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Relationship of peripheral blood neutrophil to lymphocyte ratio and irritable bowel syndrome

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Background/aim: This study aimed to determine the relationship between the peripheral blood neutrophil to lymphocyte ratio (NLR) and irritable bowel syndrome (IBS).

Materials and methods: A total of 107 patients suffering from constipation-predominant IBS, diagnosed in accordance with the ROMA III criteria and having complete blood count tests, were enrolled in this study. All patients underwent total colonoscopy in order to rule out any probable underlying organic colonic pathology.

Results: The control group consisted of 106 healthy people with no medical complaints. The peripheral blood NLR was 2.80 ± 2.52 on average in the IBS group. The NLR average was 2.37 ± 1.65 in the control group, and the average NLR ratio in the patient group was statistically significant ($P < 0.03$) and higher than that of the control group when the patient and the control groups were compared.

Conclusion: Peripheral blood NLR as a reliable, precise indicator of inflammation in constipation-predominant IBS patients, detected with a simple complete blood count, was slightly elevated but statistically significant compared to the control group.

Key words: Neutrophil to lymphocyte ratio, irritable bowel syndrome, complete blood count

1. Introduction

Irritable bowel syndrome (IBS) is a functional gastrointestinal syndrome characterized by variable disturbances of the bowel, such as abdominal pain and bloating, that are very common and nonthreatening, but that possibly impair quality of life (1–3). IBS diagnosis is made based on abdominal pain, changes in the functioning of the bowel, and stool analysis. Assessing the patient based on the Roma III criteria ensures diagnosis at a specificity of 81% (4–7). In recent years, it has been reported that enteric inflammatory events may be responsible for the pathogenesis of certain IBS cases (8–10). An increase in mast cells and proinflammatory cells in the IBS colonic mucosa, increased intestinal permeability, and subsequent subclinical minimal inflammation have also been observed (11–13). In immunohistochemical examinations, even in cases of normal histologic mucosa in IBS, there is an increase in intraepithelial lymphocytes and in lamina propria CD3- and CD25-positive T lymphocytes, both of which are indicators of immune activation. There is also an increase in mast cells in the colonic mucosa (14–16). Furthermore, increases in enterochromaffin cells, in lamina propria T lymphocytes, and in mast cells

were also seen in postinfectious IBS compared to control groups (17,18). It was also found that the ongoing minimal inflammation of treated inflammation in postinfectious IBS plays a significant role in IBS pathogenesis, and the increase in mast cells in the proximal region of enteric nerves is related to symptoms of the disease (17).

Due to the fact that the physiological response of the circulating leukocytes against stress causes an increase in the neutrophil count and a decrease in the lymphocyte count, the ratio of these two subgroups is used as a precise indicator of inflammation (18,19). Changes occur in the ratio of circulating leukocytes during inflammatory response. Lymphopenia accompanies neutrophilia. The neutrophil/lymphocyte ratio (NLR) is suggested as a simple and precise indicator of inflammatory response (20,21). It is possible to determine the NLR using a simple complete blood count measurement, which is a very inexpensive yet precise indicator. When assessed with sepsis scores such as the Acute Physiology and Chronic Health Evaluation II and the Sepsis-Related Organ Failure Assessment, such a ratio is deemed compatible with the severity and prognosis of the disease and is referred to as the neutrophil-lymphocyte stress factor (18–21).

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Peripheral blood NLR is used as a parameter that provides information about the relationship between the inflammatory setting and physiological stress. There are studies related to antibiotic usage in IBS patients such as excessive bacterial growth, subclinical inflammation, and rifaximin (18–21). A simple yet precise indicator of inflammation in IBS patients is determined based on the result of the complete blood count. The NLR may be useful in the detection and determination of a more effective usage of antibiotics in IBS patients such as rifaximin in a specific patient group. We did not encounter any studies in the literature on the place of peripheral blood NLR in IBS as an effective method in determining a noninvasive indicator; therefore, our study is the first one to address this topic.

2. Materials and methods

This study was conducted pursuant to the approval of İstanbul Medipol University's Faculty of Medicine Ethics Committee, dated 23.01.2015 and numbered 10840098-19 with decision no. 16.

A total of 213 individuals participated in the study as part of the patient and control groups. The patient group included 107 patients (55 female, 52 male) who suffered from constipation-predominant IBS according to the ROMA III criteria. All IBS patients underwent total colonoscopy and a complete blood count in order to rule out any organic colonic pathology, and the results of total colonoscopy for all patients were normal. The control group included 106 healthy people (66 female, 40 male) with no complaints. The differences between the two groups in terms of peripheral blood leukocyte count, neutrophil count, lymphocyte count, and NLR were investigated.

2.1. Statistical analysis

SPSS 21.0 for Windows was used for the statistical study (IBM Corp., Armonk, NY, USA). The differences between the patient and control groups were compared using the chi-square test and Student's t-test. The results were given as mean \pm standard deviation (mean \pm SD), and $P < 0.05$ was accepted as statistically significant.

2.2. Biochemical measurements

Blood samples were collected from the antecubital vein in vacuum tubes containing EDTA (15% K_3 EDTA, 0.054 mL/4.5 mL blood) for complete blood count and automatic blood count, and samples were tested within 1 h. Complete blood count measurements were made with automatic equipment (Sysmex XE-2100).

3. Results

When the groups were compared, no differences were detected between the control group and the IBS patient group in terms of average age and sex distributions. The peripheral blood NLR was 2.80 ± 2.52 on the average in the IBS group. The NLR average was 2.37 ± 1.65 in the control group, and the average NLR ratio in the patient group was statistically significant ($P < 0.03$) (Table; Figure). No statistically significant difference was detected for the other parameters (leukocyte, neutrophil, and lymphocyte counts) between groups when complete blood counts were measured and compared (Figure).

4. Discussion

While no anomalies are encountered in the routine analyses of IBS patients, inflammatory changes considered to be leading to changes in the colon mucosa, colon motility, and visceral perception have been recently reported (8,9,22). It has also been observed that lamina propria T lymphocytes, as well as enterochromaffin cells and the expression of interleukin-1 β , increased in the colon mucosa of patients with IBS (23–26). In a study conducted on this topic, while 30 mg/day of prednisolone did not result in any improvement in IBS symptoms compared to a placebo, it led to decreased CD3 lymphocytes in the colon mucosa (27). It was demonstrated that while intestinal immune function is improved, inflammatory or infectious events may cause permanent motility and visceral perception impairments by reprogramming the enteric nervous system (5). The beneficial effects of probiotics in IBS have been demonstrated, and detection of excessive bacterial growth in the small intestine of IBS

Table. Comparison of the control and IBS study groups.

	Control (N: 106)	IBS (N: 107)	P-value
Age (years)	44.76 \pm 17.52	55.79 \pm 14.80	0.84
Leukocytes ($10^3/\mu\text{L}$)	7.72 \pm 2.17	7.78 \pm 2.58	0.28
Neutrophils ($10^3/\mu\text{L}$)	4.66 \pm 1.79	4.83 \pm 2.27	0.10
Lymphocytes ($10^3/\mu\text{L}$)	2.22 \pm 0.70	2.07 \pm 0.64	0.54
NLR (neutrophil/lymphocyte ratio)	2.37 \pm 1.65	2.80 \pm 2.52	0.03*

* $P < 0.05$, statistically significant.

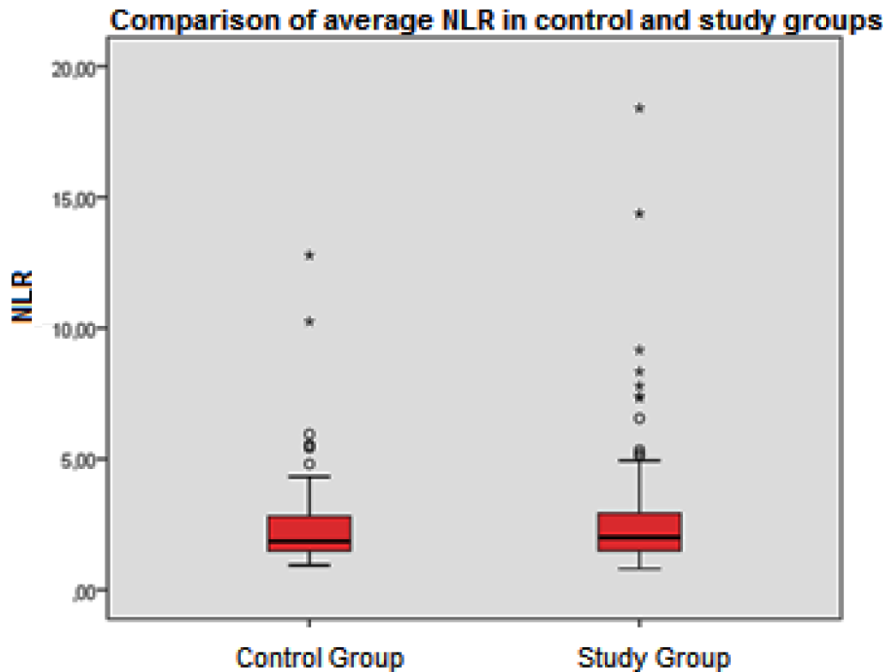


Figure. Comparison of NLR results in the control and IBS study groups. NLR: Neutrophil to lymphocyte ratio.

patients and significant improvement in IBS symptoms following antibiotic treatment support the role of infection in IBS (28,29). Host and environmental factors are also important in IBS pathogenesis. In addition, the role of genetic factors in IBS is also accepted. Disorders in natural and acquired immune response and changes in intestinal barrier function play an important role in triggering IBS with the effect of luminal factors (intestinal flora), particularly in individuals with a compatible genetic background (30–33). While the pathogenesis appears to be completely different, certain common characteristics stand out. Environmental factors, infection, and changing intestinal flora are commonly shared factors in IBS and in triggering IBS (34,35).

Evidence demonstrating that the NLR is beneficial for survival estimations of many clinical conditions increases day by day. The NLR value was investigated in patients suffering from lung cancer and colorectal cancer, and in patients who had undergone liver transplants for hepatoma, and the NLR was found to be cancer-specific and proportional to total life expectancy (36). Increased NLR is an indicator of bad prognosis in patients who have undergone cardiovascular surgical intervention and it was recently demonstrated that mortality rates are increased in acute coronary syndromes along with increased NLR (37,38). T lymphocytes detected in tissue are indicators of an immune response to lesions. New data demonstrate that a low lymphocyte count in a colorectal tumor is related to bad prognosis (37,39). However, it has been suggested that

preoperative NLR could be a simple method in identifying colorectal cancer patients with bad prognosis (37).

The NLR may be used in estimating bacteremia development in patients with community-acquired infections. A study demonstrated that cases of increased neutrophil and lymphocyte count are more susceptible to an increase in white blood cell count (39). Due to the fact that there is no perfect diagnostic testing and because of the recent topical issue of using antibiotics in IBS, we are required to collect more information on NLR as a precise test. Unfortunately, we were unable to encounter any study in the literature investigating the relationship between IBS and NLR. Our study is the first to address this topic.

While blood leukocyte counts are similar in the control group and IBS patient group in our current study and while there are no significant differences between them, the peripheral blood NLR ratio of IBS patients was slightly elevated compared to the NLR ratio of the healthy control group. This was statistically significant ($P < 0.03$), and these results demonstrate that while the peripheral blood leukocyte ratios are normal in constipation-predominant IBS patients, NLR as a precise indicator of inflammation is high, and it may support the existence of subclinical mucosal inflammation. The high NLR value detected in the IBS patients may be a reflection of inflammatory cells in colonic mucosa demonstrated in the previous studies conducted with IBS patients. These results are consistent with and supportive of what is available in the literature (23–27). Medical treatment can be planned by taking

into account the efficacy of antibiotherapy in selected IBS cases based on these results. However, it is imperative that further studies involving more patients, supported by advanced colonic histopathologic examinations in which other indicators of inflammation are included, be conducted to determine the patient groups for which antibiotherapy (rifaximin, etc.) should be preferred.

In conclusion, while the blood leukocyte counts between the groups are similar and there is no statistically

significant difference between them in our study, the peripheral blood NLR ratio of the IBS patients was slightly elevated compared to the NLR ratio of the healthy control group, and this was statistically significant. These results demonstrate that while peripheral blood leukocyte ratios are normal in constipation-predominant IBS patients, the NLR as a precise indicator of inflammation is high, and this may support the existence of subclinical mucosal inflammation.

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