

Correlation Between Helicobacter Pylori Infection and Severity of Asthma

العلاقة بين الإصابة بالملويات البوابية وشدة الربو القصبي

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الخلاصة

خلفية الدراسة: طالما كان يعتقد أن الإصابات الجرثومية توفر حماية من أمراض الحساسية، وقلة التعرض للجراثيم المعوية أعطت تفسير لزيادة انتشار الربو وزيادة شدته، ولذلك بما إن الانتشار العام للإصابة بالملويات البوابية بدأ بالانحسار، لذلك وجدنا أن نتيجة الفحص المناعي للإصابة بالملويات البوابية تتناسب عكسيا مع شدة الإصابة بالربو المزمن.

الهدف: هذه الدراسة هو تحديد هل أن الإصابة السابقة بالملويات البوابية تقلل من احتمالية حدوث حالة الربو الشديد عند مرضى الربو المزمن.

المنهجية: شارك في هذه الدراسة خمسون مريض مصابون بالربو المزمن، يتكونون من 19 ذكر و 31 أنثى تتراوح أعمارهم بين 17 و 66 سنة، من كل هؤلاء المرضى تم اخذ تاريخ مرضي شامل وخضعوا لفحص سريري كامل، بعد ذلك اجري لهم فحص وظائف الرئة، من ثم سحب من كل مريض عينة بمقدار 2 مليلتر من الدم الوريدي، من ثم تم إجراء الطرد المركزي للعينة وأرسلت لغرض إجراء فحص الملويات البوابية المناعي.

النتائج: تم إيجاد علاقة إحصائية معتبرة بين شدة الربو والنتائج الموجبة لفحص الملويات البوابية المناعي، حيث كلما زادت شدة الربو كلما قلت نسبة النتائج الموجبة للفحص المناعي، كذلك تم إثبات عدم وجود علاقة إحصائية معتبرة تربط أعمار المرضى أو أجناسهم بنتائج الفحص المناعي.

الاستنتاج: هناك علاقة عكسية بين شدة الربو القصبي ونتائج فحص الملويات البوابية المناعي.

التوصيات: نظرا لعدم وضوح العلاقة المباشرة بين الملويات البوابية والربو القصبي نوصي بالمزيد من الدراسات لاكتشاف تلك العلاقة.

ABSTRACT

Background: Microbial exposures have been suggested to confer protection from allergic disorders, and reduced exposures to gastrointestinal microbes have been proposed as an explanation for the increase in asthma severity and prevalence. Since the general prevalence of Helicobacter pylori has been decreasing, we hypothesized that H. pylori serostatus may be inversely related to the severity of asthma.

Objective: The aim of this study is to find whether infection with H.pylori reduces the probability of development of severe asthma in patients with persistent asthma.

Patients and methods: In this study fifty patients with persistent asthma includes 19 males and 31 females their ages range from (17 – 66) years For all those patients, full history and complete physical examination have been done, then after, the patients subjected to pulmonary function test. After that, two milliliters sample of venous blood have been drawn, then, the sample centrifuged and sent to assess for H.pylori infection serology. Data was analyzed by using SPSS.

Results: There is significant association between severity of asthma and result of H.pylori so with increase severity of asthma there is decrease in percentage of positive H.pylori serology. And there is no statistical significant are noted between patients sex or age and results of H.pylori infection test.

Conclusion: There is significant inverse association between severity of asthma and result of H.pylori infection serology. This association not affected by ages and sex of patients.

Recommendations: Since the exact mechanism by which H.pylori affect asthma is not clear, there is need for further studies to explore it.

Keywords: Helicobacterpylori, serology test, pulmonary function test, asthma.

Abbreviations:FEV1 (Forced expiratory volume in 1st second), FVC (Forced vital capacity), GIT (Gastro-intestinal tract), GERD (Gastro-esophageal reflex disease). H.Pylori (Helicobacter pylori), PEF (Peak expiratory flow),PEF (Peak expiratory flow).SABA (Short acting beta 2 agonist).

INTRODUCTION:

Asthma is a common pulmonary disorder characterized by airway inflammation, airway hyper-reactivity, and reversible airflow obstruction ⁽¹⁾. It is one of the most common chronic diseases globally and currently affects approximately 300 million people worldwide ⁽²⁾.

In developing countries where the prevalence of asthma had been much lower, there is a rising prevalence, which is associated with increased urbanization ⁽²⁾. The pulmonary infiltrates of asthmatic patients consist of eosinophils, mast cells, and activated Th2 and Th17 cells, which orchestrate allergen-specific immune responses ⁽³⁾. The growing prevalence of asthma has been attributed to pollution and tobacco smoke ⁽⁴⁾ and to a lack of infectious stimuli arising from modern sanitary practices and the widespread use of antibiotics ⁽⁵⁾.

Helicobacter pylori are curved, flagellated, gram-negative rods found only in gastric epithelium or in gastric metaplastic epithelium. It is the most common worldwide microbial infection, with an estimated 50% of the world's population being infected ⁽¹⁾.

The role for *H. pylori* infection in the disorders of respiratory system has been addressed for several years. *H. pylori* infection might have a role in the development of chronic bronchitis, bronchiectasis, lung cancer and tuberculosis ^(6,7). However, the role of *H. pylori* infection in the development of asthma remains controversial ^(6,8).

In developing countries, virtually all adults harbor *H. pylori*, but the prevalence is much lower in industrialized nations ⁽⁹⁾.

The prevalence of airway allergic disease such as asthma has over the years increased in developed countries. The causes of this increase remain largely unknown. Proposed associations include changes in smoking habits ⁽¹⁰⁾, exposure to food-borne and orofecal infections ^(11,12), types of dwellings ⁽¹³⁾, ownership of furry animals ⁽¹⁴⁾, number of siblings, family income/education level ⁽¹⁵⁾ and the presence of particulates in diesel exhaust ⁽¹⁶⁾. The inverse association between family size and manifestations of allergy has been consistently found, and there is also a much-published potential link between allergy and childhood infection, especially with *Helicobacter pylori* ⁽¹⁷⁾.

The "hygiene hypothesis" that reduced childhood exposure to microorganisms lead to more allergic disorders, has been proposed to explain this increase ⁽¹⁸⁾. In medicine, the hygiene hypothesis states that a lack of early childhood exposure to infectious agents, symbiotic microorganisms (e.g., gut flora or probiotics), and parasites increases susceptibility to allergic diseases by suppressing the natural development of the immune system. In particular, the lack of exposure is thought to lead to defects in the establishment of immune tolerance ⁽¹⁹⁾.

Aim of study:

The aim of this study is to find whether infection with *H. pylori* reduces the probability of development of severe asthma in patients with persistent asthma.

PATIENTS AND METHODS:

In this study fifty patients with persistent asthma includes 19 males and 31 females their ages range from (17 – 66) years who had consulted the outpatient and emergency department of AL-Sader medical city for a period of 19 months (from May 2012 – November 2013) have been enrolled to participate.

For all those 50 patients, full history and complete physical examination have been done, then after, the patients subjected to pulmonary function test with (SPIROLAB device), after that, two milliliters sample of venous blood have been drawn, then, the sample

centrifuged and sent to assess for H.pylori serology with (One step H.pylori Test Device/ABON kits) .^(20,21)

• **Inclusion criteria:**

Patients who had persistent asthma and had recurrent episodic wheeze, chest tightness, dyspnea and had pulmonary function test showing:

- (1) Reduced FEV₁, FEV₁/FVC ratio, and PEF.
- (2) Reversibility is demonstrated by a >12% and 200 mL increase in FEV₁ 15 minutes after an inhaled short –acting B₂ agonist.
- (3) Flow-volume loops show reduced peak flow and reduced maximum expiratory flow.

• **Exclusion criteria:**^(5,8)

- (1) Known cases of peptic ulcer disease.
- (2) Patients had history of upper GIT bleeding.
- (3) Current unstable cardiac disease.
- (4) Uncontrolled hypertension.
- (5) Lung disease other than asthma.
- (6) Neuromuscular disease.

Patients with persistent asthma were divided into 3 groups according to asthma severity score (table-1).

Table (1):Asthma severity score*.

Severity	Symptom frequency	Night time symptoms	%FEV ₁ of predicted	FEV ₁ Variability	SABA use
Intermittent	≤ 2 days/week	≤2/month	≥80%	<20%	≤2 days/week
Mild persistent	> 2 days/week	3–4/month	≥80%	20–30%	>2 days/week
Moderate persistent	Daily	>1/week	60–80%	>30%	Daily
Severe persistent	Continuously	Nightly	<60%	>30%	≥twice/day

*MKSAP-2013

Statistical analysis:

In this comparative study, Statistical analysis was done by using SPSS (statistical package for social sciences) version 20 in which we use chi square test for categorical data. A p-value <0.05 is statistically significant. Sensitivity calculated as the following (true positive/true positive + true negative), specificity calculated as the following (true negative/ true negative + false positive), positive predictive value calculated as (true positive / true positive + false positive), negative predictive value is calculated as (true negative / true negative + false negative).

RESULTS:

The results of this study consist of 50 patients with different degrees of asthma. The gender distribution had been shown in figure (1).

There were 17 patients with positive H.pylori and 33 negative H.pylori. The mean age of those with positive H.pylori was 46±15.6 years while those with negative H.pylori was 40.6±13.9 years with no significant difference between the two groups (P=0.22).

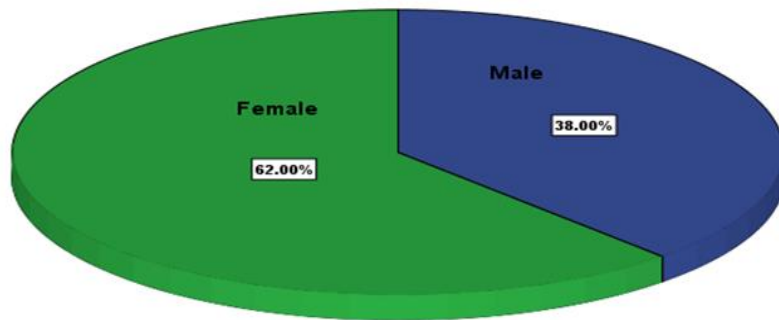


Figure (1): the distribution of patients according to gender.

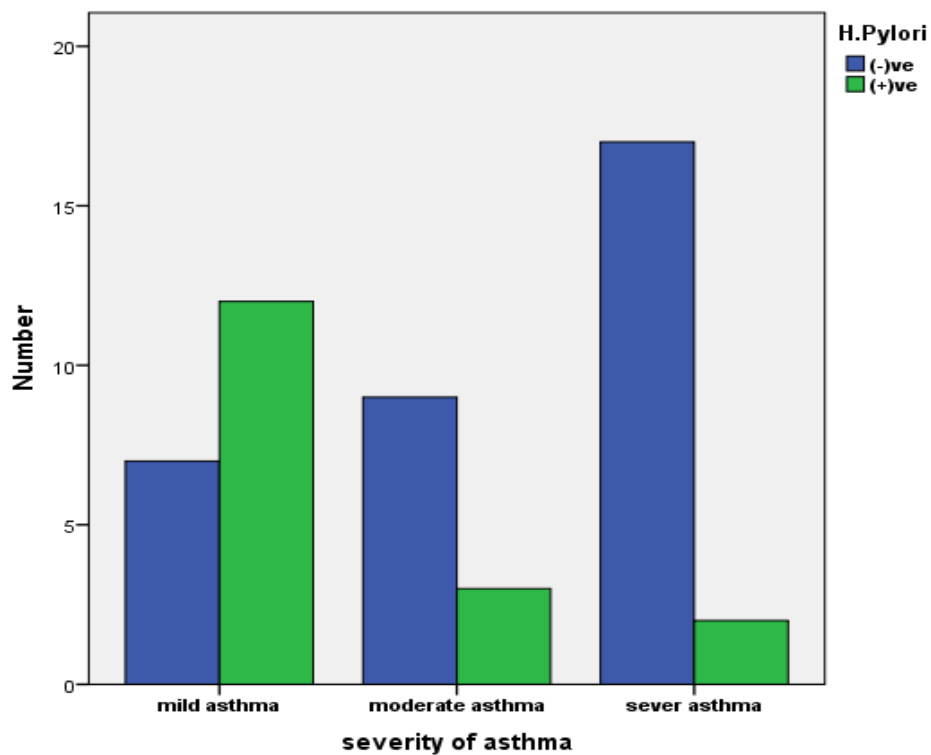


Figure (2): Number of H.pylori infection according to severity of asthma.

Figure (2) shows there is significant association between severity of asthma and result of H.pylori infection, so with increase severity of asthma there is decrease in percentage of positive H.pylori results

Table (2):Relation between severity of asthma and gender

Severity of asthma	Gender		P value
	Male	Female	
mild asthma	6 31.6%	13 41.9%	0.584
Moderate	6 31.6%	6 19.4%	
severe asthma	7 36.8%	12 38.7%	
Total(N=50)	19 100.0%	31 100.0%	

Table (2) shows that there is no significant difference between males and females regarding severity of asthma.

Table (3): Relation between gender of asthmatic patients and H.pylori infection.

H.pylori	Gender		P value
	Male	Female	
(-)ve	12 63.2%	21 67.7%	0.74
(+)ve	7 36.8%	10 32.3%	
Total(N=50)	19 100.0%	31 100.0%	

Table (3) shows there is no significant difference between males and females regarding result of H.pylori infection.

DISCUSSION:

Reduced exposure to orofecal organisms has been suggested as an explanation for the increasing prevalence of atopy and asthma, but studies of multiple organisms have had conflicting results⁽²²⁾. H. pylori are among organisms that infect humans as they colonize the gastric mucosa in early life and then produce a chronic persisting infection and an inflammatory response that persists indefinitely unless eradicated⁽²³⁾.

This study shows the relationship between H.pylori infection and severity of asthma. The result is statically significant inverse association between asthma severity and H.pylori infection (p-value =0.002), this result is consistent with Chen and Blaser (2008)⁽²⁴⁾ who proposed that in urban population asthma severity decrease in patients with positive H.pylori serology especially cagA+ strain but recommended further prospective studies to delineate the underlying mechanism.

Zevit (2012)⁽²⁵⁾ and Joan Reibman (2008)⁽²⁶⁾ also revealed that there is an inverse association between H. pylori seropositivity and pediatric asthma, and that H. pylori is an independent factor that protects against asthma.

All these studies suggest that there are several mechanisms by which H.pylori affect asthma.

First mechanism, if *H. pylori* is actually protecting against GERD⁽²⁷⁾ it also could protect against asthma, since some proportion of asthma is due to GERD⁽²⁸⁾ However, this mechanism is unlikely to be sufficient to explain protective *H. pylori* effects in hay fever and atopic dermatitis.

Second mechanism, the constellation of asthma, atopy and hay fever suggests immunological mediation. *H.pylori*-positive persons have a gastric population of immunocytes, including regulatory T cells^(29, 30) that is largely absent from *H pylori*-negative subjects. Such cells may have systemic immunomodulatory activities. This consistent with the “hygiene hypothesis” that microbial infections during early childhood may prevent or diminish atopic sensitization and asthma⁽³¹⁾ In particular, inadequate microbial stimulation of gut associated lymphoid tissue; a critical site for maturation of mucosal immunity⁽³²⁾ may be relevant to this mechanism.

Third mechanism may relate to the effects of *H pylori*-induced inflammation on gastric hormonal levels⁽³³⁾ both leptin and ghrelin have immunomodulatory activities⁽³⁴⁾ There is increasing evidence that *H.pylori* gastric colonization affects both ghrelin and leptin production^(33,34) which thus would affect the immunoregulatory environment.

Our study results are not consistent with D.Fullerton (2009)⁽³⁵⁾ They found that there was no significant association between *H. pylori* infection and asthma protection. The discrepancy between the results here may be due to the difference in the number of sampled patients and use IgE level and spirometry to assess asthma severity.

In this study, there is no statistical significant correlation between ages of asthmatic patients and status of *H.pylori* infection (p-value=0.22), this consistent with Chen and Blaser (2008)⁽²⁴⁾ but not with Zevit, (2012)⁽²⁵⁾ who reveal increase *H.pylori* infection in asthma population ages less than 15 years.

Also in this study there is no significant association between sex of asthmatic population and *H.pylori* serological status (p-value=0.74) and this consistent with all above studies that reveal there is no association with patient sex.

CONCLUSION

There is significant inverse association between severity of asthma and results of *H.pylori* infection serology. This association not affected by age and sex of patients.

RECOMMENDATIONS

Since the exact mechanism by which *H.pylori* affect asthma is not clear, there is need for further studies to explore it. These studies should include additional immunological parameters like IgE, genetics and cell mediated immune modulators that may affect this relationship.

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