6.8-20.6)	7.55(6.05-21.73)	z=0.924 P=0.355
Helicobacter pylori antigen expression [n(%)]			
-ve	13(43.3)	18(60.0)	$\chi^2=1.67$
+ve	17(56.7)	12(40.0)	P=0.196
Past drug history for previous H. pylori [n(%)]	0	3(10.0)	FET=3.16 P=0.076
Past history of chronic illness [n(%)]	0	1(3.3)	FET=1.02 P=1.0

t: Student t test, Z: Mann Whitney U test χ^2 =Chi-Square test, (Min-Max): Minimum- Maximum, FET: Fisher exact test, MC =Montcarlo test, *Statistically significant.

Table 2: Acne severity among studied cases

Acne severity	Cases (n=30)	
	N	%
Mild	6	20.0
Moderate	9	30.0
Severe	15	50.0
Global score mean \pm SD (min-max)	25.0 \pm 7.33(20-32)	

Table 3: Validity of H. pylori antigen in differentiating between cases & control groups

	AUC (95%CI)	P value	Cut of point	Sensitivity %	Specificity %
Helicobacter pylori antigen	0.569 (0.421-0.717)	0.355	8.45	63.3	56.7

AUC: Area under curve

Table 4: Correlation between Helicobacter pylori antigen and age, acne severity, global score and BMI among studied cases

	Helicobacter Pylori Antigen	
	r	p
Age/ years	-0.114	0.549
Acne severity	0.770	<0.001*
Global score	0.770	<0.001*
BMI	0.130	0.493

r: Spearman correlation coefficient, *statistically significant (P <0.05)

Table 5. Correlation between H. pylori antigen and sociodemographic characteristics of the studied cases

	Helicobacter pylori antigen	Test of significance
	Median (IQR)	
Sex		
Males	14.45(8.65-29.67)	Z=0.443
Females	11.25(6.35-19.4)	P=0.658
Residence		Z=0.357
Rural	13(6.6-19)	P=0.721
Urban	15(6.85-32.45)	
Occupation		KW=4.47
Housewife	23(19.8-58)	P=0.215
Manual worker	14(6.85-36.45)	
Employee	6.9(4.5-16.50)	
Not working	13(6.5-15.2)	
Marital status		Z=0.647
Single	13(6.5-15.2)	P=0.518
Married	16.5(6.9-26.9)	

Z: Mann Whitney U test, KW: Kruskal Wallis test, IQR: interquartile range

Table 6: Association between acne severity and H. pylori antigen quantity and expression

		Mild	Moderate	Severe	Test Result	Pairwise Comparisons
		n=6	n=9	n=15		
H. Pylori Antigen Quantity (Ng/MI)	Mean ± SD	7.68 ± 5.19	8.52 ± 3.14	25.52 ± 14.17	K=17.468, p<0.001*	p2 <0.001*
	Median (Min-Max)	5.80 (4.50-18.20)	7.90 (6.20-16.50)	19.80 (13.00-58.00)		p3 <0.001*
H. Pylori Antigen Expression, N(%)	Negative	5(83.3%)	8(88.9%)	0(0.0%)	X2=22.986, p<0.001*	p4 = 0.068
	Positive	1(16.7%)	1(11.1%)	15(100.0%)		p2 <0.001*
						p3 <0.001*
						p4= 1.000

K: Kruskal Wallis test, p2: comparison between mild and moderate groups, p3: comparison between mild and severe groups, p4: comparison between moderate and severe groups

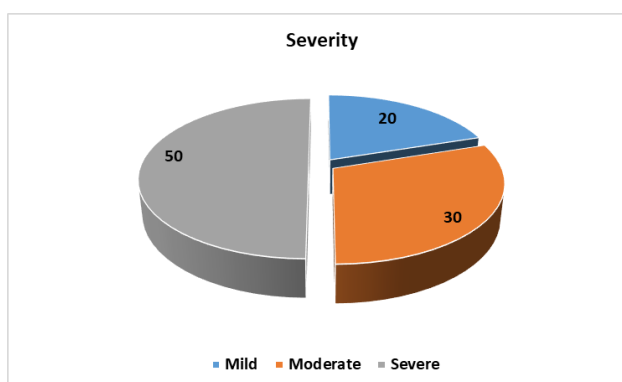


Fig. 1: Distribution of the studied cases according To acne severity

DISCUSSION

The current study's sociodemographic data analysis showed that, every demographic parameter, there was a nonstatistically significant difference between the analyzed groups. The mean age of the studied cases was 25.47 years versus 26.2 years for the control group. It was found that the control group had a higher mean body mass index than the patients, and this difference was statistically significant. A study by Saleh et al.¹³ examined 100 cases with AV (male to female (M/F) ratio of 37/63) and 100 sex matched HC cases. The median age of patients with AV was 20 years which wasn't significantly different from that of the HC (P=0.135). The median duration of AV was ten months.

In terms of disease severity, the present study demonstrated that 50% of the studied cases had severe degree acne, 30% had moderate degree acne and 20% had mild degree acne. In addition, the mean Global score was 25.0±7.33(20-32). In contrast, Saleh et al.¹³ have revealed that, based on the GAGS evaluation, AV severity was classified as mild in 31/100 (31%), moderate in 54/100 (54%), and severe in 15/100 (15%) of the cases.

Also, in Khashaba et al study¹⁴ cases were classified based on GAGS into mild, moderate, and severe AV. Group I (mild AV) comprised 22 cases, group II (moderate AV) comprised 22 patients, group III (severe AV) comprised 22 cases with severe acne; and group IV (control group) comprised 22 normal subjects.

Our analysis of the *H. pylori* antigen comparison showed that the expression and quantity of *H. pylori* antigen varied nonstatistically significantly between the case and control groups. In addition, Saleh et al.¹³ displayed that there was a non-statistically significant difference between both groups with regard to the serum levels and the rate of positivity of *H. pylori* antibodies (65% in acne patient, 64% in control group). Similarly, Khodaeiani et al.¹⁵ has displayed that; with regarding the rate of HP infection, there was a non-statistically significant difference between the controls and the cases with mild AV (p>0.05), and between the controls and the patients with moderate AV (p=0.24). They also showed that; there were non-statistically significant differences in anti-Helicobacter Ig G index between control group and cases with mild and moderate acne.

As regard to correlation between *H. pylori* antigen and age, acne severity, global score and BMI, our study demonstrated that; there was a statistically significant positive relationship between *H. pylori* antigen and each of AV severity & Global score (p<0.005, each). Our research demonstrated a strong and statistically significant correlation between the amount and expression of *H. pylori* antigen and the severity of acne. Notably, the mean quantity of *H. pylori* antigen (measured in ng/ml) increased significantly with acne severity; mean ± SD values increased from 7.68 ± 5.19

in the moderate group to 25.52 ± 14.17 in the severe group. A very high statistical significance (p<0.001) supports this pattern.

Pairwise comparisons revealed a significant difference between mild and moderate groups and mild and severe groups (p<0.001*). In the same line with the present study, Saleh et al.¹³ revealed that the cases with severe AV were associated with significantly higher values of fecal *H. pylori* Ag than the cases with mild AV, moderate AV, and normal controls (P<0.001).

In addition, *H. pylori* antigen could differentiate between cases & control groups with 63.3% sensitivity and 56.7% specificity. Similarly, it was demonstrated that; patients with severe AV were associated with a significantly higher levels of *H. pylori* AB in comparison with those with mild and moderate AV, and normal controls¹³.

In accordance, Khodaeiani et al.¹⁵ have displayed that; the rate of *H. Pylori* infection, was significantly higher in the cases with severe AV compared to the controls (p=0.01). In addition, IgG level was significantly higher in the same group. This was consistent with the findings of Khashaba et al.¹⁵, who showed that the group with severe acne had a statistically significant rise in anti-Helicobacter Ig G levels (P<0.001), positive relationship between antibody index and acne score was found (P=0.02), and a significant improvement in AV following triple therapy in all the studied groups (P<0.05)¹⁴.

Mush research observed that, on comparing cases with AV either mild or moderate or severe and control group there wasn't only a greater incidence of *H. pylori* was detected but also a significantly increased titer of fecal antigen or serum IgG to *H. pylori* were recognized¹⁵⁻¹³.

Our investigation showed that there was a non-statistically significant relationship between the *H. pylori* antigen and every sociodemographic variable. This relationship pertained to the association between the antigen and these characteristics.

CONCLUSION

The current study revealed that AV severity and global score were correlated positively with *H.pylori* infection. *H. pylori* antigen could discriminate between cases and control groups 'but' with mild sensitivity and specificity.

Declarations:

Consent for publication: Not applicable

Availability of data and material: Data are available upon request.

Competing interests: The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article. This manuscript has not been previously published and is not under consideration in another journal.

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