*Turk J Gastroenterol 2002; 13 (3): 154-158*

# Relationship between gastritis severity, Helicobacter pylori intensity and mast cell density in the antrum and corpus

## Antrum ve korpusda gastritis şiddeti, Helicobacter pylori yükü ve mast hücre yoğunluğu arasındaki ilişki

Fazilet KAYASELÇUK[1], Ender SERİN[2], Yüksel GÜMÜRDÜLÜ[2], Sema BİRCAN[1], İlhan TUNCER[1]

*Başkent University, Adana Medical Center, Departments of Pathology[1] and Gastroenterology[2], Adana*

***Background/aims:*** *The aim of this study was to investigate the relationship between mast cell density, Helicobacter pylori intensity and histopathological severity of gastritis in the corpus and antrum mucosa.* ***Methods:*** *The study included 59 Helicobacter pylori-positive and 20 Helicobacter pylori-negative patients. All cases underwent endoscopy, and biopsies were obtained for the evaluation of Helicobacter pylori and histopathological examination. All biopsies were evaluated according to the Sydney system and mast cell density in both the corpus and antrum mucosa was analyzed by modified Giemsa stain. Spearman's correlation test was used to determine the relationship between mast cell density and other histopathological parameters. The comparision of mast cell density between H. pylori positive and negative groups was analysed by Mann Whitney U test.* ***Results:*** *Both in the antrum and the corpus, mast cell density was significantly higher in the Helicobacter pylori-positive group than in the Helicobacter pylori-negative group (p<0.001). The higher mast cell distribution was correlated with increased inflammation, activity and Helicobacter pylori in the antrum and corpus (p<0.001). No relationship was found between mast cell distribution and intestinal metaplasia or atrophy.* ***Conclusions:*** *In the light of the results of our study, mast cells may play a role in the development of Helicobacter pylori gastritis.*

**Key words:** Gastritis, mast cell, Helicobacter pylori.

***Amaç:*** *Bu çalışmanın amacı korpus ve antrum mukozasında gastritis şiddeti, Helicobacter pylori yükü ve mast hücre dansitesi arasındaki ilişkiyi araştırmakdır.* ***Yöntem:*** *Bu çalışmaya 59 Helicobacter pylori- pozitif ve 20 Helicobacter pylori- negatif hasta alınmıştır. Tüm vakalara endoskopi uygulandı ve histopatolojik tanı için antrum ve korpusdan biyopsiler alındı. Tüm biyopsiler Sydney sistemine göre değerlendirildi ve modifiye Giemsa boyasında mast hücre yoğunluğu ölçüldü. İstatistik analiz için Spearman's korelasyonu ve Mann Whitney U testi kullanıldı.* ***Bulgular:*** *Antrum ve korpusda, mast hücre yoğunluğu Helicobacter pylori –pozitif grupta negatif olanlara gore anlamlı derecede yüksektir (p<0.001). Mast hücre dağılımı antrum ve korpusda inflamasyon, aktivite indeksi ve Helicobacter pylori yoğunluğu ile anlamlı korelasyon göstermektedir. İnflamasyonun varlığı ve yokluğu ile mast hücre dağılımı arasındaki fark istatistiksel olarak anlamlıdır (p<0.001). Atrofi ve intestinal metaplazi ile mast hücre dağılımı arasında ilişki bulunamamıştır.* ***Sonuçlar:*** *Bu çalışmanın sonuçlarına göre mast hücreleri Helicobacter pylori gastritinin gelişiminde midenin farklı bölgelerinde benzer rol oynamaktadır.*

Anahtar kelimeler: Gastritis, mast hücre, Helicobacter pylori.

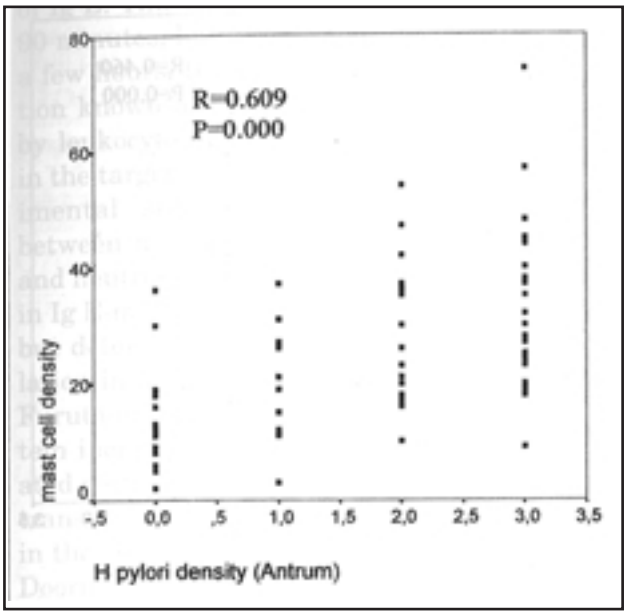
## INTRODUCTION

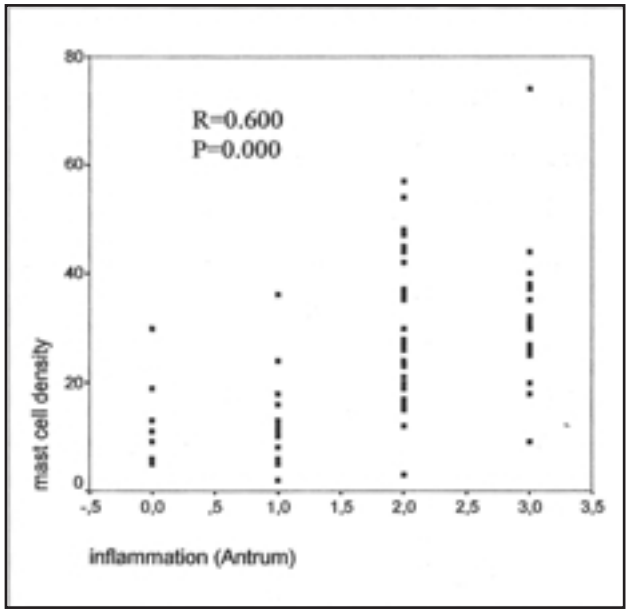
Helicobacter pylori (H. pylori) is the most frequent and significant factor in the etiology of chronic active gastritis, in addition to being implicated in various illnesses such as peptic ulcer, gastric adenocarcinoma, and lymphoma (1,2) In H. pylori gastritis, the gastric mucosa is subject to infiltration by neutrophilic leukocytes, lymphocytes and plasma cells. This inflammation and other mucosal changes may be classified by using the Sydney system, in which five morphological variables (inflammation, activity, atrophy, intestinal metaplasia and H. pylori) are graded according to the 30% rule (1).

Mast cells originate from bone marrow, which plays a role in the onset and regulation of inflammation. These cells mature within tissue, and con-

**Address for correspondence:** Dr. Fazilet KAYASELÇUK
Başkent Üniversitesi, Tıp Fakültesi, Adana Araştırma ve Uygulama Hastanesi,Dadaloğlu mah. Serinevler 39 sok. Yüreğir/Adana
Tel: 0322 3217272/1157 E mail: faziletks @ baskent-adn.edu.tr

**Manuscript received:** 10.1.2002 **Accepted:** 3.7.2002



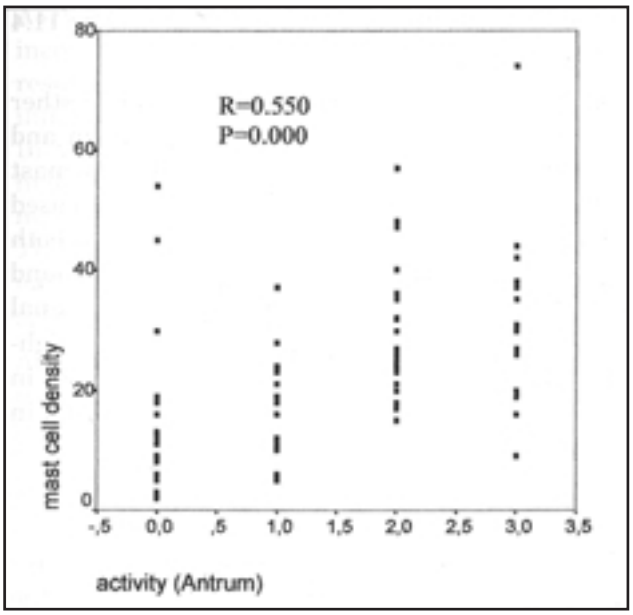




**Figure 1.** The relationship between mast cell density and inflammation, activity index and H. pylori intensity in the antrum

tain cytoplasmic granules, which are involved in allergic reactions associated with Ig E (2,3). Mast cells store and release a number of chemical mediators such as heparin, histamine, eosinophilic chemotactic factor, and chondroitin sulfate, as well as prostaglandin D2, leukotriene $C_4$, $D_4$, $E_4$, IL-4,5,6,8 and tumor necrosis factor alpha (TNF-α) cytokines (2-9). Gastric mucosa levels of promoter cytokines such as IL-1,6,8 and TNF-α have been shown to increase at the onset and course of inflammation of the stomach (1,5,10).

The purpose of this study was to investigate the relationship between mast cell density and histopathological scores of gastritis in the antrum and corpus mucosa.

## MATERIALS AND METHODS

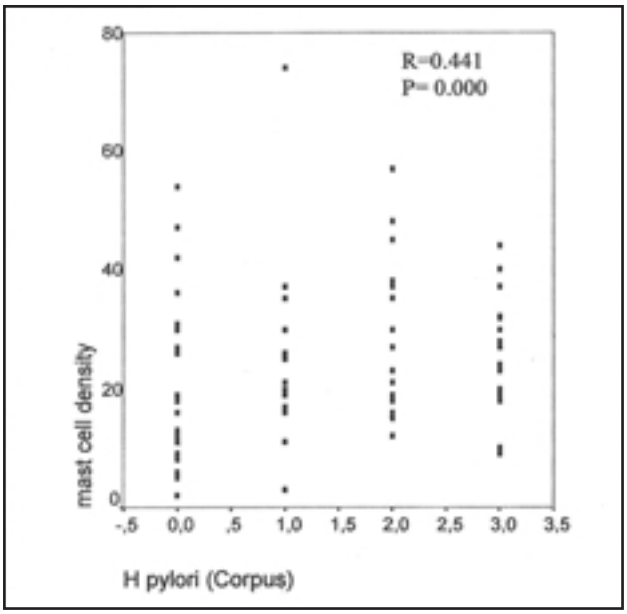
Antrum and corpus biopsies from 59 H. pylori-positive and 20 H. pylori-negative patients were selected from the pathology archive at Baskent University Hospital, Adana. The hematoxylin-eosin stain, mucicarmine, PAS-Alcian blue and modified Giemsa-stained preparations of each patient were reviewed and the values obtained by the Sydney system

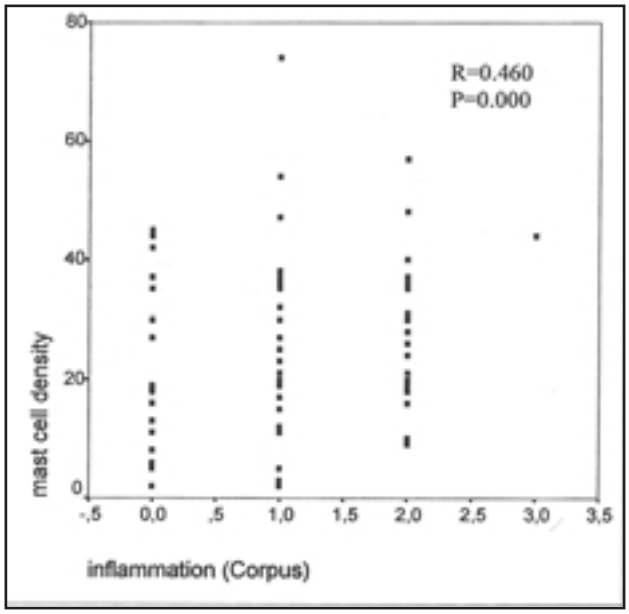
were recorded. The epithelial and submucosal mast cells were counted by modified giemsa stain in all patients at x400 magnification in five regions. Statistical analysis of the results was carried out by the Spearman's correlation and Mann Whitney U test with SPSSPC statistical software.

## RESULTS

The mean age of the 79 patients (21 men, 58 women) included in the study was 46.4 ±14.2 years.

Both in the antrum and the corpus, mast cell density was significantly higher in the H. pylori-posi-



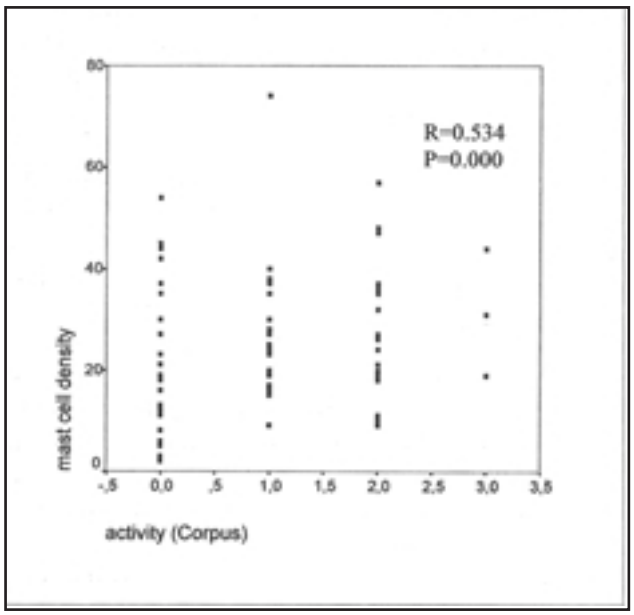




**Figure 2.** Relationships between mast cell density and inflammation, activation index and H. pylori intensity in the corpus.

tive than the H. pylori negative group (28.6 ± 13.0 vs 11.4 ± 9.0 and 18.2 ± 8.2 vs 9.7 ± 7.8, respectively; p<0,001).

We compared the mast cell densities in patients with mild activity and no activity based on neutrophilic accumulation in order to determine the role of mast cells during active inflammation. The mean mast cell density was higher in patients with mild activity than in those with none but the difference was not significant (28.6 ± 13.0 vs 11.4 ± 9.0 , p=0.06).

Relationships between mast cell density and other histopathological parameters in the antrum and corpus are shown in Figure 1-2. The higher mast cell distribution was correlated with increased inflammation, activity, and H. pylori in both antrum and corpus. No relationship was found between mast cell distribution and intestinal metaplasia or atrophy. Nonetheless, slightly higher values for mast cells were determined in patients with atrophy or intestinal metaplasia in the antrum and corpus.

## DISCUSSION

Throughout the world, the rate of Helicobacter pylori infection increases with age (1). In the stomach, it induces significant cellular and humoral immune responses via the antigenic stimulus of mucosal monocytes and T-lymphocytes. Various cytokines, proteases, prostaglandins, and reactive $O_2$ metabolites released from these inflammatory cells increase the endothelial adhesion of neutrophilic leukocytes. Local humoral mediators such as mucosal Ig A lead to leukocyte accumulation, and the degranulation of eosinophilic leukocytes brings about the secretion of various cytokines, contributing to the progress of tissue damage (1).

Mast cells are the most important cells in acute allergic reactions occurring through the mediation

of Ig E. This early reaction generally ends within 90 minutes, but in the event of recurrence within a few hours, there may be an inflammatory reaction known as late-phase reaction, characterized by leukocyte and mononuclear cell accumulation in the target tissue (2). Wershil et al., in an experimental study, demonstrated a relationship between mast cell degranulation in the stomach and neutrophilic and mononuclear cell infiltration in Ig E-mediated gastric reactions in normal mice, but determined no significant leukocyte accumulation in mast cell deficient $Kit^{W}/Kit^{W\text{-}v}$ mice (3). Furuta et al. showed that TNF-α mRNA and protein increase in inflamed gastric tissue is associated with Ig E (4). Mast cells are necessary in the transcription of TNF-α which is released by cells in the stomach(4). In a study with CD1 mice, van Doorn et al. found not only a significant increase in T-lymphocytes in the stomach beginning in the $3^{rd}$ or $4^{th}$ week and resulting from type I (Cag A+/Vac A+) H. pylori infection, but also an increase in mast cells in 50% of the mice (5). These results suggest that mast cells play a role in the inflammatory reaction in the course of gastritis. In the present study, there was a tendency for higher mast cell density even in patients with mild activity compared to those with no activity. This may be concordant with Furuta et al.'s opinion that mast cells are mediators in neutrophil accumulation.

Although the role of mast cells in chronic inflammatory intestinal illnesses has not been completely explained, studies in which increased mast cell count has been shown during the active phase of disease support continuous mast cell activity in these illnesses (2,6,7). Nonetheless, the events initiating mast cell degranulation in the stomach or the colon are not completely clear. In addition to allergic stimuli, luminal invasive bacteria such as H. pylori and neuropeptides can initiate degranulation with nonallergic stimuli (2). The study of Nakajima et al., demonstrated that mast cell density was higher in the gastric mucosa of patients with gastritis than in healthy subjects, and higher in patients with H. pylori + peptic ulcer disease than in those with gastritis. They also observed mast cell degranulation by electron microscope in patients with H. pylori (positive) peptic ulcus disease (8). In a number of clinical studies, mast cell density has been found to be different in H. pylori-negative and positive cases of gastritis (8-12). The results of the present study are in agreement with the literature.

In this study, we observed increased mast cell activity during H. pylori gastritis as in other recent studies. However, our data is not sufficient to comment on whether H. pylori affects mast cell density directly or whether the inflammation secondary to H. pylori infection is responsible for the increase in gastric mucosa mast cell number since H.pylori density is a well estabalished factor in the severity of inflammation (1). We determined a significant correlation between H.pylori density, severity of inflammation and activity and mast cell density, in both antrum and corpus. This suggests that mast cells assume similar functions in different regions of the stomach in the development of H. pylori gastritis and that the luminal binding of H. pylori in both mucosa may initiate mast cell degranulation by a nonallergic stimulus. In the present study, the difference between the mast cell density in the antrum and that in the corpus was significant for all three variables. These results can be explained by inflammation, activity and H. pylori intensity generally having high values such as 2-3 in the antrum and values of 1-2 in the corpus.

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