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Is there a difference concerning red cell distribution width in patient with or without helicobacter pylori and gastric inflammation severity?

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Abstract

Helicobacter pylori (H.Pylori) which is a widespread pathogen leading a slow chronic inflammation, may cause many clinical outcomes including gastric cancer. Red cell distribution width (RDW) is a new and promising indicator of inflammation. The primary aim of this study was to compare the red cell distribution width in patients with chronic gastric inflammation, either Helicobacter pylori positive or negative and also in gastric inflammation sub-groups. A total of 2500 patients who underwent upper gastro- intestinal system endoscopy were screened Of these 156 eligible patients, between 18 and 85 years old with no chronic disease and anemia as well as a normal of C-reactive protein and iron storage condition, were enrolled in this study. At least four gastric biopsies were taken from each patient and evaluated by the Sydney Classification. Serum RDW level and Helicobacter pylori positivity were compared as well as gastric inflammation severity. Of 156 patients, 84 (53.8%) were H.pylori positive, while 72 (46.2%) were H.pylori negative. There were no statistical differences between two groups according to mean age, gender, hemoglobin, mean corpuscular volume, ferritin, serum iron, platelet count and C-reactive protein ($p>0.05$). The median RDW level of H.Pylori positive and negative was not statistically different [13.4 (11.8-17.9) vs.13.4 (11.6-16), %95 confidential interval], respectively ($p=0.89$). Moreover, the median RDW level was not different among the groups of gastric inflammation severity according to Sydney Classification (all p-values >0.05). Our results demonstrated that there were no differences as regards to the median RDW result in patients with H.Pylori positive and negative . Also no disparity was observed between the median RDW and among the different subgroups of chronic gastric inflammation.

Keywords: Red cell distribution width, helicobacter pylori, gastric inflammation

Introduction

Many infective diseases with chronic inflammatory features affecting any part of the gastrointestinal tract still necessitate examining with minimally invasive endoscopic methods that are not available everywhere and suitable for every patient [1]. From another point of view, advanced immune histopathological examinations of endoscopic biopsies to identify a potential causative agent are also both expensive and time-consuming [2]. Consequently, a new diagnostic tool as a reliable and straightforward blood indicator of chronic inflammation is needed to avoid unnecessary costly and invasive processing [3].

Helicobacter pylori (H.pylori) is a common cause of infection agent causing chronic inflammation and thereby leading to various gastric diseases including gastric cancer and has an endemic feature in certain parts of the world, especially in the developing countries [1]. This chronic inflammation and its associated clinical condition have recently been linked with many other conditions and diseases outside of the stomach such as hematological and cardiovascular diseases [4-6]. Moreover, in recent years, the researchers regarding host immune responses occurred against the chronic H.pylori infection have begun to attract much more scientists attention before now [7]. Consequently, the identification of potential patients, who need further endoscopic investigation and need for H.pylori eradication, with simple, reliable and cheap blood markers, has become the increasingly significant subject of research studies.

It is a well-known entity that there is a relationship between subgroup parameters of complete blood count (CBC) and low-grade chronic inflammation [8]. Notably, some of these parameters are significantly elevated as correlated with the severity and duration of inflammation [9]. Red cell distribution width (RDW), which display the degree of variability of red blood cells, is one of the fundamental components of CBC and commonly used to differentiate anemia types from each other [6]. In addition to this essential function, in recent years, it is also used as a predictor

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and prognostic marker for various types of chronic diseases such as from diabetes mellitus, hypertension and heart failure to liver fibrosis and hepatocellular carcinoma [10-12]. New studies have clearly demonstrated this relationship [13,14].

Although there are many studies related to RDW in the gastrointestinal system, the critical role, and importance of RDW in H.pylori related chronic gastric inflammation have not been studied before. Hence, the primary aim of this study is to compare serum RDW between H.pylori positive and negative patients as well as in various degree of chronic gastric inflammation according to Sydney classification.

Material and Methods

This retrospective study was conducted at the department of gastroenterology in Zonguldak Bülent Ecevit University Farabi Hospital between from January 2015 and June 2017. A total of 2500 upper GIS endoscopic reports and their laboratory data were checked according to eligibility for this study. Patients between the ages of 18-85 who underwent upper endoscopy and received at least four gastric biopsies obtained from a different part of the stomach during this procedure were primarily included. The pathological report was accepted if the investigation is made according to Sydney Classification. H.pylori infection and other parameters were recorded as the degree of intensification and severity such as none, mild (+), moderate (++) and severe (+++) in this way. The measurements of CBC was accepted if done on the same day as the endoscopy procedure. It was clearly stated that if any patient had certain anemia or low and high mean corpuscular volume as well as low ferritin level, they were excluded. Since any part of anemia and anisocytosis were tightly linked and this could have caused a change in RDW values. Patients with confounding factors known to be possibly associated with anisocytosis were excluded. Besides, patients with a high level of C-reactive protein, white blood, and platelet count occurred any reason, or with any acute or chronic inflammatory disease and cancer were also excluded. Patients with gastric polyps and early gastric lesion or dysplasia during upper endoscopy were not included. A local ethics committee decision was made for this study and, consequently, this study was done according to the declaration of Helsinki, with the obtaining of approval of informant consent of each patient.

For statistical analysis, Windows compatible SPSS 18 version was used. The data distribution of all groups was checked with at least three tests including the Kolmogorov Smirnov test. Parametric and non-parametric values were expressed as a mean ± standard deviation and as median with minimum and maximum levels, respectively. For mean±standard deviation type values, Student's t-test was applied to compare the two groups, but if there were more than two groups, the individual comparisons were made with one-way ANOVA test. For median values (means as non-parametric), The Mann Whitney U test was used to compare two groups, but if there were more than two groups, the Kruskal Wallis test was used to compare among the groups. P-value <0.05 was accepted as significant.

Results

A total of 156 patients were enrolled in this study after the initial assessment as mentioned above. The most important demographic data were summarized in Table I. The study population was first analyzed as H. Pylori positive and H.pylori negative groups. Of these, 84 patients (53.8%) were H.Pylori positive, whereas 72 patients (46.2%) were H.pylori negative. There were no differences between the two groups according to the mean age, gender, hemoglobin level, endoscopic findings, mean corpuscular volume, platelet count, ferritin, serum iron and C-reactive levels (all p-values >0.05). As to the result of Sydney Classification; 1- Helicobacter Pylori; as expected the H. pylori positivity was detected only in H. pylori positive group (p<0.001), 2- Inflammation; the number of patients with mild and moderate inflammation was not different in both groups, but patients with severe inflammation were significantly higher in H. pylori group (p<0.001), 3- Activation; none (0) type activation was higher in H.pylori negative group than those with H.pylori positive (p<0.05), but mild and moderate activation was higher in H.pylori positive patients than those H.pylori negative (p<0.005), 4- Metaplasia and Atrophia; there was no difference between the two groups according to metaplasia and atrpohia.

The median RDW levels of H.pylori positive and negative were not statistically different in two groups, [13.4 (11.80-17.9) vs.13.4 (11.6-16), %95 Confidential Interval], respectively (p=0.89). In groups structured according to Sidney classification, there was no difference in median RDW among the five groups (all p values>0.05) (Table-II). Also, when analyzed by stratification in pairs or triple group formats, no statistical difference was found in median RDW among the groups (all p values>0.05) (Table-II).

Discussion

In that presenting study, the first time in literature, we investigated the comparison of the RDW levels in chronic gastric inflammation, whether H.pylori positive or negative, and clearly demonstrated that there were no differences the median RDW between H.pylori-positive and H.pylori-negative patients and also found no differences the median RDW in different subgroups of chronic gastric inflammation according to Sydney Classification. Consequently, we say that the RDW measurement does not work for demonstrating the gastric inflation severity and the presence of Helicobacter pylori. Also, it is not possible to make a decision with RDW in the inflammation of the stomach.

Helicobacter pylori is a prevalent problem for all over the world, especially developing countries. Because it could lead to many gastrointestinal issues including gastric cancer, consequently, it should be eradicated in patients with high-risk features [1]. For H .pylori eradication in many countries, two weeks of dual antibiotics are recommended [1,15]. Also, the empirical H.pylori eradication therapy is not suggested without clearly H.plori detection mainly in low endemic countries, because the recommended dual drugs can cause many side effects including liver toxicity. The standard gold method for the detection of this pathogen is still upper endoscopy with histological examination [15]. Although these procedures are minimally invasive, they are expensive in some country, and time-consuming as well as are not available, suitable for every patient and everywhere [1,2]. A reliable and straightforward indicator of inflammation is needed to avoid unnecessary invasive and expensive processing attempts [3].

Table 1. The essential critical demographic data of the study

	H.PLORI (+) n,%	H.PLORI (-) n,%	P
	Mean ± standard deviation		
Patients	84 (53.8%)	72 (46.2%)	0.337
Age	53.6 ±13.3	54.4 ±15.4	0.724
Gender			
Male	45	40	0.804
Female	39	32	
Hemoglobin (mg/dL) (NR:12-18)	14.1 ±1.14	14.2 ±1.1	0.304
MCV (fL) (NR:80-99)	87.4 ±3.5	88.1 ±3.9	0.274
Serum Iron ʋg/dl (NR:60-180)	72.2 ±12.8	67.8 ±9.7	0.689
Platelet x106 µ/mL (NR:140-400)	232 ±69	220 ±57	0.724
CRP mg/dl (NR:0-8)	2.2 ±1.5	3.06 ±1.1	0.854
	Median (minimum-maximum)		
RDW (%) (NR:11.5-15.5)	13.45 (11.6-16)	13.4 (11.8-17.9)	0.890
Ferritin mg/dl (NR:11-308.6)	48.2 (9.5-253)	44.65 (11-323)	0.986
Endoscopic findings			
1-Erythematous superficial gastritis(ESG)	30	24	
2-LES dysfunction +ESG	48	45	NS
3-ESG+ Ulcer or erosion of duodenum	6	3	
Histological Examination			
1-H.Pylori			
None	0	0	
Mild (+)	50 (59.5%)		
Moderate (++)	22 (26.1%)		<0.001
Severe (+++)	12 (14.2%)		
2-Inflammation			
None	0	2 (2.7%)	NS
Mild (+)	15 (17.8%)	27 (37.5%)	NS
Moderate (++)	34 (40.4%)	39 (54.1%)	NS
Severe (+++)	35 (41.6%)	4 (5.5%)	<0.001
3-Activation			
None	34 (40.4%)	64 (88.8%)	<0.05
Mild (+)	25 (29.7%)	6 (8.3%)	<0.05
Moderate (++)	24 (28.5%)	2 (2.7%)	<0.05
Severe (+++)	1 (1.1%)	0 (0%)	NS
4-Metaplasia			
None	63 (75%)	52 (72.2%)	
Mild (+)	17 (20.2%)	15 (20.8%)	NS
Moderate (++)	4 (4.7%)	2 (2.7%)	
Severe (+++)	0 (0%)	0 (0%)	
5-Atrophia			
None	69	66	NS
Exist	15	6	

NR: Normal Range, NS: Not significant, CRP:C reactive protein, MCV: Mean corpuscular volume, RDW: Red cell distribution width, LES: Lower esophageal sphincter

Table 2. There were no differences between the median RDW and among the chronic gastric inflammation sub-groups according to Sydney Classification (all p-values >0.05). (RDW: red cell distribution width)

Sydney Classification (n)	Red Cell Distribution Width Median (minimum-maximum)	p
1-Helicobacter pylori (n)		0.954
None (-) (72)	13.4 (11.6-16)	
Mild (+) (50)	13.4 (12.7-15.3)	
Moderate (++) (22)	13.5 (11.8-17.9)	
Severe (+++) (12)	13.3 (12.8-14.6)	
2-Inflammation (n)		0.995
None (-) (2)	13.4 (13.2-13.7)	
Mild (+) (40)	13.3 (12.5-16)	
Moderate (++) (69)	13.5 (11.6-15)	
Severe (+++) (38)	13.5 (11.8-17.9)	
3-Activation (n)		0.280
None (-) (98)	13.5 (11.6-16)	
Mild (+) (31)	13.4 (12.7-17.9)	
Moderate (++) (26)	13.2 (11.8-15.3)	
Severe (+++) (1)	13.1	
4-Metaplasia (n)		0.756
None (-) (115)	13.4 (11.6-17.9)	
Mild (+) (32)	13.5 (12.5-15.4)	
Moderate (++) (9)	13.6 (12.8-14.2)	
Severe (+++) (0)	0	
5-Atrophia (n)		0.944
None (-) (135)	13.4 (11.6-16)	
Exist (+) (21)	13.4 (12.8-17.9)	

RDW is a part of routine CBC and used commonly to differentiate iron deficiency anemia and various part anemia [6]. Recently, RDW has been very popular and promising marker for predicting chronic diseases such as cardiovascular, hematological and metabolic diseases [5,16]. RDW has so far been studied in many different diseases and slow inflammation as an indicator of prognosis or as a marker of subclinical inflammation, but, no current study is available related RDW and H.pylori [14]. To best of knowledge, our study is first to paper evaluating the relationship between RDW and H.pylori and the severity of slow gastric inflammation that primarly related with H.pylori .

RDW is mainly affected by age and iron storage [6]. Therefore, when evaluating the RDW, the iron storage condition should be investigated in the right way. In this study, we carefully selected our patients and, in our population, no patient was anemia and also even iron deficiency [6]. Unlike the previous studies, for evaluation of iron storage, we used the serum ferritin level and serum iron concentration as well [11]. Even in the same patients with hemoglobin and MCV levels, the serum RDW can become high if ferritin is low. In literature, because a few numbers of the studies evaluated the RDW with ferritin and serum iron, therefore, conflicting results could also be obtained.

Unlike the many previous RDW related studies, we found no relationship between RDW and gastric inflammation severity, whether H.pylori positive or negative. There may be a few reasons for this. First, the RDW is mainly affected by changes in the stock of iron storage. When looked at the literature much more closely, the iron storage condition with ferritin has not taken into count in many RDW related studies [14,16-18]. To us and current literature, RDW should be evaluated with serum ferritin level. In our work, we checked this matter correctly and did not include any patient who had no evident anemia with low ferritin level and serum iron. It can be clearly seen that only a small number of study take care of this situation [11,19]. Second, some conditions and agents cause a more serious systemic inflammatory response than H. Pylori. Thus, RDW may be more affected by these situations. For example, Yılmaz et al. concluded that RDW could an easy and inexpensive marker for intrahepatic cholestasis of pregnancy, and Xanthopoulos et al. claimed that RDW levels might be a prognostic marker in patients with heart failure and diabetes mellitus [9,11,14]. In these exemplified studies, CRP, the indicator of systemic inflammatory response, was not considered as a reason to influence the results [20,21]. For this, in our study, we studied CRP level and found a similar result in groups both H. H.pylori positive and negative.

Consequently, our result may be more reliable. Third, previous studies have clearly demonstrated that H. pylori-associated chronic gastric inflammation does not produce systemic cytokines such as in serum levels of tumor necrosis factor-alpha, interleukin-6 and interleukin-8 [22]. In this article, the authors concluded that since the H.pylori pylori lives only in the stomach mucosa and causes a unique form of local inflammation, thus, this inflammation cannot produce a systemic response. Conflicting results have already been reported in RDW related studies performed in local inflammatory diseases [23,24]. To us, the reason why the RDW does not differ in gastric inflammation severity and presence of H.pylori is only limited inflammation.

The limitations of our study as follows; retrospective design and relatively small case number. We also believed that if we added the mean platelet volume in this study, the results could be more meaningful.

Conclusion

Our results demonstrated that there were no differences in the median RDW in H.pylori positive and negative patients and no association between the median RDW and among the different subgroups of chronic gastric inflammation. Consequently, RDW is not a suitable marker to differentiate H.pylori positive and negative patients and severity of gastric inflammation.

Competing interests
The authors declare that they have no competing interest

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Ethical approval
The ethics committee approval (date: 29.6.2017 and clinical trial number; 2017-79- 29/06) was obtained by local department.

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