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ORIGINAL ARTICLE

DETERMINATION OF ASSOCIATION BETWEEN KERATOCONJUNCTIVITIS SICCA AND HELICOBACTER PYLORI INFECTIONS IN MIDDLE AGED ADULTS: CROSS SECTIONAL STUDY

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ABSTRACT

Background: *H. pylori* can lead to chronic gastritis, peptic ulcers, and gastric adenocarcinoma along with several extra gastric manifestations, such as glaucoma, other dry eye illnesses, and several autoimmune diseases. The purpose of this was to determine the association of patients' clinical aspects with dry eye disease along with *Helicobacter pylori* (H. pylori) using serology IgG antibody & urea breath test, which is a non-invasive to find out the relationship of Keratoconjunctivitis sicca and *H. pylori* chronic gastritis.

Materials & Methods: This cross-sectional, observational study was conducted at Baghdad Teaching Hospital and other medical city hospitals in Baghdad, Iraq, from October to December 2022. One hundred eyes from 50 patients were examined using physical assessments and modern techniques to detect various dry eye diseases based on the severity of sicca stages (0–3). Blood samples were collected from all patients to determine serological IgG antibody levels for chronic gastritis diagnosis, along with more specific urea breath tests for *H. pylori* detection.

Results: patients diagnosed with H. pylori-induced chronic gastritis were positive for serology IgG antibody & urea breath test IN 30 (60%) cases and negative for both tests in 20 (40%) cases from a total of 50 patients. Patients were aged between (40-60) years old with mean age 50, most patients 20(40%) belong to sicca stage 3 suffered from severe dry eye diseases along with most prevalent investigated 14(28%) positive chronic gastritis caused by *H. pylori*.

Conclusions: There is a strong relationship between the frequency of dry eye diseases in patients suffering from chronic gastritis caused by the *H. pylori* bacterium.

KEY WORDS: Conjunctivitis; Dry eye disease; Gastritis; *Helicobacter pylori*.

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INTRODUCTION

The multifactorial condition known as dry eye disease (DED) affects the ocular surface and is marked by symptoms on the ocular surface and instability of the tear film. With the advancement of science and technology, as well as lifestyle changes, the prevalence of dry eyes has been rising yearly. Dry eye irritation has increasingly becoming the leading cause of clinical consultations.[1,2] Dry eye causes irritation and can also lead to incapacitating pain and erratic vision, significantly reducing tasks like driving and reading as well as leisure time. The inability to use a computer or read for extended periods, a decreased tolerance for specific settings, and a reduced work time are all ways that dry eye affects productivity at work.[3]

There are numerous reasons for dry eyes, which frequently interact and overlap. It often coexists with oth-

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er diseases, is brought on by outside stressors, or is a side effect of medications, including over-the-counter treatments like antihistamines. Computer usage, contact lens use, low humidity, and ocular surgery are all risk factors for the illness. However, focusing on the several forms of dry eye subtypes, categorized according to risk factors and pathophysiological characteristics.[4] Along with its well-known relationship with gastrointestinal illnesses, *Helicobacter pylori* has been linked to several extra digestive diseases. Several studies conducted during the past year have revealed a connection between *H. pylori* infection and several additional digestive disorders, including cardiovascular and immunological conditions.[5,6] Numerous disorders can be linked to this bacteria, including glaucoma, central serous chorioretinopathy, ocular adnexal mucosa-related lymphoid tissue lymphoma, anterior uveitis, and blepharitis.[7]

Ongoing researches report a link between *Helicobacter pylori* infection and eye problems. It has been proposed that this bacterium may have a role in chronic eye conditions such as blepharitis, glaucoma, central serous chorioretinopathy, and others. This investigation aimed to determine if *Helicobacter pylori* infection and dry eye diseases share a pathogenic link and are responsible for the inflammation of human eyes, despite the mechanisms by which this interaction occurs are currently unclear.[8]

Despite the growing evidence of *H. pylori*'s systemic impact, there is a lack of comprehensive research evaluating its role in the pathogenesis of dry eye disease. Most studies focus on gastrointestinal and cardiovascular implications, leaving ocular manifestations understudied. Given the increasing prevalence of both DED and *H. pylori* infection, understanding their potential pathogenic link is critical. This study addressed the gap by exploring whether *H. pylori* contribute with Keratoconjunctivitis sicca providing novel insights into its pathophysiology. The findings from this research could have significant clinical implications for ophthalmologists, gastroenterologists, and primary care physicians. By identifying *H. pylori* as a potential risk factor for DED, targeted screening and eradication therapies may improve patient outcomes and reduce the burden of chronic dry eye disease.

MATERIALS AND METHODS

The study was conducted in accordance with ethical guidelines outlined by dental college, Ibn Sina university of medical and pharmaceutical sciences. All these samples were collected and diagnosed in laboratories & eyes consultant clinics of Baghdad Teaching Hospital and other hospitals of medical cities from October to December 2022. One hundred eye swab specimens were collected from 50 patients with different dry eye diseases & 50 blood samples collected from those patients who suffered from chronic gastritis diagnosed with rapid serological IgG antibody test to investigate Helicobacter *pylori* bacteria as well as urea breath test were done to all patients as a confirmatory test for these bacteria. Also, doctors did endoscopies on all patients to investigate the frequency of chronic gastritis caused by targeted *H. pylori* bacteria.

Patients included in this study were, suffering from chronic gastritis with severe abdominal pain who were diagnosed with *H. Pylori* bacteria and different dry eye diseases, aged from 40-60 years and who were not receiving any treatment. Children, patients taking any medications for the last three months, patients with slight abdominal pain not diagnosed as gastritis, and those subjected to any other bacterial or viral infections of the eyes were excluded.

Bacterial Infections Diagnosis

IgG antibody test for *H. pylori:* The Babio® Helicobacter pylori (H. pylori) IgG Antibody Test Kit was used to detect IgG antibodies against *H. pylori* in serum samples. The test was performed according to the manufacturer's instructions. Venous blood was collected, allowed to clot, and centrifuged to obtain serum. A total of 10 μL of serum was applied to the sample well of the Babio® *H. pylori* IgG Test Cassette, followed by the addition of 2–3 drops of the buffer solution provided with the kit. The test cassette was left undisturbed at room temperature for 10–15 minutes to allow for result development. Results were interpreted as positive if two colored bands appeared (test line and control line), negative if only one colored band appeared (control line), and invalid if no control line appeared, in which case the test was repeated. The internal control on the cassette ensured the validity of the results. All steps were carried out meticulously to comply with the manufacturer's protocol and ensure the accuracy of the findings. The babio antibody kit test should only be used to assess people exhibiting clinical symptoms and indications of gastrointestinal illness; it is not meant to be used with asymptomatic patients. A positive test result makes it impossible to differentiate between *H. pylori* colonization and active infection. A positive test results in chronic gastritis and solely shows the existence of IgG antibodies to *H. pylori*. A negative result means that there is either no IgG antibody to *H. pylori* present or that the amount is too low to be identified by the assay.[9] Figure 1.

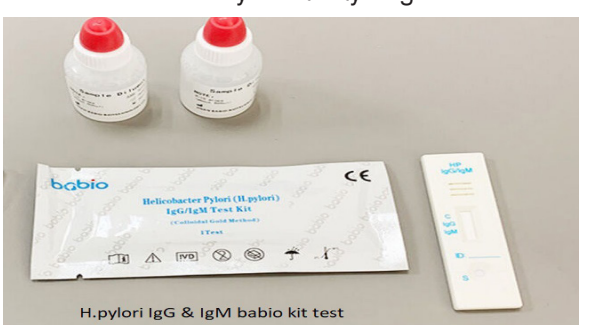

Fig. 1: *H. pylori* IgG & IgM babio antibody kit test

Urea breathing test: Breathing into a bag that resembles a balloon is part of the *H. pylori* breath test. *H. pylori* generates an enzyme called urease that breaks down urea into ammonia and carbon dioxide, making it a simple and safe technique to diagnose *H. pylori* infection. A urea pill is taken during the test, and the amount of carbon dioxide exhaled is calculated. This suggests that the stomach has *H. pylori.*[10] figure 2.

Fig. 2: Heliforce urea breath test kit to diagnose *H. pylori* bacterium

Gastroscopy: It is the examination that can establish gastritis. During this examination, a doctor inserts a small, flexible telescope down your throat to see inside your stomach. They can see any infection or other abnormalities, such as a stomach ulcer. Not every person with gastritis symptoms requires a referral for an endoscopy. Small samples (biopsies) of the stomach lining are often obtained during an endoscopy. These were delivered to the lab to be examined under a microscope to check for bacterial infection.

Dry eyes examination: The doctor must be guided by careful and thorough exams when assessing and evaluating dry eye patients:

Slit-lamp biomicroscopy: A doctor should assess the anatomical features of the lid using slit-lamp biomicroscopy, particularly any changes to the lid margins and eyelashes. Hyperaemia, telangiectasia, thickening, scarring, keratinization, ulceration, tear debris, abnormalities of the meibomian orifices, metaplasia, and the nature of expressed meibomian secretions are among the changes to the lid margins; changes to the eyelashes include misdirection (trichiasis), malposition (distichiasis), encrustations, collarettes, and districts.[11]

Schirmer's test: When there is a suspicion of insufficient tear secretion, the Schirmer's test is the most often used examination. Schirmer, who initially proposed the test in 1903, was honored with the test's name. In essence, the test assesses total (primary and reflex) tear secretion when performed without anesthesia, but when performed under anesthesia, it only measures essential tear production. This is still the most typical test for determining the number of tears. Schirmer I and Schirmer II tests can be used to categorize it.[12,13]

RESULTS

All 50 patients who suffered from mild to severe dry eye diseases (sicca) were categorized into four stages from 0 to stage 3, according to the degree of the dry eye affected when examined physically and by slit microscopy, our results revealed that 20 patients belonging to stage 3 with 40% of patients suffering from chronic severe dry eye disturbances as shown in Table :1. The Table :2, show that out of 50 patients, 30 (60%) had positive *H. pylori*.

Table 1: Patients distributed according to Sicca stage classification

Sicca stage	Signs	No. of dry eye patients
Stage 0	No dry eye	2(4%)
Stage 1	Mild	12(24%)
Stage 2	Moderate	16(32%)
Stage 3	Severe sicca	20(40%)
Total		50(100%)

Table 2: Diagnosis of *H. pylori* bacteria in all sicca patients

Tests	Positive *H. pylori*	Negative *H. pylori*	Total patients
IgG Ab test	30(60%)	20(40%)	50
Urea breath test	30(60%)	20(40%)	50
Total	30 (60%)	20(40%)	100

The severity of sicca stages in patients with chronic gastritis determines the association between the frequency of dry eye disease and *H. pylori*-positive chronic gastritis. In our study, the strongest association was observed in sicca stage 3, where approximately 40% of patients had severe dry eye complications, and 28% of patients experienced chronic gastritis with intense abdominal pain. The second most common stage was sicca stage 2, which included 32% of patients with dry eye disease, along with roughly 18% of patients who reported moderate abdominal pain. To compare the prevalence of *H. pylori* infection across different groups, appropriate statistical analyses were conducted. Categorical variables were compared using the Chi-

square test. A 95% confidence interval (CI) was used to assess the precision of the estimates. All statistical analyses were performed using SPSS version 26.0 software (IBM Corporation, Armonk, NY, USA), with a significance level of $p < 0.05$ considered statistically significant.

Table 3: patients distributed according to frequency of gastritis & dry eye

Sicca stage	Sicca No.	*H. pylori* detected	p-value
Stage 0	2(4%)	0	0.03 NS*
Stage 1	12(24%)	7(14%)	
Stage 2	16(32%)	9(18%)	
Stage 3	20(40%)	14(28%)	
Total	50(100%)	30(60%)	

*p-value p<0.05considered statistically non-significant (NS)

DISCUSSION

A breakdown of the tear film's equilibrium results in the multifactorial ocular surface disorder known as dry eye disease (DED), also referred to as dry eye syndrome (DES), keratoconjunctivitis sicca (KCS), and keratitis sicca. Numerous techniques and procedures have been developed to evaluate DED for both initial diagnosis and regular follow-up.[14,15]

In our study, 20 patients (40%) belonged to stage 3, 16 patients (32%) belonged to stage 2, 12 patients (24%) were in stage 1, and only 2 patients (4%) were classified under stage 0 with no sicca signs. These results align with the findings of L. Blomberg (2004), where most patients (19 out of 53; 35.8%) belonged to sicca stage 1, while the remaining patients were distributed across stages 2, 3, and 4.[16]

Regarding the frequency of *Helicobacter pylori* (*H. pylori*) infection, which causes chronic gastritis, our results showed a non-significant statistical correlation between chronic gastritis and sicca stages. However, a notable association was observed in specific stages. In sicca stage 3, 14 out of 50 patients (28%) had chronic gastritis and experienced intense abdominal pain. In sicca stage 2, 9 out of 50 patients (18%) reported moderate abdominal pain. These findings are consistent with the results of JM Kim et al., who reported that 69.7% of seropositive *H. pylori*-infected patients had anterior uveitis.[17]

Furthermore, the relationship between *H. pylori* infection and dry eye diseases in our study aligns with the findings of Michael Doulberis, who demonstrated a significant correlation (with a 95% confidence interval) between active *H. pylori* infection and glaucoma.[18] Similarly, our study concurs with Jannis Kountouras, who detected *H. pylori* bacteria in 88% of glaucoma patients, with 83% of those cases showing improvement after *H. pylori* eradication therapy.[19]

Finally, a larger sample size would enhance the statistical power and generalizability of the findings. Future studies should aim to include a larger, more diverse cohort to verify the findings and explore the potential mechanisms behind the observed associations. Longitudinal studies could provide more insight into the temporal relationship between H. pylori infection and the progression of dry eye disease.

CONCLUSIONS

Our study results conclude, there is a significant correlation exists between the frequency of *H. pylori* infection in patients with different dry eye diseases (sicca). There is a solid relationship between chronic gastritis of patients diagnosed with *H. pylori* and dry eye. These bacteria can trigger autoimmunity represented by autoantigens and inflammatory cytokines that affect different sites in the body, like eyes and their content accessories.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	DBI, SKI
Acquisition, Analysis or Interpretation of Data:	DBI, SKI, SAJ
Manuscript Writing & Approval:	DBI, SKI, SAJ

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.