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Histopathological evaluation of H. pylori and brucellosis relationship

Hakan Sezgin Sayiner[1], Sezgin Barutcu[2], Sefer Aslan[3], Bilge Aydın Turk[4], Aysun Gurbuzcan[5], Sadik Akgun[6]
[1] Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Adıyaman University, Adıyaman
[2] Department of Gastroenterology, Faculty of Medicine, Gaziantep University, Gaziantep
[3] Department of İnternal Diseases, Adiyaman Education Research Hospital, Adıyaman
[4] Department of Pathology, Faculty of Medicine, Adıyaman University, Adıyaman
[5] Department of İnternal Diseases, Harran State Hospital, Sanliurfa
[6] Department of Microbiology, Faculty of Medicine, Adıyaman University, Adıyaman, Turkey

Abstract
Aim: Helicobacter pylori (HP) is a common infection that can increase the pH of the stomach. Situations in which stomach protection is removed cause an increase in susceptibility to brucellosis.
Material and Methods: Pathological examination results of our patients who underwent gastroscopy and gastric biopsy with the diagnosis of retrospective brucellosis and the control group, who were not diagnosed with brucellosis, were included in the study. In the period from 01.07.2012 to 01.07.2019, the pathology investigation results of 39 patients diagnosed with brucellosis through Brucella agglutination or with 1/160 and above on Brucella coombs agglutination test were compared with 113 control group patients.
Results: There was no significant difference (P <0,185) in HP positivity between the two groups. A significant decrease (P<0,007) was determined in terms of lymphoid aggregation between the brucellosis HP- positive and the control group with HP- positive patients.
Discussion: HP was not found to be significant as a facilitating factor in terms of brucellosis, however, a negative correlation was determined in terms of lymphoid aggregation (MALT lymphoma precursor) in the brucellosis patient group.

Keywords
Brucellosis, H. pylori, Intestinal Metaplasia, Lymphoid Aggregate

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Corresponding Author: Sefer Aslan, Department of Internal Medicine, Adıyaman Training and Research Hospital, 02100, Adıyaman, Turkey.
E-mail: drseferaslan02@hotmail.com P: +90 505 220 27 03
Corresponding Author ORCID ID: https://orcid.org/0000-0002-5926-5375

Introduction

H. pylori (HP) is one of the most common infections in the world that can raise gastric pH level and infects approximately 50% of the world's population and plays a causal role in ulcer disease and gastric cancer [1,2]. Stomach fluid provides protection through pH level, but the use of antacid drugs or H2 receptor blockers that remove the protective feature of the stomach increases the transmission of food-borne bacteria and the possibility of infection [3].

Stomach fluid provides protection due to the pH level, but the lack of protective properties for various reasons increases the transmission of foodborne bacteria and the possibility of infection [3]. Brucellosis is a zoonotic disease and causes disease in humans with milk and dairy products, particularly in endemic areas [4,5]. Significant positivity was found in a study comparing HP positivity rates of patients with brucellosis with those in the normal population [6]. Contrary to this finding, another study found a reduction in HP in patients with brucellosis [7].

In our study, patients who underwent gastroscopy and gastric biopsy, which we retrospectively followed up with the diagnosis of brucellosis, were compared with patients who underwent gastroscopy for dyspepsia due to the absence of concomitant disease. In this study, we aimed to investigate the relationship between HP and patients with brucellosis.

Material and Methods

Our study was started after obtaining ethical approval from the Ethics Department of Adıyaman University Faculty of Medicine with the date of 21.05.2019 and the decision number 2019/4-14.

Patients

In this study, retrospectively, 39 patients over 18 years of age who were diagnosed with Brucella agglutination or Brucella coombs agglutination 1/160 and above who had complaints such as joint pain, night sweating in the period from 01.07.2012 to 01.07.2019 were included in the Infectious Diseases outpatient clinic. Patients who were admitted to the Gastroenterology outpatient clinic during the diagnosis period or in the last 6 months due to dyspepsia, who had no other comorbid diseases, and who received two biopsies from the corpus and antrum were considered. In this process, patients in the control group were admitted to the gastroenterology outpatient clinic and were selected from 113 patients without brucellosis and comorbid disease who underwent gastroscopy for dyspepsia. All the cases involved in this study were informed about the study and informed consent was obtained.

All patients were evaluated using Hematoxylene-Eosin, PAS-AB and Giemza histochemical staining (Rosche). The Sydney classification was used to rate gastritis activity, H.pylori density, atrophy, intestinal metaplasia and lymphoid aggregate; 0 = none, 1 = mild, 2 = medium, 3 = severe. In the classification of gastritis according to Sydney system, it is aimed to combine topographic, morphological and etiological information in a diagram. This makes the clinical diagnosis more efficient and useful [8]. The Sydney system also emphasizes the importance of topographic differences in the distribution of gastritis. Acute, chronic, and special forms of gastritis are defined in the classification of chronic gastritis. The most important feature of this system is the grading of changes in the gastric mucosa in terms of the five main histological features (chronic inflammation, neutrophil activity, glandular atrophy, intestinal metaplasia and HP density [8]. In the classification of gastritis according to Sydney system, it is aimed to combine topographic, morphological and etiological information in a diagram. This makes the clinical diagnosis more efficient and useful.

The criteria for inclusion in the study

-Age 18 or over

-Gastroscopy and gastric biopsy performed

-Brucella agglutination test and/or Brucella coombs agglutination test results 1/160 and above

-Receiving brucellosis treatment or treatment planned

-No previous HP treatment

The results of the participants who had positive Brucella agglutination test and had gastric biopsy by gastroscopy and the results of the control group who underwent gastric biopsy by gastroscopy were compared.

Devices used to analyze parameters

-Biopsy Results were evaluated using Olympus BX53 light microscope.

-Microscopic photographs were taken with Olympus DP73 camera

Statistical Method

Data were analyzed using SPSS (Statistical Package for Social Sciences Statistical Software) version 23.0 (SPSS, Inc., Chicago, IL). Descriptive statistics were carried out. The Chi-square test was used to evaluate categorical data. The Kolmogorov-Smirnov test was carried out to determine whether continuous data showed normal distribution. Data with a normal distribution were expressed as mean ± standard deviation and evaluated using Independent Two Sample T test, data without normal distribution were expressed as median (minimum-maximum) and evaluated with the Man-Witney U test. $P<0.05$ was considered significant. We declared that the study was approved by the ethics committee.

Results

In our study, 39 cases (F: 25 M: 14) from the brucellosis (+) group and 113 cases (F: 59 M: 54) from the control group were evaluated (Table 1).

No significant difference between brucellosis and control group in terms of age, gender and HP was determined.

In patients with brucellosis, there was no difference in HP (+) (Figure 1) and HP (-) groups in terms of lymphoid aggregate, intestinal metaplasia and inflammation, while a significant difference in activation ($P <0.011$) was determined (Figure 2).

HP (-) groups in terms of intestinal metaplasia, while the difference was significant in terms of inflammation ($P <0.005$),

Table 1. Distribution of patients included in the study

	H.P (+)	H.P (-)	Total
Brucella (+)	21	18	39
Brucella (-)	47	66	113
Total	68	84	152

Table 2. Comparison of intestinal metaplasia and lymphoid aggregate positivity in the groups with H. pylori (+) and H. pylori (-) in the control group

	H. pylori positive (n=47)	H. pylori negative (n=66)	P
Activation	35	18	<0,001*
Inflammation	47	55	0,005*
Intestinal metaplasia	8	10	0.816
Lenfoid agregat	32	18	<0,001*

Table 3. Comparison of the pathology results of the Brucella positive group and the control group

	Brucella group (n=39)	Control Group (n=113)	P
Activation	22	53	0.260
Inflammation	37	102	0.198
Intestinal metaplasia	4	18	0.442
Lymphoid Aggregate	9	50	0,022*

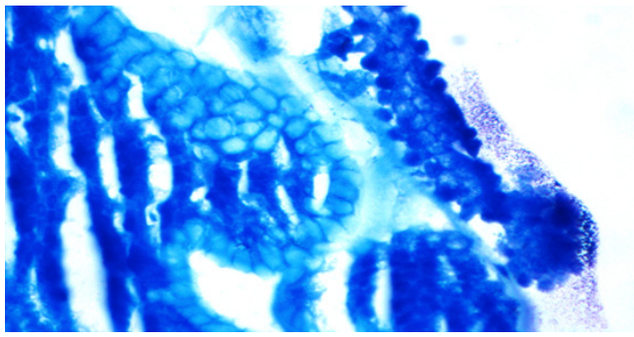


Figure 1. H.pylori in superficial mucus at 20X magnification with Giemza dye in Brucella group.

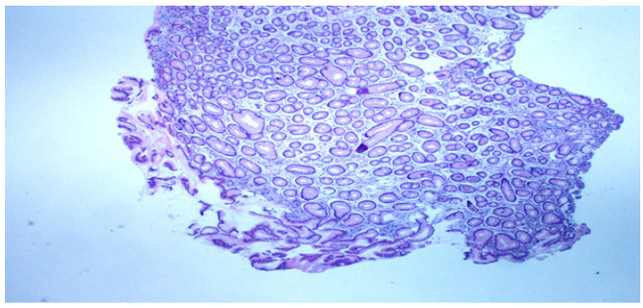


Figure 2. 4X Hematoxylin-eosin stained H.pylori positive case in Brucella group does not contain lymphoid aggregate

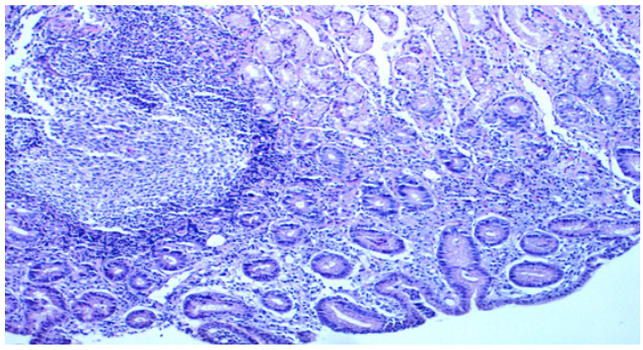


Figure 3. H.pylori positive case with Hematoxylin eosin stained 4X magnification with germinal center marked lymphoid aggregate in the control group

Activation (P <0.001) and lymphoid aggregation (P <0.001). (Table 2). (Figure 3).

In the comparison of the pathology results of the brucellosis group (n: 39) and the control group (n: 113),there was no significant difference in terms of activation, inflammation and intestinal metaplasia, however a significant difference in terms of lymphoid aggregate was determined (P <0.022) (Table 3).

In the comparison of pathology findings of those who are brucellosis and control group in the HP positive group, a significant difference in terms of lymphoid aggregate was determined. (P<0.007)

In the comparison of pathology findings of patients with brucellosis and the control group in the HP negative group, no difference was determined in terms of lymphoid aggregate, intestinal metaplasia, activation and inflammation.

Discussion

Because HP infection is very common and affects gastric pH level, many studies have been conducted on the relationship between HP infection and other infectious and non- infectious diseases. However, studies related to brucellosis are few. In a study conducted by Afrasiabian et al., HP positivity rates were investigated in the normal population with those who had brucellosis and significant positivity was found [6].

In the same study, HP was positive in 30 (30%) the case group and 27 (13%) patients in the control group. In addition, the prevalence of positive IgM antibody to HP in the case group was 2.74 times higher than in the control group. (p = 0.001)

In the multivariate analysis, it was found that there was a significant relationship between brucellosis and HP positive IgM antibody (p = 0.001) and the prevalence of IgM antibody against HP in people infected with brucellosis was found to be higher [6].

In a study by Esen R. et al., it was determined that the prevalence of HP decreased in patients with brucellosis compared to the control group (P <0.001), and a negative correlation between HP infection and brucellosis infection may be considered [7].

In our study, unlike previous studies, an evaluation was made according to histopathological results, and no significant difference was determined in their comparison in terms of HP, with 53.8% in patients with brucellosis, and 41.6% in the control group (p<0,185).

HP is a bacterial pathogen that causes gastroduodenal inflammation and can lead to gastric and duodenal ulcers and atrophic gastritis and even stomach cancer [9-11].

In the study of Safaan et al., HP infection was significantly more associated with each of the follicular gastritis and lymphoid aggregates compared to normal samples (P < 0.0001) [12].

In a study carried out by Bashiri et al., a significant correlation was determined between gastric lymphoid follicle and aggregate formation to HP infection. Lymphoid follicles were detected more frequently in HP-positive patients (59%) compared to HP-negative cases (3%).

In the same study, the prevalence of lymphoid follicles and aggregates as precursors of MALT lymphoma was evaluated [13].

The close relationship between HP infection and gastric MALT lymphoma is well known, especially due to the regression of

gastric MALT lymphoma with the eradication of HP infection [14-16].

In our study, we found a significantly lower rate of lymphoid aggregation in brucellosis patients in the comparison of the brucellosis group and control group histopathology results (p<0,022).

In the comparison of pathology findings of patients with brucellosis and the control group in the HP positive group, we found a significantly lower rate of lymphoid aggregation in Brucellosis patients (P<0,007).

In our study, the pathology findings of HP positive people were compared according to brucellosis and control group results. Unlike previous studies, an evaluation was made based on histopathological results. The weak point of this study may be that the number of patients with brucellosis is low and when the diagnosis of brucellosis is made, the pathology result and stomach biopsy cannot be performed simultaneously.

Conclusion

While HP increases susceptibility to infections by increasing stomach acid pH, in our histopathological study, it was shown that the presence of HP is not a risk factor for brucellosis infection. In addition, a negative correlation was found in terms of lymphoid aggregate in patients with HP who had brucellosis. Since lymphoid aggregate is considered to be a precursor to gastric MALT lymphoma, we believe that it may reduce the risk of gastric Maltoma development. The limitation of this study was the low number of cases. Studies with larger case numbers are needed to support this negative correlation.

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Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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