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# Measurement of Helicobacter Pylori in Patients with Bronchial Asthma

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## ABSTRACT

**Background:** Current evidence indicates an inverse association between *Helicobacter pylori* and asthma and allergy. *H. pylori* is a Gram-negative bacterium which represents the major cause of peptic ulcer and gastric cancer, and preferentially elicits a T helper (Th)-1 response. Many *H. pylori* factors, such as the neutrophil-activating factor of *H. pylori* (HP-NAP), are able to drive Th-1 polarization and to display a powerful inhibition of allergic Th-2 response. Special attention has been drawn to HP-NAP as a potential novel strategy for the prevention and treatment of asthma and atopy.

**Aim of the Work:** This study was aimed to measure helicobacter pylori in patient with bronchial asthma.

**Subjects and Methods:** This study included a total of 50 patients with bronchial asthma and 20 age-matched control individuals attending at AL-Hussein, Al-Azhar University Hospitals in the period between April 2018 and December 2018. All patients underwent full history taking, complete clinical examination, plain chest X-ray, routine lab investigations, spirometry before and after bronchodilators and H. pylori antigen in stool by ELISA.

**Results:** The results of this study revealed that there is a relation between bronchial asthma and helicobacter pylori.

**Conclusion:** There were improvement in pulmonary function tests in asthmatic patients with H. pylori positive more than asthmatic patients with H. pylori negative.

**Keywords:** Helicobacter pylori neutrophil-activating factor, protein, Th-1/Th-2, Treg, asthma.

## INTRODUCTION

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[(1)] exposure to food-borne and orofecal infections[(2)], types of dwellings,[(3)] ownership of furry animals,[(4)] number of siblings, family income/education level,[(5)]and the presence of particulates in diesel exhaust.[(6)]

The inverse association between family size and manifestations of allergy has been consistently found,[(7)] and there is also a much-published potential link between allergy and childhood infection, especially with Helicobacter pylori[(8)]. Until the late 1980s, interest in the role of infections in allergic diseases focused principally upon the process of primary allergic sensitization.

The literature of the time contained several observations which argued for a role for infections, including the ability of bacterial-derived immune-stimulants such as pertussigen to selectively improve priming for immunoglobulin (Ig)E antibody production[(8)], and the potential of lipopolysaccharide to bypass tolerance to mucosally applied allergens. Also, other studies reported that respiratory viral infections such as influenza could subvert the generation of protective "inhalation tolerance" to aeroallergens[(9)]. Signals such as enterotoxins from skin-dwelling bacteria have been invoked as important contributors to the pathogenesis of atopic dermatitis[(10)].

However, it was also clear from other observations that microbial exposure per se could not be considered in generic terms as "pro-atopic". For example, other microbial-derived agents exemplified by the components of Freund's adjuvant displayed atopy-antagonistic activity[(11)], and stimuli derived from normal gut flora were demonstrated to be necessary to facilitate the expression of oral tolerance to fed allergens[(12)], and also inhalation tolerance to aeroallergens [(13)]. These observations suggested that microbial-derived stimuli had potential to modulate the etiology and pathogenesis of atopic diseases in dichotomous ways, their ultimate effects perhaps being context-dependent.

The current study was aimed to measure helicobacter pylori in patient with bronchial asthma.

## SUBJECTS AND METHODS

This study included a total of 50 patients with bronchial asthma and 20 age-matched control individuals attending at AL-Hussein, Al-Azhar University Hospitals. This study was conducted between April 2018 and December 2018.

All patients underwent full history taking, complete clinical examination, plain chest X-ray, routine lab investigations, spirometry before and after bronchodilators and H. pylori antigen in stool by ELISA.

**Exclusion criteria include:** Patients with respiratory failure, acute severe asthma , patients on mechanical ventilation, Patients unable to do pulmonary function tests, Patients on proton pump inhibitors ,



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patients with gastroesophageal reflux disease [14], Patients on H. Pylori treatment, patients under 18 years old and above 65 years old, patients were current smokers; had a history more than 10 pack years tobacco use , patients who had unstable cardiac disease, un controlled hypertensive patients, patients with lung disease other than asthma and patients with neuro-muscular disease.

**Ethical consideration**

Privacy and confidentiality were maintained throughout the study process. Subjects or their relatives received written notification of the results. Approval of the ethical committee and a written informed consent from all the subjects were obtained.

**Statistical analysis:**

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data.

Comparisons between quantitative variables were done using the non-parametric Mann-Whitney test. For comparison of serial measurements within each patient the non-parametric Wilcoxon signed rank test was used . For comparing categorical data, Chi square ($\chi 2$) test was performed.

Exact test was used instead when the expected frequency is less than 5.

Correlations between quantitative variables were done using Spearman correlation coefficient. P-values less than 0.05 were considered as statistically significant.

**RESULTS**

This study was carried out on 70 patients attended to Hussein University hospital, Al-Azhar University, in which 50 patients presented with bronchial asthma and 20 age-matched control individuals. They included 62 males and 8 females. This study was designed to evaluate the effect of H. pylori on bronchial asthma. In this study spirometry was done before and after bronchodilators, liver and kidney function tests, chest x ray and complete blood count.

**Table(1):** Distribution of patients according to age

| | Mean | Standard Deviation | Median | Minimum | Maximum |
|---|---|---|---|---|---|
| **age** | 45.14 | ±12.42 | 47.00 | 25.00 | 65.00 |

**Table(2)** Distribution of patients according to sex

| | | Count | Column N % |
|---|---|---|---|
| **sex** | **female** | 8 | 11.4% |
| | **male** | 62 | 88.6% |

This table shows that there were 62 patients are male and 8 patients are female.

**Table(3)** Distribution of patients as regard h.pylori antigen in stool

| | | Count | % |
|---|---|---|---|
| **H.Pylori antigen** | **Positive** | 43 | 61.4% |
| | **Negative** | 27 | 38.6% |

This table shows that there were 43patients are positive and 27 are negative

**Table(4)** Distribution of Normal X-Ray and Abnormal X-Ray among H. pylori Positive.

| | | H. Pylori antigen Positive | |
|---|---|---|---|
| | | Count | % |
| **Chest X Ray** | **Normal** | 12 | 27.9% |
| | **Abnormal** | 31 | 72.1% |

This table shows that there were 12 patients are normal and 31patients are abnormal.

**Table (5)** Distribution of Normal X-Ray and Abnormal X-Ray among H. pylori Negative.

| | | H. Pylori antigen Negative | |
|---|---|---|---|
| | | Count | % |
| **Chest X Ray** | **Normal** | 8 | 29.6% |
| | **Abnormal** | 19 | 70.4% |

This table shows that there were 8 patients are normal and 19 patients are abnormal.

**Table (6)** comparison between Asthmatic and control as regard H. Pylori antigen

| | | Control | | Asthmatic | | P value |
|---|---|---|---|---|---|---|
| | | Count | % | Count | % | |
| **H. Pylori antigen** | **Positive** | 12 | 60.0% | 31 | 62.0% | 0.877 |
| | **Negative** | 8 | 40.0% | 19 | 38.0% | |

This table shows that there was no statistically significance between asthmatic and control as regard H. Pylori antigen.

**Table (7)** comparison between Asthmatic and control as regard complete blood count.

| | Control | | Asthmatic | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| **WBCs** ($x10^9$ /l) | 8.08 | 1.91 | 8.10 | 1.42 | 0.861 |
| **Platelets** ($x10^9$ /l) | 223.40 | 47.59 | 270.04 | 60.79 | < 0.001 |
| **Hb (g/dl)** | 12.53 | 1.62 | 12.45 | 0.57 | 0.715 |

This table shows that there were statistically significance increasing number of platelets between asthmatic patients more than control.

**Table (8)** comparison between Asthmatic patients and control as regard liver –kidney function tests

| | Control | | Asthmatic | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| **AST (units/L)** | 19.70 | 2.54 | 20.38 | 2.47 | 0.676 |
| **ALT (units/L)** | 21.85 | 4.67 | 21.44 | 4.52 | 0.634 |
| **Urea (mg/dl)** | 22.10 | 5.51 | 26.62 | 4.87 | 0.015 |
| **Creatinine (mg/dl)** | 0.85 | 0.14 | 0.81 | 0.15 | 0.273 |

This table shows that there were statistically significance increasing level of urea between asthmatic patients more than control.

**Table (9)** comparison between asthmatic patients and control as regard FEV1, FVC, FEV1/FVC (pre-bronchodilator)

| | Control | | Asthmatic | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| **FEV1 Pre-bronchodilator** | 3.78 | .71 | 2.21 | .93 | < 0.001 |
| **FVC Pre-bronchodilator** | 4.48 | .95 | 3.34 | 1.20 | < 0.001 |
| **FEV1/FVC Pre-bronchodilator** | 0.85 | 0.05 | 0.65 | 0.13 | < 0.001 |

This table shows that there were statistically significance decreasing in FEV1, FVC and no significantly change as regard FEV1/FVC between asthmatic and control patients.

**Table (10)** comparison between asthmatic patients and control as regard MEF25, MEF75, PEF(pre-bronchodilator)

| | Control | | Asthmatic | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| **MEF25 Pre-bronchodilator** | 1.92 | .44 | 1.28 | 1.45 | < 0.001 |
| **MEF75 Pre-bronchodilator** | 8.02 | 1.48 | 2.63 | 1.58 | < 0.001 |
| **PEF Pre-bronchodilator** | 8.59 | 1.37 | 5.17 | 1.89 | < 0.001 |

This table shows that there were statistically significance decreasing in MEF25, MEF75and PEF between asthmatic and control patients.

**Table (11)** comparison between asthmatic patients and control as regard FEV1,FVC, FEV1/FVC (post-bronchodilator)

| | Control | | Asthmatic | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| **FEV1 post-bronchodilator** | 3.91 | .75 | 2.69 | 1.06 | < 0.001 |
| **FVC post-bronchodilator** | 4.54 | .95 | 3.72 | 1.25 | < 0.001 |
| **FEV1/FVC post-bronchodilator** | 0.87 | 0.05 | .72 | 0.13 | < 0.001 |

This table shows that there were significant difference decreasing in FEV1, FVC between asthmatic and control but no significant difference in FEV1/FVC between them.

**Table (12)** comparison between asthmatic patients and control as regard MEF25, MEF75, PEF(post-bronchodilator)

| | Control | | Asthmatic | | P value |
|---|---|---|---|---|---|
| | Mean | ±SD | Mean | ±SD | |
| **MEF25 post-bronchodilator** | 2.13 | .59 | 1.75 | 2.08 | 0.002 |
| **MEF75 post-bronchodilator** | 8.14 | 1.64 | 3.65 | 1.91 | < 0.001 |
| **PEF post-bronchodilator** | 8.70 | 1.49 | 5.69 | 1.96 | < 0.001 |

This table shows that there were statistically significance decreasing in MEF75and PEF with no significant change as regard MEF25 between asthmatic and control patients.

**Table (13)** Comparison between asthmatic patients with positive and negative h.pylori as regard pre-bronchodilator pulmonary function tests.

| | H. Pylori antigen | | | | P value |
|---|---|---|---|---|---|
| | Control | | Asthmatic | | |
| | Mean | ±SD | Mean | ±SD | |
| **FEV1 Pre-bronchodilator** | 2.06 | 0.93 | 2.45 | 0.92 | 0.131 |
| **FVC Pre-bronchodilator** | 3.27 | 1.16 | 3.47 | 1.27 | 0.535 |
| **FEV1/FVC Pre-bronchodilator** | 0.61 | 0.12 | 0.71 | 0.11 | 0.003 |
| **MEF25 Pre-bronchodilator** | 1.05 | 1.19 | 1.65 | 1.77 | 0.131 |
| **MEF75 Pre-bronchodilator** | 2.43 | 1.57 | 2.97 | 1.58 | 0.223 |
| **FEV1 Pre-bronchodilator** | 4.93 | 1.99 | 5.56 | 1.68 | 0.158 |

This table shows that there were no statistically significant change as regard FEV1, MEF25, MEF75 PEF and FVC and statistically significant change increasing FEV1/FVC between asthmatic patients positive and negative as regard H. Pylori antigen.

**Table (14)** Comparison between asthmatic patients with positive and negative h.pylori as regard post-bronchodilator pulmonary function tests.

| | H. Pylori antigen | | | | P value |
|---|---|---|---|---|---|
| | Control | | Asthmatic | | |
| | Mean | ±SD | Mean | ±SD | |
| **FEV1 post-bronchodilator** | 2.94 | 1.06 | 2.54 | 1.05 | 0.201 |
| **FVC post-bronchodilator** | 3.84 | 1.41 | 3.64 | 1.16 | 0.726 |
| **FEV1/FVC post-bronchodilator** | 0.77 | 0.12 | 0.69 | 0.13 | 0.010 |
| **MEF25 post-bronchodilator** | 2.19 | 2.43 | 1.47 | 1.82 | 0.126 |
| **MEF75 post-bronchodilator** | 3.95 | 2.01 | 3.47 | 1.86 | 0.441 |
| **PEF post-bronchodilator** | 6.13 | 1.69 | 5.42 | 2.09 | 0.207 |

This table shows that there were significant statistically improvement In FEV1, MEF25, MEF75 and PEF and no statistically significant change in FVC and FEV1/FVC between asthmatic patients positive and negative as regard H.pylori antigen.

## DISCUSSION

Helicobacter pylori and humans have co-evolved for at least 50,000 years and probably for much longer as such H. Pylori colonization has been essentially universal, and the usual pattern of inflammation has likely been pan-gastric[15].

H. Pylori is the main cause of peptic ulceration, gastric lymphoma and gastric adeno carcinoma. The loss of this ancient, dominant and persistent member of the normal biota of humans would be predicted to have consequences, and now there is much information's about the beneficial and deleterious

aspects of this change on the health and disease of gastrointestinal tract. However, increasing evidence is pointing to extra intestinal manifestations of the disappearance of H. Pylori including asthma[16].

In our study, the age distribution ranged from 25 years to 65 years. This is agreed with **Reibman et al.** who discuss the asthma is inversely associated with helicobacter pylori status in urban populations, cases and control were similar in age and gender. Cases were more often Hispanic and income levels were lower in the cases than in the controls. Hispanic ethically was not associated with asthma status, once income and race were adjusted for via logistic regression.[17]

The current study disagreed with Wang **et al**. who show that is helicobacter pylori infection associated with asthma risk due to probably large number of patients taken in that study . In our study there were gender distribution of patients to be 8 females and 62 males. This is in agreement with **Wang *et al.*** who take metanalysis based on 770 cases of asthma and 785 as control and sub group analysis regarding other can founding such as age not conducted in this study[18].

These results were in agreement with **Reibman *et al*.** who had taken 318 of patients as asthmatics, and 208 subjects as control. In our study there was 50 patients asthmatic and 20 subjects control , 43 patients were positive and 27 patients were negative, as regard H. Pylori positive in asthmatic patients, 31 patients ,12 patients in control and 19 patients was negative in asthmatic patients and 8 patients in control[17]. And this in agreement with **Hessein *et al.*** who stated that helicobacter pylori inversely related to clinical and functional severity of adult asthma. In our study we found that increase number of platelets and level of urea in asthmatic patients more than control.

In our study there are decrease in pulmonary function tests as regard (FEV1 , FVC, FEV1/FVC % , MEF25 , MEF75 and PEF) between patients and control .[19] And this disagreement with **Wang *et al.*** who found no associated effect of H.pylori on asthma. In this study because several limitations; first, the papers identified in this study were limited to those openly published up to July 2012, Second, limited number of small size, third, sub group analysis regarding other confiding such as smoking status, age and gender. And this in agreement with **Reibman *et al.*** this due to reduced this parameters in asthmatic patients compare to control.[17]

In the current study, there are no statistically significance change in pre-bronchodilator (pulmonary function tests) as regard FEV1 , FVC , PEF , MEF25 and MEF75 between asthmatic patients negative and positive as regard H. Pylori. There were only statistically significance in FEV1/FVC % (H. Pylori positive more than negative).And there were statistically significant improvement of post-bronchodilator (pulmonary function tests) as regard FEV1 , FVC , PEF , MEF25 and MEF75 and no statistically significant change in FEV1/FVC % .

And these results were in agreement with **Reibman *et al.*** who examined whether h.pylori serostatus was an asthma modifier using post-bronchodilator FEV1 and FEV1/FVC as surrogates of asthma severity.

There were significant difference in FEV1 among the individuals with asthma who were cag(+ve), compared to those who were negative although FEV1/FVC was not different between two groups.And next asked whether H. Pylori serostatus was associated with the age of onset of asthma. Age of onset of asthma was similar among the H. Pylori (+ve) and (-ve) individuals but was substantially lower among the H. Pylori negative individuals , similar difference in age were noted when them assessed age at onset of symptoms [17]. And in agreement with **Hessein *et al.*** who show that there was statistically negative association between asthma severity and H. Pylori infection.[19]

And it is also in agreement with **Matricardi *et al*.** who found that there was an inverse relationship between rhinitis and bronchial asthma as regard exposure to micro organism.[20]

And is also in agreement with **Zevit *et al***. also stated that H. Pylori seropositivity and pediatric asthma were presented with inverse association between them and that H. Pylori is an independent factor that protects against asthma.[21]

The current study disagreement with **Martin blasser** who show Does helicobacter pylori protect against asthma and allergy[22] ,And our study in disagreement with **Wang *et al.*** who study is helicobacter pylori infection associated with asthma risk meta-analysis based on 770 cases , 785 cases and disagreement was previously discussed.[18]

However, a realistic hypothesis based on clinical and experimental evidence in humans and animal models.

Is that the allergic TH2 response is reduced by TH1 response elicited by H.pylori that able to induce the production of INFγ , IL12 , IL23 , several studies were devoted to the definition of new immune modulating factors all to inhibit TH2 responses and different compounds have been proposed for the treatment and prevention of asthma and atopy diseases.

## CONCLUSION

It could be concluded that there is a relation between H. Pylori and pulmonary function tests by

improving pulmonary function tests in asthmatic patients with H. Pylori positive more than asthmatic patients with H. Pylori negative.

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