

Research Article

What do the White Spots in the Second Part of Duodenum Tell Us?

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Abstract: Objective: The underlying conditions/diseases of scattered white spots in the duodenum are rather not very clear in the literature. We aimed to find out whether *Helicobacter pylori*, diabetes mellitus or inflammation has an impact on the presence of duodenal white spots.

Materials & Methods: We included all patients who underwent endoscopy between the time-period 2007-2017 in the Endoscopy Unit of Cumhuriyet University and had scattered white spots in the duodenum. Our control group was formed by randomly selected patients who underwent endoscopy at the same time period in whom duodenal biopsy was taken. The demographic data of both the patient and the control group, the presence of diabetes, endoscopic and histological diagnoses, neutrophil lymphocyte ratio, thrombocyte lymphocyte ratio, mean platelet volume and erythrocyte distribution width were obtained from the computer system of the hospital in detail.

Results: Peptic ulcer disease was found to be significantly more prevalent in patients with white spots than the control group. We could not find any difference between the patient and control groups by means of either neutrophil lymphocyte ratio, platelet lymphocyte ratio, mean platelet volume and erythrocyte distribution width, *Helicobacter pylori*, positivity or presence of diabetes.

Conclusion: Both diabetes mellitus and *H. pylori* are causes of systemic inflammation. In our study, we evaluated whether patients with white spots were associated with systemic inflammation by looking at popular inflammation markers. We could not find any difference between the two groups in terms of these markers.

Keywords: White spots, Duodenum, Diabetes mellitus, Systemic inflammation, Lymphangiectasia, Giardiasis, Chronic nonspecific duodenitis.

INTRODUCTION

The scattered white spots on the duodenum is a relatively rare endoscopic finding during upper gastrointestinal endoscopy [1]. There is no exact definition of white spots in the literature, it is a visual finding identified at the endoscopy procedure. Although its pathogenesis is not known, there are publications showing that these white spots have been seen in patients with giardia, lymphangiectasia and chronic nonspecific duodenitis [2-4]. There is a great variation among studies. The other unknown area about duodenal white spots is the issue of underlying conditions. Both *Helicobacter pylori* (*H. pylori*) and diabetes mellitus (DM) can induce chronic inflammation in the body and we don't whether chronic inflammation can be an underlying condition for duodenal white spots.

For this reason, we performed this study to delineate the most prevalent endoscopic and histopathological findings that have co-existence with duodenal white spots and also to determine whether the associated conditions such as *H. pylori*, diabetes mellitus and inflammation which we investigated by popular serum markers like neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), mean platelet volume (MPV) and erythrocyte distribution width (RDW) have an impact on the

presence of duodenal white spots. As far as we have searched this is the first study in the literature that investigates these correlations.

MATERIALS AND METHODS

In present retrospective study, we included all patients who underwent endoscopy between the time-period 2007-2017 in the Endoscopy Unit of Cumhuriyet University and had scattered white spots in the duodenum, by random sampling. Patients were determined retrospectively by examining them from hospital files. Our control group was formed by randomly selected patients who underwent endoscopy at the same time period. The number of subjects in the study and control group was 205 each respectively. Following an at least 8-hour fasting upper gastrointestinal endoscopy was performed on each patient. Written informed consent was obtained prior to each procedure from all patients. After premedication with topical anesthesia of the oropharynx, patients assumed the left lateral decubitus position. At least two duodenal biopsies were obtained from the second part of the duodenum for histological investigation. Gastric antrum biopsy specimens (at least two biopsies) were also obtained from all participants. Duodenal biopsy was taken from the control group due to indications other than white spots.

Demographic data, presence of chronic disease, endoscopic

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and histological diagnoses of both the patient and control groups were noted, and complete blood count results were obtained through the hospital computer recording system. Patients under 18 and over 80 years old and pregnant women were not included in the study, neither in study nor in control group.

STATISTICAL ANALYSIS

The statistical analyses were conducted with SPSS software (SPSS 22.0 for Widows, IBM, Chicago, IL, USA). Analyses of the variables whether they show normal distribution or not between study groups were done with Kolmogorov Smirnov test. Independent samples t test was used in comparison of the variables with normal distribution and these variables were expressed as mean ± standard deviation. Comparison of the categorical variables were done with chi-square test and expressed as n (percentage). Statistical significance level was set on a p-value lower than 0.05.

RESULTS

In this study, peptic ulcer were found in 21 (10.2%) of the patients with white spots, and in 9 (4.4%) of the control group patients respectively and this was significantly important (p=0.023). There was no difference by means of age, gender, DM, and anemia between the two groups (Table 1). We also did not find any difference between the two groups by means of the chronic inflammation parameters derived from the complete blood count such as, neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), mean platelet volume (MPV) and erythrocyte distribution width (RDW) (Table 2). There was no difference by means of the presence of gastritis, duodenitis, esophagitis, lower esophageal sphincter (LES) relaxation, hiatal hernia, or erosive gastritis between the two groups (Table 3). We also did not find any difference between the two groups by means of the gastric histological findings such as atrophy, intestinal metaplasia, chronic gastritis and *H. Pylori* presence (Table 3). Duodenal biopsy results such as, non-specific duodenitis, giardiasis and lymphangiectasia were also not significantly different between the two groups (Table 3).

Table 1. Demographic Data of Control and Study Groups.

	Study group (n=205)	Control group (n=205)	p-value
Age (years)	53.36±16.37	54.74±17.20	0.404
Gender			
Woman (n (%))	115 (%56.1)	102 (%49.3)	0.166
Man (n (%))	90 (%43.9)	103 (%50.7)	
DM (n (%))	23 (%11.2)	15 (%7.3)	0.173
Anemia (n (%))	53 (%25.9)	67 (%32.7)	0.129

Table 2. Chronic Inflammation Parameters in the Control and Study Groups.

	Study group (n=205)	Control group (n=205)	p-value
NLR (%)	3.07±4.50	3.35±3.54	0.263
PLR (%)	148.56±87.01	152.12±76.58	0.188
MPV (fL)	9.40±1.30	9.36±1.24	0.408
RDW (%)	14.28±2.16	14.47±2.69	0.431

(NLR: Neutrophil Lymphocyte Ratio, PLR: Platelet Lymphocyte Ratio, MPV: Mean Platelet Volume and RDW: Red Cell Distribution Width).

Table 3. Endoscopic and Histopathological Findings in Control and Study Groups.

Endoscopic Findings	Study group (n=205)	Control group (n=205)	p-value
Gastritis (n (%))	165 (%80.5)	174(%84.9)	0.240
Peptic ulcer (n (%))	21 (%10.2)	9(%4.4)	0.023 *
Duodenit (n (%))	9 (%4.4)	16(%7.8)	0.149
Esophagitis (n (%))	47 (%22.9)	61(%29.8)	0.116
LES Relaxation (n (%))	61 (%29.8)	59(%28.8)	0.828
Hiatal hernia (n (%))	19 (%9.3)	14(%6.8)	0.364
Erosive gastritis (n (%))	10 (%4.9)	7(%3.4)	0.457
Gastric Histopathological Findings			
Atrophy (n (%))	61 (%29.8)	64 (%31.3)	0.755
Intestinal metaplasia (n (%))	55 (%27)	40 (%19.8)	0.900
Chronic gastritis (n (%))	199 (%97.4)	194 (%94.9)	0.191
<i>Helicobacter pylori</i> (n (%))	129 (%63.3)	127 (%62.4)	0.865
Duodenal Histopathological Findings			
Duodenal mucosa (n (%))	49 (%25.3)	7 (%22.6)	0.345
Non-specific duodenitis (n (%))	138 (%71.1)	23 (%74.2)	0.468
Giardiasis (n (%))	2 (%1)	0 (%0)	0.289
Lymphangiectasia (n (%))	2 (%1)	0 (%0)	0.290

* Statistically significant.

DISCUSSION

White spots is a visual finding determined by the endoscopist. It is also defined by some gastroenterologists as a view of salt thrown in the duodenum. As the associated conditions accompanying this lesion is not clear in the literature; we conducted this study and found that peptic ulcer disease is significantly more common than the control group in these patients. We also investigated whether diabetes mellitus or chronic inflammation parameters derived from the complete blood count have any impact on the prevalence of white spots and could not find a significant difference between the study and control groups.

The demographic findings of our study group yielded a slight

female predominant middle-aged profile of patients. We also used a control group in our study and found no difference by means of age and sex between the study and control groups. The number of subjects in each group was 205. In a similar study conducted by Biyikoglu *et al.* which aimed to show the spectrum of pathologies in patients with duodenal white spots; we can see that female predominance is overt in this study (65.5% vs 34.5 %) and the patients are mostly middle-aged. But this study included a lesser number of patients with no control group [2]. In our study, we compared the results of duodenum and gastric biopsy results of our patient and control groups. While the most common lesion was gastritis in both the study and control groups; peptic ulcer disease was significantly more common in the study group than the control group. Chronic gastritis and chronic non-specific duodenitis were the most common histopathological diagnoses of our study group. In the study of Tas *et al.* just as it was in our study the most common duodenal histopathology was chronic non-specific duodenitis while it was intestinal lymphangiectasia in the study of Biyikoglu *et al.* [2].

In our study, we compared the incidence of DM among patients with white punctuation and in the control group. In DM and hyperglycemia infectious diseases are common. The main reason for this is the emergence of an immunosuppressive condition as a result of natural and acquired immunity disorders. In mouse DM models, phagocytosis, chemotaxis and cytokine production with neutrophil functions are decreased. In patients with DM, the belt toward the TH2-axis leads to a decrease in Th1-dependent immunity [5]. In a study involving 200 diabetic and 200 dyspeptic patients in Turkey, giardia intestinalis was investigated in the stool by ELISA method and giardiasis was found in 7% of dyspeptic patients and 15% in diabetic patients [6].

Giardiasis is one of the pathologies that accompany white spots and. It is very common in our country [7]. Therefore, we hypothesized that DM may be the underlying disease of the white spots. But when we investigated the relationship between DM and white spots; we could not find a significant relationship. We could detect giardiasis in only 2 patients histopathologically and we think that our study could have been more valuable if we had also tested giardia antigen in stool by Enzyme-Linked ImmunoSorbent Assay (ELISA) in these patients which is the most sensitive method. In the literature, there is no study investigating the relations between DM and white spots.

Anemia is also a finding in giardiasis [8]. The cause of anemia is the disruption of iron absorption by this parasite. In 302 children who went to kindergarten in Tunisia, giardiasis and anemia were investigated and the rate of anemia was 23.17% in the presence of giardiasis infection [9]. We also thought that there might be a relationship between anemia and

white spots, and we compared patients with white spots to those who did not. We could not detect any relationship between anemia and white spots. In the literature, there are no studies on the relationship between anemia and white spots.

Helicobacter pylori (*H. pylori*) are present in roughly 50% of the human population worldwide and infection levels reach over 70% in developing countries. One of the main mechanisms by which *H. pylori* is thought to damage the host is by inducing local and systemic inflammation [10, 11]. From this point of view, we investigated the relationship of white spots in duodenum with MPV and RDW, PLR, NLR, which are nowadays used as markers of inflammation in many systemic diseases.

Neutrophil lymphocyte ratio is a parameter of neutrophil count associated with lymphocyte division. In recent studies, NLR is said to be a marker of systemic inflammation in many diseases such as atherosclerosis, myocardial infarction, DM, ulcerative colitis, and malignancies [12, 13]. NLR has been shown to be superior to the white blood cell (WBC) in predicting adverse effects in various inflammatory and surgical conditions (i.e, pancreatitis, appendicitis, acute coronary syndrome, major vascular surgery and critical care disease) [12, 14]. We compared the NLR between the patients with white spots and those who were not present in order to determine whether the white spots are related to inflammation. However, we could not find any significant difference. In the literature, there are no studies investigating the relation between white pointing and NLR. The platelet lymphocyte ratio (PLR) is the parameter of the number of platelets divided by the number of lymphocytes. In recent studies, PLR is said to be an indicator of systemic inflammation [15, 16]. Therefore, we compared the patients with white spots and those who were not. However, we could not find a significant difference. There is no study investigating the relationship between white pointing with PLR in the literature. In recent years, it has been reported that MPV can be used as a marker of inflammation in different inflammatory diseases. Inflammatory, pro-inflammatory cytokines and acute phase markers in the inflammatory process on the bone marrow affect megakaryopoiesis and this may cause a decrease in platelet volume [17]. In the study of Kapsoritakis, MPV levels were found lower in inflammatory bowel disease compared to the healthy group [18]. Cardiovascular risk factors such as smoking, hypertension, dyslipidemia and diabetes may affect MPV. Active platelets play a role in cancer progression and metastases. Mean platelet volume (MPV) is an indicator of activated platelets and is associated with gastric, breast, lung, colon and ovarian cancers [19]. We compared whether there is a difference in MPV between patients with white spots and non-patients. However, we could not detect significant differences. In the literature, there is no study investigating the relationship between MPV and white spots.

Two limitations of present work are retrospective design and relatively small study population. However, our results may contribute to current literature, significantly.

It has been suggested that RDW is associated with a strong and independent risk of cardiovascular morbidity and mortality in patients with previous myocardial infarction and higher RDW levels may reflect an underlying chronic inflammation that would increase the risk of cardiovascular disease [20]. RDW's studies have shown that it is a marker of inflammation. We did not find a relationship between RDW and white spots. In the literature, there is no study investigating the relationship between RDW and white spots.

CONCLUSION

Both diabetes mellitus and *H. pylori* are causes of systemic inflammation. In our study, we evaluated whether patients with white spots were associated with systemic inflammation by looking at popular inflammation markers. We could not find any difference between the two groups in terms of these markers.

AUTHORS' CONTRIBUTION

Ozge Kurtkulagi did the retrospective investigation, analyzed the data and wrote the paper. Ozlem Yonem designed the study and wrote the paper.

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CONFLICT OF INTEREST

Declared none.

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