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Investigating the Relationship Between Helicobacter pylori Infection and the Severity of Bronchial Asthma

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ABSTRACT

Background: It has been found in many studies that 50% of the population were infected by Helicobacter pylori (H. pylori), hence, infections due to H. pylori are considered as most commonly occurring infections in the population. Numerous studies indicate that H.pylorimay impact organs outside the gastrointestinal tract, including the respiratory system.

Objective: To find out the potential connection between the severity of bronchial asthma and H.pylori infection, aiming to improve disease management.

Methodology: A cross-sectional study was performed at the outpatient clinic of the Chest Department at Lady Reading Hospital in Peshawar, taking place from January 2020 to December 2021.. Sample size included 150 asthmatic patients which were selected randomly. Spirometry and H.pylori tests were done on all study participants. They were 112 females with mean age ± SD (37.34 ± 4.99) years and 38 males with mean age ± SD (37.89 ± 5.19) years & with age range from 28–42 years.

Results: The severity of bronchial asthma is inversely related to H. pylori infections; as asthma severity increases, the frequency of H. pylori infections decreases. A significant difference in H. pylori IgG levels was found among patients with mild, moderate, and severe persistent asthma, with a P value of less than 0.002. Asthmatic patients were mostly positive for H. pylori infections (59.1%), while patients with moderate and severe cases of asthma were positive for H. pylori infections as (30.9%) and (11.1%), respectively.

Conclusion: H. pylori seropositivity appears to provide a protective effect against childhood asthma and is negatively correlated with its clinical and functional severity. Furthermore, H. pylori infection may lead to enhanced control of asthma symptoms.

Keywords: Respiratory Disease; Helicobacter Pylori; Asthma

Introduction

Helicobacter pylori (H. pylori) is a prevalent type of bacteria known for its ability to infect the stomach lining and the first part of the small intestine. It is estimated that nearly 50% of the global population is infected by H. pylori.[1] The bacteria possess an enzyme called urease, which plays a crucial role in its survival. Urease neutralizes stomach acidity, creating a more favorable environment for the bacteria, but at the same time, it weakens the stomach lining. While most individuals with H. pylori infections remain asymptomatic, the bacteria can cause significant gastrointestinal disturbances in others, including peptic ulcers and gastritis.[2] Gastritis, or inflammation of the stomach lining, is one of the more common outcomes of H. pylori infection, and if left untreated, this condition can progress, significantly increasing the risk of developing gastric cancer.[3]

Beyond the gastrointestinal tract, H. pylori has been implicated in various systemic conditions. Research has demonstrated its potential role in liver and biliary disorders, ear and eye conditions, cardiovascular diseases, neurological conditions, and even immune system dysregulation. Respiratory disorders are also among the extra-gastrointestinal manifestations of H. pylori infection. Despite these associations, H. pylori is primarily recognized for its impact on the stomach, which has drawn the majority of research attention.[4]

On the other hand, asthma is a chronic inflammatory disorder of the airways characterized by airflow obstruction, excessive mucus production, airway hyper-responsiveness, and bronchial inflammation. Asthma is a significant public health concern worldwide, affecting millions of individuals and leading to substantial morbidity. The pathophysiology of asthma involves a complex interplay of genetic and environmental factors. Common risk factors include exposure to cigarette smoke, allergens, air pollution, microbial infections, obesity, and genetic predisposition. Asthma has become increasingly prevalent, especially in developed countries, where other allergic conditions such as atopy and hay fever have also risen in tandem.[5]

Interestingly, the rise in asthma and allergic disorders has paralleled the decline in H. pylori prevalence in many parts of the developed world. This inverse relationship between the two conditions has sparked research into a possible connection. While studies remain limited, emerging evidence suggests that H. pylori infection may influence immune responses in a way that could reduce the risk of asthma. Specifically, H. pylori appears to promote the activation of T-helper type 1 (Th1) immune cells while suppressing T-helper type 2 (Th2) cells. Since asthma is associated with Th2-driven inflammation, this immunomodulatory effect of H. pylori may offer a protective benefit by mitigating bronchial inflammation, which is central to asthma pathogenesis.[6]

One possible explanation for this relationship is that H. pylori influences the balance of the gut microbiome, which in turn can have downstream effects on the immune system and respiratory health. The gut-lung axis has been a subject of increasing research interest, as studies have revealed that the health of the gastrointestinal system can significantly impact respiratory outcomes. By modifying the gut microbiota and promoting a Th1-dominant immune response, H. pylori may reduce the hyper-reactivity and inflammation that are characteristic of asthma. Additionally, certain microbial products released during H. pylori infection may regulate immune tolerance in distant organs, including the lungs, helping to prevent excessive allergic responses.

Another hypothesis involves the hygiene hypothesis, which suggests that reduced exposure to certain infections or microbes in early life, such as H. pylori, may lead to an overactive immune system that is prone to allergic diseases.[7] This theory posits that in environments where H. pylori is less prevalent due to improved sanitation and widespread antibiotic use, individuals may be more susceptible to asthma and allergies because their immune systems are not adequately "trained" by early microbial exposures. In this context, the presence of H. pylori may play a protective role by helping to balance immune responses and prevent the overactivation of pathways that lead to asthma and other allergic conditions.

Several studies have already suggested a significant inverse relationship between H. pylori infection and asthma, hypothesizing that H. pylori may play a protective role against the development of allergic diseases by regulating immune responses. Despite these findings, the potential association between H. pylori and asthma severity remains underexplored, especially in terms of clinical and functional outcomes. Given the widespread prevalence of both H. pylori infection and asthma, understanding their potential connection could have important implications for disease prevention and management.[8,9]

The purpose of this study is to investigate the potential association between H. pylori infection and the clinical and functional severity of bronchial asthma. By exploring this relationship, we aim to better understand how H. pylori might influence the course of asthma and whether its presence can impact disease control. This study could offer insights into novel approaches for managing asthma, particularly in individuals co-infected with H. pylori. Understanding this association could also contribute to broader discussions on the role of gut-respiratory interactions and their influence on immune-mediated diseases like asthma.

Objective

To find out the potential connection between the severity

Table 1. Baseline Characteristics of study Participents

Parameter	Total N = 150			
	M	F	T	P
Age (Mean ± SD)	37.73 ± 5.01	37.41 ± 4.99	1.9	0.06
Smoking	N	%	X^2	P
Smoking History	28	18.7%	62.2	0.00
	122	81.3%		
Positive family history of Asthma	37	24.6%		

of bronchial asthma and H. pylori infection, aiming to improve disease management.

Methodology

The present study was carried out with cross-sectional study design which was carried out at the Department of Pulmonology, lady Reading Hospital, Peshawar (LRH). This study was carried out during the period from March 2021 to April 2022. Sample size included 150 asthmatic patients which were selected randomly.

This study followed strict Inclusion criteria which included asthmatic patients with recurrent episodic wheeze, chest tightness, and dyspnea. Exclusive criteria included those cases and controls with age <19 or ≥60 years old; patients with current unstable cardiac diseases, people with uncontrolled hypertension, lung diseases other than asthma, diseases of CNS, and uncooperative patients.

Asthma diagnosis in patients was based on the 2015 GINA guidelines, which included evaluating their medical history for respiratory symptoms like wheezing, breathlessness, chest discomfort, or coughing. Symptoms often intensified at night or in the early hours and could be provoked by factors such as viral infections, physical activity, allergens, weather changes, laughter, or irritants like vehicle emissions, strong odors, or smoke. Furthermore, pulmonary function tests were conducted to assess lung function for the diagnosis of asthma.

Consent was acquired from all participants prior to the administration of spirometry and other evaluations necessary for determining asthma severity. A thorough personal background was collected from each individual, including their name, age, gender, place of residence, job, and any particular habits. This background included information about current respiratory complaints, atopic conditions such as asthma, eczema, and rhinitis, as well as any associated health issues (like diabetes, high blood pressure, heart conditions, liver problems, gastroesophageal reflux disease, and tuberculosis). Significant past medical history, especially related to tuberculosis, and family history of respiratory conditions, particularly asthma, were documented. All participants underwent a detailed physical examination, and spirometry was performed. Short-acting bronchodilators were withheld for about 8-9 hours before the spirometry testing. Asthma was classified into categories of mild, moderate, or severe. Each patient was assessed by healthcare providers with extensive experience in diagnosing and managing asthma. Our study confirmed the diagnoses using the framework proposed by Enright et al.[10]

After administering appropriate treatments tailored to the severity of asthma in each patient, the level of asthma control was assessed using a series of key questions. Patients were asked to reflect on their symptoms over the past four weeks, providing answers categorized as "well controlled," "partly controlled," or "uncontrolled." The assessment focused on four critical areas: whether they experienced daytime asthma symptoms more than twice per week, any nighttime awakenings due to asthma, the need for a reliever more than twice per week, and whether

Table 2. Distribution of Bronchial Asthma Severity Among Participants

BA Patients	Mild	Moderate	Severe	Total
N	57	59	34	150
%	38	39.3	22.7	100

Table 3. Asthma Classification Based on Control Levels

Classification of Asthma	Frequency	Percentage (%)
Controlled	75	50
Partially controlled	57	38
Uncontrolled	18	12

variable, while other factors were grouped into categories. Smoking status was classified as never, occasional, or daily; alcohol consumption as never, infrequent (once a week or less), or frequent (more than once a week); and physical activity as inactive (no or less than one hour of light activity per week), moderately active (1–2 hours of light activity or under one hour of vigorous exercise per week), or highly active (3 or more hours of light activity or at least one hour of vigorous exercise per week). Education was divided into three levels: primary school, high school, and college/university. All statistical tests were two-tailed, with a significance level set at 0.05.

Results:

In this study, a significant proportion of asthmatic patients were female (76.6%), with an average age of 37.41 ± 4.99 years. There was no statistically significant age difference between genders ($p > 0.06\%$). Among the participants, 81.3% were nonsmokers ($p < 0.002$). Additionally, 57.7% of patients had gastroesophageal reflux disease (GERD), and 24.6% reported a family history of asthma. Most patients with persistent bronchial asthma were classified as having moderate severity (38.30%). Control levels indicated that 50% of patients were well-controlled, 36.7% were partially controlled, and only 13.3% were uncontrolled. Regarding H. pylori status, 33.3% tested positive for the antigen, while 66.7% were negative. In blood tests, 40% were H. pylori positive, compared to 60% who were negative.

Table 2 showed the degree of severity of asthma in mild, moderate and severe pattern. Moderate cases of asthma were more as compared to the other cases i.e., 39.3%.

It has been showed in Table 3 that majority of the patients of asthma were under control i.e., 50% while 38% patients were partially controlled and 12% patients were uncontrolled.

It has been shown in Table 4 that there were 32.6% patients with H. pylori +ve Ag, while H.pylori negative patients were 67.3%. On the other hand, +ve H. pylori cases in blood were 41.3%, while H. pylori–ve cases were 58.6%.

Table 5 demonstrates an inverse relationship between the severity of bronchial asthma and the incidence of positive H.pylori cases; as asthma severity increases, the occurrence of H.pylori infections decrease.

Table 6 illustrates the differences in H.pylori IgG levels among mild, moderate, and severe asthma cases. Notably, 59.6% of patients with mild asthma tested positive for H.pylori, while the positive rates for moderate and severe cases were 32.2% and 8.0%, respectively.

Table 7 indicates that all negative H.pylori cases identified through serum IgG testing were also negative in the stool antigen test.

Discussion

Asthma is a long-lasting inflammatory disease of the lungs that can affect individuals of all ages. In asthma, inflammation occur and muscles become very tight around the airways, which makes it difficult for the patients to breathe. It is triggered by allergens such as dusts, pollens, molds and pet dander. While the non-allergic causes include extreme stress, illness, and exercise. According to the recent studies, it has been shown that asthma currently affects over 300 million

Table 4. Distribution of H. pylori Stool and Blood Samples of Patients

H. Pylori Findings	Positive		Negative	
	Frequency	Percentage	Frequency	Percentage
Ag in stool	49	32.6	101	67.3
H. Pylori in Blood	62	41.3	88	58.6

Table 5. Analysis of Asthma Severity Based on H.pylori Status (According to Stool Antigen)

BA severity		H. pylori stool Ag		Total	X^2	P
		Positive H. pylori	Negative H. pylori			
Mild	N	25	30	55	11.01	0.008
	%	51.0	29.7	36.6		
Moderate	N	18	42	60		
	%	36.7	41.5	40		
Severe	N	6	29	35		
	%	12.2	28.7	23.3		
Total		49	101	150		

asthma symptoms led to any limitations in their daily activities. This comprehensive evaluation helped gauge the effectiveness of the treatment and provided valuable insights into each patient's asthma management and overall quality of life.

We measured serum anti-H. pylori IgG antibody levels using ELISA with whole cell antigens, while Cag A status was assessed through a separate ELISA. Patients were deemed negative for H. pylori if their antibody levels were undetectable. A positive antibody results combined with a negative antigen result indicated a prior infection, whereas both positive results indicated active disease. Data collection and analysis were conducted using SPSS version 20.0, where we tabulated and analyzed the information statistically.

We reported variables as either counts and percentages or as means with standard deviations (SD). A P-value below 0.05 was regarded as statistically significant, while values under 0.001 were considered highly significant. In fully adjusted analyses, age was treated as a continuous

Table 6. Association Between H.pylori IgG Levels and Asthma Severity

Asthma severity		H. pylori IgG		Total	X^2	P
		Positive IgG	Negative IgG			
Mild	N	37	22	59	15.9	0.00
	%	59.6	25.0	39.3		
Moderate	N	20	37	57		
	%	32.2	42.0	38		
Severe	N	5	29	34		
	%	8.0	32.9	22.6		
Total		62	88	150		

Table 7. Comparison of Diagnostic Methods for H. pylori

H. pylori IgG		H. pylori stool Ag		Total	X^2	P
		Negative stool Ag	Positive stool Ag			
Negative IgG	N	92	0	92	91	0.00
	%	91.0	0.00	61.3		
Positive IgG	N	9	49	58		
	%	8.9	100	38.6		
Total		101	49	150		

individuals in the World.[11] Without treatment, asthma can pose serious risks to life.

Helicobacter pylori is a rod-shaped bacterium which is able to infect the inning of stomach. It can lead to lesions and irritation in the lining of the stomach or the upper section of the small intestine, referred to as the duodenum. In some cases, the infection can lead to the cancer of stomach. However, it is estimated that in 30% people who were suffering from infections of H pylori develop other conditions, such as gastritis and peptic ulcers. This is because the bacteria could damage the inner protective lining of stomach.[3]

In the present present study, we compare the cases of severity of asthma with those patients who were also suffering from H pylori along with asthma. We found that generally there is no direct association between H pylori infection and asthma or allergic diseases. But we have also found that there was reduced risk of asthma in those patients who were already infected with H pylori. A study conducted in the United States supported these findings. Chen and Blaser identified an inverse relationship between asthma severity and the prevalence of H. pylori infections, suggesting that higher asthma severity is associated with lower rates of H. pylori. This research highlights the complex interplay between respiratory conditions and gastrointestinal infections.[12]

The current study provides a comprehensive overview of the relationship between Helicobacter pylori (H. pylori) infection and the severity of bronchial asthma in patients. In this study, a significant proportion of asthmatic patients were female (76.6%) with an average age of 37.41 ± 4.99 years, which aligns with previous research that suggests

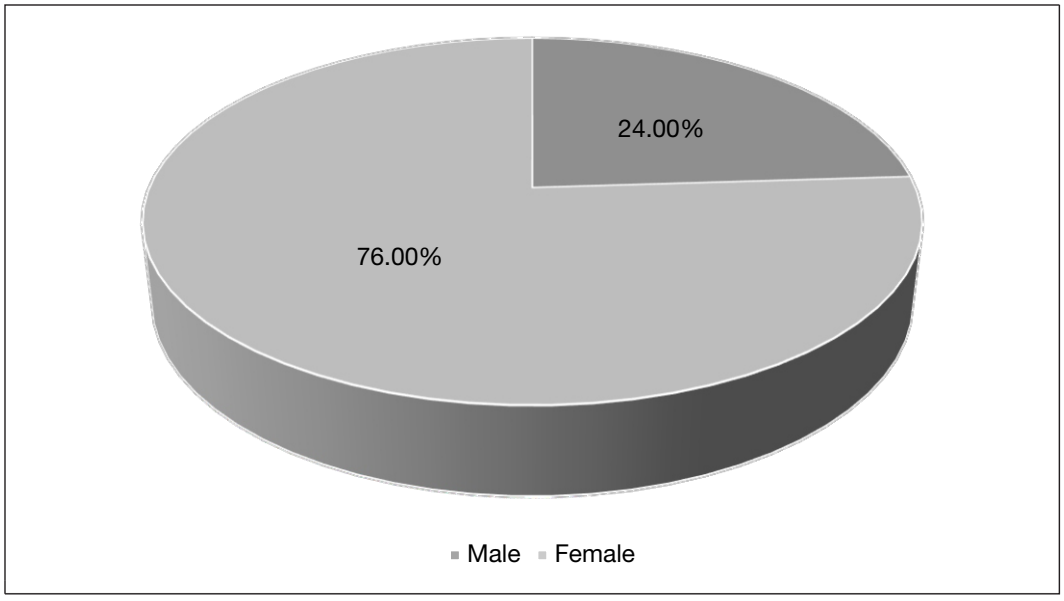

Figure 1. Presentation of study cases by gender

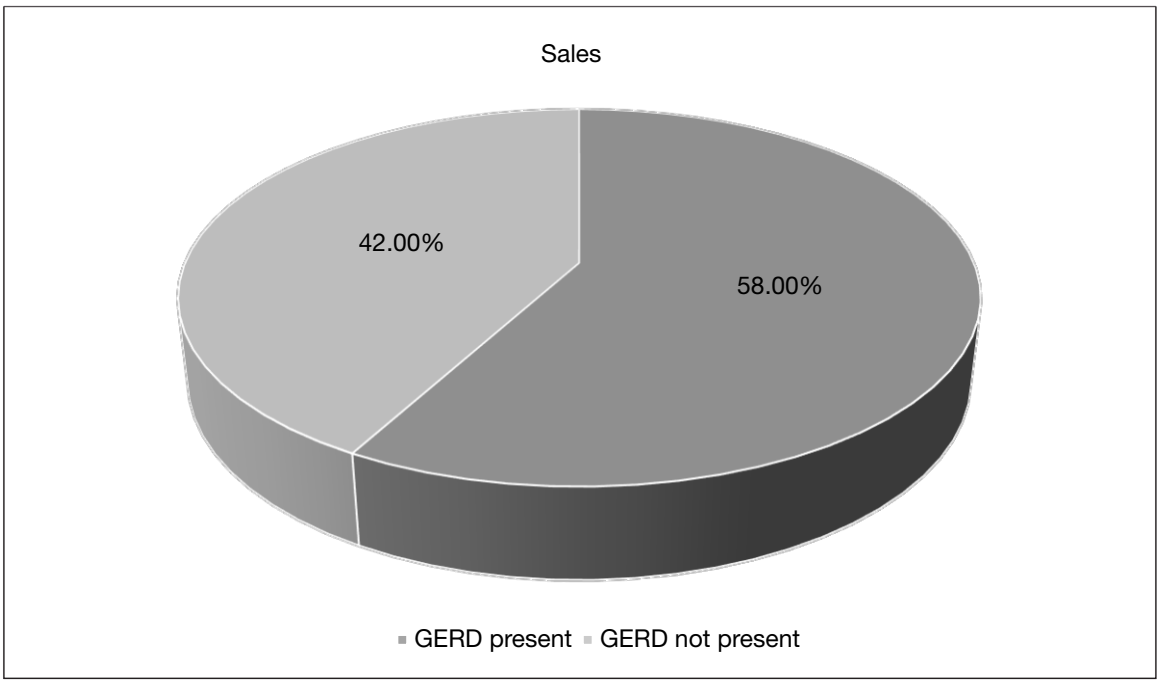

Figure 2. Occurrence of GERD comorbidity

asthma is more prevalent in females, especially post-adolescence, due to hormonal and immunological factors. The majority of patients fell into the moderate chronic asthma category, which corresponds with the findings of few other studies. These studies suggests that moderate persistent asthma is a common diagnosis in this cohort, highlighting the need for effective management strategies tailored to these individuals.[9,12,13]

Among the study participants, the prevalence of H. pylori infection was found to be 32.6% based on stool antigen tests and 41.3% based on blood tests. These figures are in line with global trends indicating variability in H. pylori prevalence depending on the geographical location and the diagnostic method used. The inverse relationship observed between H. pylori infection and asthma severity in this study, where more severe asthma cases were associated with a lower prevalence of H. pylori, raises important considerations. Specifically, 59.6% of mild asthma patients tested positive for H. pylori IgG, while only 8% of severe asthma patients had positive IgG tests. This finding is consistent with studies suggesting a protective role of H. pylori against certain allergic conditions, including asthma. For instance, Blaser et al. proposed that H. pylori might help regulate immune responses, thereby decreasing the risk of allergic diseases, including asthma. Similarly, Zhou et al. found a lower prevalence of H. pylori in patients with severe asthma compared to those with milder forms, supporting the hypothesis that H. pylori infection may modulate immune responses and reduce asthma severity.[8]

However, some studies have reported conflicting results, suggesting a positive association between H. pylori infection and the severity of asthma. For example, a study by Reibman et al. indicated that patients with more severe asthma exhibited higher rates of H. pylori infection, hypothesizing that the chronic inflammation induced by H. pylori may exacerbate airway inflammation and worsen asthma symptoms.[9] These contrasting findings highlight the complexity of the relationship between H. pylori and asthma, suggesting that various factors such as genetic predisposition, environmental influences, and different strains of H. pylori may influence the outcome.

The presence of comorbidities, such as gastroesophageal reflux disease (GERD), was also notable in this study, with 57.7% of patients reporting GERD. Previous research has shown a strong association between GERD and asthma, as acid reflux can exacerbate airway inflammation and contribute to poor asthma control. The current findings support this, as a significant portion of the study participants with moderate and severe asthma also had GERD, suggesting that management of GERD could play an essential role in improving asthma outcomes. This findings in line with the study of Tempera.[3]

In terms of asthma control, the study revealed that 50% of the patients were well-controlled, while 38% were partially controlled, and 12% were uncontrolled. This is consistent with the global asthma control rates reported by the Global Initiative for Asthma (GINA), which indicate that a significant proportion of asthmatic patients remain uncontrolled despite treatment.[15] The challenge of achieving full asthma control could be due to factors such as poor medication adherence, environmental triggers,

and the presence of comorbid conditions like GERD.

Conclusion

The recent study indicates an inverse relationship between H pylori infection and asthma, with this association remaining consistent regardless of age and gender. However, further large-scale studies are necessary to elucidate the precise mechanisms through which H pylori influences asthma, as the underlying pathways remain unclear. Understanding how H. pylori' interacts with the immune system and potentially alters T-helper cell responses could provide valuable insights. Additionally, investigating genetic factors, environmental influences, and variations in microbial exposure may enhance our comprehension of this relationship, ultimately guiding targeted interventions and treatment strategies for asthma management.

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