

# Diagnostic value of neutrophil to lymphocyte ratio, platelet to lymphocyte ratio and mean thrombocyte volume in irritable bowel syndrome-constipation according to Rome IV criteria

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## Abstract

**Aim:** Structural and biochemical reagents that could help diagnose irritable bowel syndrome (IBS) are still lacking. Moreover, use of certain diagnosis criteria in the diagnosis of the disease decreases the need for making over-diagnostic tests in order to rule out other diseases. Rome IV criteria include new parameters for the diagnosis of IBS. Our objective in this study is to research the diagnostic value of neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR) and mean platelet volume (MPV) count in IBS-Constipation (IBS-C).

**Material and Methods:** Data of the cases among patients who applied to general surgery polyclinics of Ordu University Medical Faculty who were diagnosed with IBS and have Rome IV IBS-C diagnosis criteria. Healthy volunteers were selected from adult healthy patients who applied to general surgery polyclinics of our hospital for general health check purposes. The age, sex, WBC (white blood cell), NLR, PLR, MPV values of the cases were analyzed.

**Results:** Average age of IBS-C group was 39.47±9.97 (min 19-max 57). Average age of the control group was 40.16±11.50 (min 18-max 59). Out of 78 IBS-C group patients, 48 (61.5%) were women and 30 (38.5%) were men. Of 82 patients 54 (65.9%) were women, 28 (34.1%) were men. Average age of the patients was 39.83±10.75 (min 18-max 59). A significant result was obtained for NLR when control group was compared with IBS-C group (p=0.01). No significant difference was determined between two groups for MPV, PLR (p>0.05). Cut-off value of NLR was calculated as 1.895, and the sensitivity in IBS diagnosis was calculated as 51.3%, and the specificity was calculated as 59.8%.

**Conclusion:** We have determined significant results with NLR, which is an inflammatory reagent, in IBS-C according to Rome IV Criteria. However, NLR has low sensitivity and specificity for IBS-C diagnosis from the other causes of constipation. We are of the opinion that inflammatory reagents such as NLR, PLR, MPV are not useful in the diagnosis of this disease. We consider that our study will shed a light on future studies with larger research populations.

**Keywords:** Rome IV criteria; irritable bowel syndrome; neutrophil to lymphocyte ratio (NLR); platelet to lymphocyte ratio (PLR); mean platelet volume (MPV).

## INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic disease with no organic pathology in clinical terms, characterized by such gastrointestinal symptoms as change in the bowel habits (constipation or diarrhea), abdominal pain, dyspeptic complaints (gas, swelling), of which etiology is not fully known, and its newest symptom criteria are the Rome IV criteria (1,2). IBS has four subtypes and a distinction is made between the following subtypes of IBS:

IBS with constipation (IBS-C), IBS with diarrhea (IBS-D), mixed IBS (IBS-M) and unsubtyped IBS (IBS-U) (2). Since the structural or biochemical reagents which will help diagnose IBS are not still present today, the diagnosis relies on well evaluation of the symptoms and ruling out other organic diseases that lead to similar situations. Use of certain diagnosis criteria in the diagnosis of the disease decreases the need for making excessive diagnostic tests in order to rule out other diseases (3). Considering that this causes inadequacy in diagnosis, Rome IV criteria

Received: 14.06.2019 Accepted: 22.09.2019 Available online: 24.10.2019

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have been released. In Rome IV criteria, it is emphasized that, in addition to excretion habits, the shape of the feces is also important for diagnosis. The most significant difference between Rome III and Rome IV is that one of the major symptoms in Rome III, "abdominal pain that has been repeating recently and suffering from discomfort in the abdomen" was changed in Rome IV into "abdominal pain that has been repeating recently", making it more restrictive (4).

In recent years, neutrophil to lymphocyte ratio (NLR) has been used as a reagent of the systemic inflammatory condition. NLR has a diagnostic value in certain diseases characterized by systemic inflammatory response such as ulcerative colitis and inflammatory arthritis (5,6). PLR is used as an indicator of inflammatory and pre-coagulative response that frequently appears in malignity and is considered to be a prognostic factor in breast cancer and colorectal cancer (7). Mean platelet volume (MPV) is considered as an indicator of the number and activity of thrombocytes. It was suggested that thrombocytes played important roles in the inflammatory process (8).

Our purpose in this study is to research whether NLR, PLR, and MPV have any diagnostic value in IBS-C according to Rome IV criteria.

## MATERIAL and METHODS

Ethical approval for the study was obtained from Clinical Research Ethics Committee of Ordu University Faculty of Medicine (Date: 7/2/2019, approval number:2019-21). Data of the cases among patients who applied to general surgery polyclinics of Ordu University Faculty of Medicine University Medical Faculty between June 1, 2017 - December 1, 2018 and who were diagnosed with IBS and have Rome IV (IBS-C) diagnosis criteria, was screened retrospectively. According to this, "patients who had recurrent abdominal pain sensation start of which was at least 6 months ago and which lasted for minimum 3 days in each month of the last three months", were determined. Besides, for constipation dominant IBS diagnosis, the Bristol feces form scale scores were used, which is among Rome IV diagnosis criteria. After performing basic biochemical analysis and colonoscopies of the patients were done for ruling out purposes, cases with IBS-C diagnosis on the basis of Rome IV criteria were included in the study. Our ruling out criteria for study were as follows:

1. Cases younger than 18 or older than 80 years of age;
2. Cases with severe chronic disease;
3. Patients with diarrhea;
4. Pregnant women;
5. Cases with malignity;
6. In case of occurrence of other alarm symptoms such as fever, gastrointestinal bleeding, weight loss, anemia, abdominal mass or functional bowel disorders and other unexplainable symptoms, organic diseases were thought of and were excluded from the study.

Healthy volunteers were selected from adult healthy patients who applied to general surgery policlinics of our hospital for general health check purposes.

WBC, NLR, PLR, and MPV values were obtained from complete blood analysis. NLR was calculated in complete blood analysis by dividing the number of neutrophils to the number of lymphocytes; and PLR was calculated by dividing the number of platelets to the number of lymphocytes. For complete blood count (CBC), blood analysis was made in vacuum tubes containing EDTA (15% K3 EDTA 0.054 ml / 4.5 ml blood). CBC measurements were made in an automatic device (Sysmex XN-1000, Tokyo, Japan).

Reference ranges of the tests studied; it was accepted as 3500-11000 microliters ( $\mu$ l) for WBC, 1800-7920  $\mu$ l for neutrophils, 1500-4000  $\mu$ l for lymphocytes, 8-12 fentoliters (fl) for MPV and 150000- 450000  $\mu$ l for platelets.

## Statistical Analysis

Whereas the descriptive statistics for continuous variables in our study were expressed as mean, median, standard deviation, minimum and maximum values; they were expressed as number and percentage for categorical variables. Mann-Whitney U test was performed in relation to continuous variables. Chi-square test was used in determining the relationship between categorical variables. Receiver operating characteristics (ROC) analysis was done in order to determine the diagnostic value of NLR, PLR, and MPV. The statistical significance level was set to 5% ( $p=0.05$ ) and the SPSS (IBM SPSS for Windows, V.24) statistical package software was used for calculations.

## RESULTS

160 cases were included in the study. 78 (48.7%) patients constituted the IBS-C group, and 82 (51.3%) patients constituted the control group. Of 160 cases, 102 (63.8%) were female, and 58 (36.2%) were male. The age average of female was  $39.19 \pm 11.03$ , and the age average of male was  $40.95 \pm 10.24$ . The control group patients, 48 (61.5%) were female and 30 (38.5%) were male. Of 82 patients, 54 (65.9%) were female, 28 (34.1%) were male. Average age of the patients was  $39.83 \pm 10.75$  (min 18 - max 59). Average age of IBS-C group was  $39.47 \pm 9.97$  (min 19 - max 57). Average age of the control group was  $40.16 \pm 11.50$  (min 18-max 59).

The demographic information of the patients and our descriptive statistical findings determined in hemogram values are given in Table 1.

ROC slopes were drawn in order to define efficiency of NLR, PLR, and MPV in diagnosis of IBS (Figure 1, 2, 3).

In ROC analysis, the cut-off value of NLR was calculated as 1.895, and the sensitivity in IBS diagnosis was calculated as 51.3%, and the specificity was calculated as 59.8%, which was statistically significant ( $p < 0.05$ ). The predictive value of PLR and MPV in IBS diagnosis was not found statistically significant ( $p > 0.05$ ). The ROC analysis of NLR, PLR, and MPV for IBS diagnosis value is given in Table 2.

Table 1. Definitive statistical values of groups

Variables	IBS-C group (n=78)	Control group (n=82)	P
Age (mean±std) (min-max)	39.47±9.97 (19-57)	40.16±11.50 (18-59)	0.71*
sex			0.57‡
female (n)	48	54	
male (n)	30	28	
WBC (µl)	7.47±1.66 (3.70-11.40)	7.29±1.72 (3.87-11.41)	0.67*
Neutrophil (µl)	4.48±1.31 (2-7.56)	4.12±1.18 (1.7-6.43)	0.31*
Lymphocyte (µl)	2.27±0.57 (1-3.78)	2.42±0.77 (1.23-6.26)	0.48*
Platelet (µl)	254.679±6.11 (131-431)	245.695±5.89 (148-503)	0.35*
NLR	2.09±0.80 (0.57-5.47)	1.82±0.82 (0.66-4.37)	0.014‡
PLR	51.77±50.58 (0.7-168.11)	57.13±51.08 (0.63-183.33)	0.053‡
MPV (fl)	8.61±1.63 (6.30-14.40)	8.35±1.44 (5.34-12.20)	0.40‡

\*: Mann-Whitney U test was used, †: Chi-Square test was used, ‡: ROC analysis was used. IBS-C: Irritable bowel syndrome-constipation, mean±std (min-max): mean±standard deviation (minimum-maximum), WBC: White blood cells, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, MPV: Mean platelet volume, (µl): microliter, (fl): fentoliter.

Table 2. The ROC analysis of parameters in the prediction of IBS-C

Variables	AUROC	95% CI	Cut-off	Sensitivity (%)	Specificity (%)	P
NLR	0.613	(0.526-0.700)	>1.895	51.3	59.8	0.014
PLR	0.589	(0.500-0.677)	>106.350	56.4	58.5	0.053
MPV (fl)	0.538	(0.449-0.628)	>8.075	52.6	45.1	0.401

IBS-C: Irritable bowel syndrome-constipation, ROC: Receiver operating characteristic; AUROC: Area under the ROC curve, CI: Confidence Interval, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio, MPV: Mean platelet volume, (fl): fentoliter.

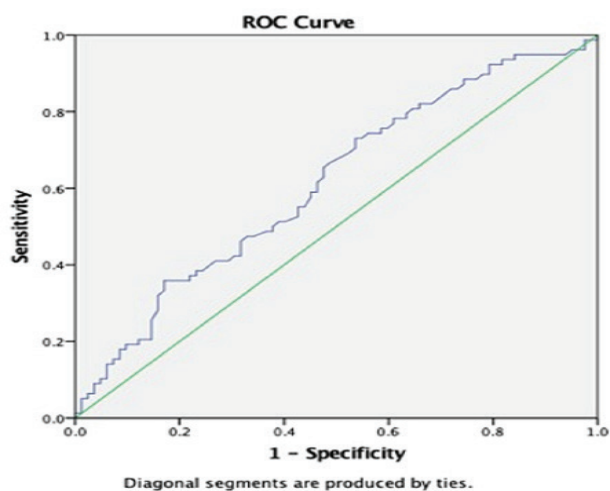


Figure 1. ROC analysis of NLR

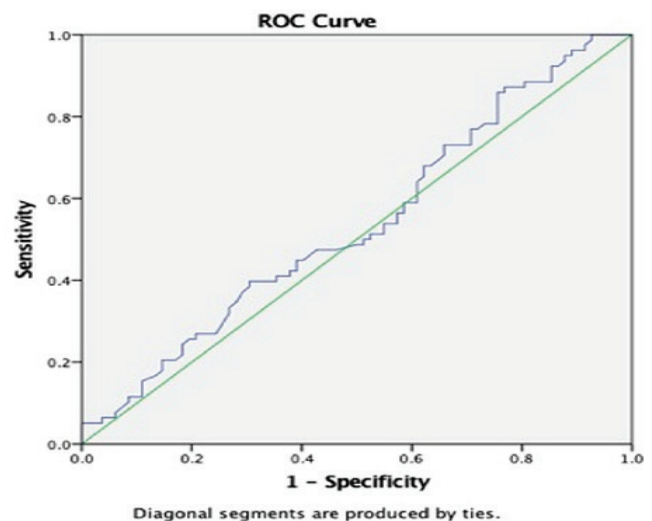
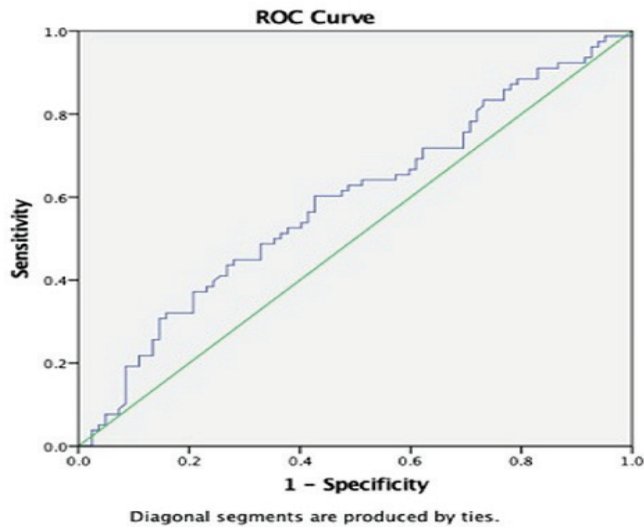


Figure 2. ROC analysis of PLR



**Figure 3.** ROC analysis of MPV

## DISCUSSION

In this study, a significant result was obtained for NLR between IBS-C group and the control group. No statistically significant result was determined between two groups for PLR and MPV. In addition to that, NLR had low sensitivity and specificity for IBS-C diagnosis. It is not considered that determination of NLR, PLR and MPV, which are reagent of inflammation, suggests that inflammation takes role in IBS pathogenesis.

Irritable bowel syndrome is a frequently seen functional bowel disorder. It demonstrates abdominal pain, discomfort in abdomen and change in excretion habits (9). It's pathogenesis includes irregular bowel motility, bowel visceral over-sensitivity, post-infectious reactivity, brain bowel relationship, altered bowel flora, food intolerance, diet habits and bowel inflammations (10). IBS prevalence is around 5-20% overall the world. It is seen more frequently among females than males, and among those aged below 50 than those aged above 50 (11). IBS constitutes excessive burden on patients and on the health system. This is due to its high prevalence and unsuccessful medical methods (12,13). For that reason, IBS is a disease with important diagnosis and treatment prospects.

In the analysis of Lovell et al., it was seen that IBS was 1.67 times more frequent in females compared to male (13). In the studies carried out in Asia, the frequency of IBS among females was not evidenced, and a male dominant on the contrary was determined in India (14,15). On the other hand, it is slightly in favor of females in Hong Kong (16). When considered in general, studies demonstrating that IBS is more frequent in females outweigh in the literature. In this study, the number of patients diagnosed with IBS-C was significantly higher among females. Our results are in compliance with literature in terms of sex. In the study conducted by Drossman et al. (17), it was notified that IBS prevalence decreased with increasing age. 67.3% of the cases in America were determined between ages 25-54, and in another study in North America, the starting age of IBS disease was found to be between 20-39 (18,19). In a

meta-analysis conducted by Lovell et al. IBS prevalence decreases by age overall the world (13). The studies conducted determined more frequently under age 50. In this study, age homogenization was ensured among healthy volunteers and patients diagnosed with IBS-C. The age average of both control and study group was around 40. Our results are similar to the literature in terms of age average.

In a study on 427 participants with clinical IBS diagnosis by experienced gastroenterologists under negative endoscopy conducted in nine different academic medical centers in three different countries, the participants completed questions involving Rome III and Rome IV criteria over internet. As a result of the study, the specificity of Rome IV criteria was found 97%, sensitivity 62%, positivity rate 21%, and negativity rate 38%. In Rome III, the specificity was found 93%, sensitivity 73%, positivity rate 10%, and negativity rate 28%. In China, the diagnosis test values were found for Rome IV as 97% for specificity and 46% for sensitivity (20,21). In this study, we used Rome IV criteria for IBS-C diagnosis. We think that Rome IV criteria are more up to date and sensitive.

In a study conducted by Unal et al. the relationship between the disease magnitude and NLR, PLR, and MPV in psoriasis patients was researched (22). Due to the fact that there is a positive relationship between PLR and both the erythrocyte sedimentation rate and CRP compared to NLR and MPV, it is a better reagent compared to MPV and NLR as inflammation reagent in psoriasis patients. In addition, as opposed to studies conducted before, Unal M. et al., did not determine a significant relation between NLR, PLR, and MPV and the disease magnitude, joint uptake, disease period in psoriasis patients. In our study, a significant relationship was found only with NLR in IBS-C patients, and no significant relationship was determined with PLR and MPV. Our conclusions are partially in compliance with literature findings. In the study conducted by Yavuzcan et al., the authors have studied the predictivity value of NLR, PLR, and MPV in advanced phase endometriosis patients in whom endometrioma was diagnosed and they could not determine significant results for all three variables (23). The authors have demonstrated in the study that NLR, PLR, and MPV values could not be used for predictive purposes in advanced phase endometriosis patients in whom strong inflammation existence was proven at cellular or molecular level. In our study, significant results were determined only for NLR, and no significant results were obtained for PLR and MPV. Our results partially coincide with the literature.

In a study conducted by Guclu et al., significant results were obtained between IBS-C patients diagnosed with Rome III criteria, and the NLR (24). Our study is in compliance with the study of Guclu et al. in the sense that it is constipation oriented which is the subgroup of IBS and significant results were obtained from the point of NLR. Besides, using Rome IV criteria for IBS diagnosis could be counted as an advantage of our study.

Our study has certain limitations. The data has been retrospectively obtained only from the information management system of our hospital, so as to rule out IBS with colonoscopy and radiologic imaging. Since IBS final diagnosis is made with retraction, comprehensive laboratory tests were not used due to economic constraints. Our study was not conducted in the general population, but among those who applied in our tertiary care center.

## CONCLUSION

As a conclusion, we have determined significant results with NLR, which is an inflammatory reagent in IBS-C. However, we believe that it has low sensitivity and specificity. We are of the opinion that inflammatory reagents such as NLR, PLR and MPV are not useful in the diagnosis of IBS. We consider that our study will shed a light on future studies with larger research populations.

*Competing interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Ethical approval: Ethical approval for the study was obtained from Clinical Research Ethics Committee of Ordu University Faculty of Medicine (Date: 7/2/2019, approval number:2019-21).*

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