Red cell distribution width-to-platelet count ratio is a promising predictor of functional bowel disease


Background. Hemogram parameters are not only diagnostic tools in haematological diseases, but their role in inflammatory conditions is also important. One of these haematological markers is a derived index, the so-called red cell distribution width-to-platelet count ratio (RPR). The role of RPR has been well established in various inflammatory conditions.

Objectives. In the present study, we aimed to observe the RPR levels of patients with functional bowel disease (FBD), which is also considered as an inflammatory process, and to compare this to the healthy population.

Material and methods. Patients diagnosed with FBD according to Rome IV criteria were included as the study group. Healthy volunteers were enrolled as control subjects. Patients with any form of anaemia or haematological disorders or inflammatory diseases were excluded. Age, gender and hemogram parameters were obtained from institutional databases. The data of the study and control groups was compared.

Results. 158 subjects were enrolled in the study; 87 in the FBD group and 71 in the control group. The RPR of the FBD and control groups were 7% (2%) and 5% (1%), respectively. The difference in RPR between the FBD and control groups was statistically significant (p = 0.008). A RPR value higher than 6% has a 70% sensitivity and 52% specificity in detecting FBD. There was a significant and positive correlation between RPR levels and the presence of FBD (r = 0.22, p = 0.007).

Conclusions. We suggest that elevated RPR levels could yield potential diagnostic benefits in the diagnosis of FBD. However, prospective studies with a larger population are needed to confirm our results.

Key words: erythrocyte indices, blood platelets, inflammation.

Background

Hemogram parameters have gained the attention of scientists in recent years. Both diagnostic potential in haematological diseases and predictive role in inflammatory condition of hemogram parameters make them the subject of recent studies in literature. One of these haematological markers is a derived index, the so-called red cell distribution width-to-platelet count ratio (RPR). RPR has been associated with various clinical conditions in medical literature. These conditions include rheumatoid arthritis, autoimmune hepatitis, cardiovascular morbidities, mortality of burned patients and acute pancreatitis [1–5].

Functional bowel disease (FBD) is characterised by abdominal discomfort and pain, a change in bowel habits and flatulence. Interactions between mucosal immunity and microbiological gut flora, infections and inflammation are three possible mechanisms of the development of functional bowel disease [6–9]. Since it affects nearly one third of the world population, it could not be classified as a rare condition [10]. Therefore, FBD imposes an enormous burden on healthcare systems and makes up a large proportion of hospital visits [11].

An association between inflammatory markers and one of the functional bowel diseases, irritable bowel syndrome (IBS), has been well established in literature [12, 13].

Objectives

There is strong evidence of a correlation between FBD and inflammation; therefore, in the present study, we aimed to observe the RPR levels of patients with FBD and to compare this to the healthy population.

Material and methods

Study design and setting

Patients visiting the outpatient internal medicine clinics of our institution with a diagnosis of FBD between January 2020 and April 2021 were enrolled in the present retrospective analysis. The institutional ethics committee approved the study (approval no: 2021-141). Rome IV criteria were used in the establishment of FBD. These subjects were grouped in the FBD group, while healthy volunteers visiting the institutional outpatient internal medicine clinics for a routine check-up were grouped as the control group. Patients with any kind of anaemia or haematological disorders, inflammatory diseases, such as inflammatory bowel disease, rheumatoid arthritis, with recent infectious diseases, with cancer, type 2 diabetes mellitus, chronic renal insufficiency and advanced heart failure were excluded.
Laboratory analyses

Age, gender and hemogram parameters including white blood cell count (WBC), haemoglobin (HB), haematocrit (HTC), mean erythrocyte volume (MCV), erythrocyte distribution width (RDW) and platelet count (PLT) were obtained from institutional databases. A RPR value was calculated by division of RDW by PLT.

All haematological analyses were carried out within 15 minutes after drawing of blood samples into sterile tubes containing a constant amount of EDTA. The LH 780 automatic analyser (Beckman Coulter Inc., Brea, CA, USA) was used in hemogram analyses. The study variables of FBD and control groups were compared.

Statistical analyses

SPSS software (SPSS 15.0; SPSS Inc., Chicago, IL, USA) was used in statistical analyses. Normality of the study variables was conducted using the Kolmogorov-Smirnov test. Either the independent samples t-Test (for variables with normal distribution) or the Mann-Whitney U test (for variables without normal distribution) were used in the comparison of parametric variables. These variables were expressed either as mean ± standard deviation (variables with normal distribution) or median (IQR) (variables without normal distribution). Comparison of non-parametric variables were carried out with the X² test and were expressed as numbers and percentage. The sensitivity and specificity of RPR in determining FBD were analysed with the ROC curve test. The correlation between FBD and RPR was analysed with the Spearman’s correlation analysis. When the p-value was lower than 5%, it was considered statistically significant.

Results

158 subjects were enrolled to the study; 87 in the FBD group and 71 in the control group. 27 (31%) were men and 60 (69%) were women in the FBD group, and 31 (43%) were men and 40 (57%) were women in the control group. Gender was not statistically different between the study groups (p = 0.15). The mean age of the FBD and control groups were 41 ± 14 years and 41 ± 11 years, respectively (p = 0.85). The WBC (p = 0.17), HB (p = 0.18), HTC (p = 0.38), MCV (p = 0.95) and PLT (p = 0.08) levels of the FBD and control groups were not statistically different. The RDW of the FBD group was higher than that of the control group (p = 0.03).

The RPR of the FBD and control groups were 7% (2%) and 5% (1%), respectively. The difference in RPR between the FBD and control groups was statistically significant (p = 0.008). Table 1 shows the data of the study groups.

A RPR value higher than 6% has 70% sensitivity and 52% specificity in detecting FBD (AUC: 0.63, p = 0.008, 95% CI: 0.53–0.72). Figure 1 shows the sensitivity and specificity of RPR in detecting FBD.

There was a significant and positive correlation between RPR levels and the presence of FBD (r = 0.22, p = 0.007).

![ROC Curve](image)

**Figure 1.** Sensitivity and specificity of RPR in detecting FBD

Discussion

The present study showed that RPR is a reliable and sensitive marker of FBD. Moreover, we showed that RPR has a significant positive correlation with the disease and has high sensitivity and considerable specificity in selecting patients with FBD.

Inflammatory diseases have been reported to be associated with elevated RPR levels in recent literature. Taefi et al. found increased RPR levels in subjects with chronic hepatitis, and they also concluded that the degree of fibrosis was better correlated with the RPR than MELD score [14]. Subsequently, fibrosis in patients with chronic hepatitis C was found to be associated with blood RPR levels in a study by Karagöz et al. in 2016 [15]. Not only fibrosis in chronic hepatitis but also in non-alcoholic fatty liver disease has been reported to be correlated with blood RPR levels [16]. Moreover, RPR was suggested to be correlated with the severity of primary biliary cirrhosis [17]. In another study, RPR has been suggested as a diagnostic and follow-up tool in pa-
patients with patent ductus arteriosus [18]. Increased RPR yields potential diagnostic or prognostic benefits in systemic lupus erythematosus [19], colorectal cancer [20], myocardial infarction [21], breast cancer [22] and acute traumatic brain injury [23]. All of these conditions are associated with subtle or prominent levels of inflammatory burden. Since FBD is also associated with inflammatory response in the microvasculature of the bowel, increased RPR in FBD is not a surprising finding.

The association between inflammation and functional bowel disease is well established. There are numerous studies in literature that report upon the correlation between inflammation and irritable bowel syndrome, a type of FBD [12, 13, 24]. Moreover, there is evidence that chronic, low-grade inflammation at the microscopic level in the bowel of patients with FBD accompanies the disease [25]. Inflammatory cytokines, such as interleukin-6 and interleukin-8, were also found to be increased in patients with irritable bowel disease [26]. This evidence suggests that inflammation may be somewhat involved in the pathogenesis of FBD. Since RPR is a novel inflammatory marker, it is increased in FBD, another inflammatory condition.

Overlap syndrome of inflammatory bowel disease and FBD (especially irritable bowel syndrome) has been reported in recent studies. A recent meta-analysis suggested that 40% of patients with inflammatory bowel disease experience symptoms of FBD [27]. Subsequently, Gracie et al.’s study supported those findings in this meta-analysis [28]. Bowel functions and intestinal permeability are suggested to be altered by ongoing, chronic inflammation in inflammatory bowel disease and irritable bowel syndrome, thus causing similar symptoms in these conditions [29]. Histological examination of the intestinal biopsy materials of patients with inflammatory bowel disease and irritable bowel syndrome reveal a common pathology – increased permeability of the intestines [29]. This data suggests that inflammation could be a triggering factor in irritable bowel syndrome, a type of FBD, as in inflammatory bowel disease. Increased RPR in FBD could be also explained by this phenomenon.

Limitations of the study

The present study has two important limitations. The design of the study was retrospective, which could cause selection bias. Control of the accompanied factors is also difficult in a retrospective analysis. The second possible limitation could be the small size of study cohort. However, to the best of our knowledge, this is the first study in literature that showed a significant association between FBD and blood RPR levels.

Conclusions

We think that elevated RPR levels could yield potential diagnostic benefits in the diagnosis of FBD. However, prospective studies with a larger population are needed to confirm our results.

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References


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