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Blood Count Parameters as Inflammation Indicators in Children and Adolescents Diagnosed with Depressive Disorder

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ABSTRACT

Aim: There is increasing evidence that immunological and inflammatory dysfunctions play an essential role in the initiation and progression of major psychiatric disorders. Neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume can be used as markers of systemic inflammation in different diseases. We aimed to investigate these blood count parameters in children and adolescents diagnosed with major depressive disorder.

Methods: Designed as a case–control study, our sample consisted of patients aged 9-16 years referred to Child and Adolescent Psychiatry and pediatrics outpatient clinics for the first time and diagnosed with major depressive disorder according to *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* diagnostic criteria, and healthy children and adolescents matched at a ratio of 1 to 2. Data of 58 cases and 90 healthy controls evaluated between 01.07.2019 and 01.07.2020 were included.

Results: Platelet-to-lymphocyte ratio values were significantly higher in the case group. No significant difference was found between patient and control groups regarding other blood count parameters. When depression group was compared in terms of all parameters as those who committed suicide and those did not, significant difference was found between the 3 groups in terms of platelet-to-lymphocyte ratio values. The intergroup difference in platelet-to-lymphocyte ratio was found between the depression group without suicide and the control group. No significant relationship was found between other parameters and Children's Depression Inventory Scale scores. We determined a cut-off value of 112.5 for platelet-to-lymphocyte ratio (with sensitivity of 70% and specificity of 63%).

Conclusion: Platelet-to-lymphocyte ratio might be an important parameter in the clinical follow-up of major depressive disorder.

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KEYWORDS: Depression, inflammation, mean platelet volume, neutrophil lymphocyte ratio, platelet lymphocyte ratio

INTRODUCTION

Research on the role of inflammation in the etiology of psychiatric disorders has increased in recent years. One of the depression hypotheses is the chronic, low-grade inflammation hypothesis. There is increasing evidence that immunological and inflammatory dysfunctions play an essential role in the initiation and progression of major psychiatric disorders, which have a multifactorial and heterogeneous etiology.[1] The mechanism underlying chronic low-grade inflammation in major depressive disorder (MDD) remains unclear.[2]

It was found that MDD can suppress the immune system and cause an increase in the production of proinflammatory cytokines.[3] While studies on the relationship between depression and inflammation increase daily in the national and international literature, it is noteworthy that the number of studies evaluating these parameters in children and adolescents is relatively low.

Neutrophil lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), and mean platelet volume (MPV) can be used as markers of systemic inflammation in different diseases. These blood count parameters and indices (BCPI) can be obtained by a simple hemogram analysis. Lymphocytes play a critical role in chronic inflammation. Lymphocytopenia, which means a significant decrease in the number of circulating lymphocytes during severe trauma, surgical procedures, sepsis, and systemic inflammation, has been described in many studies.[4] It was shown that not only white blood cells (neutrophils, lymphocytes, and

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monocytes) but also platelets are altered in inflammatory processes.[5] Increased platelet sizes indicate increased platelet activity, which plays a vital role in inflammatory processes. Platelet lymphocyte ratio can predict inflammatory response by considering platelets together with lymphocytes.[6]

With BCPI among the hemogram parameters, which are already requested during follow-up of psychiatric disorders, easily calculated, and cost-effective in routine use instead of measurements such as cytokines and tryptophan metabolites with high economic costs, it may be possible to reach inflammation markers.[7,8] Although standardization cannot be achieved in measuring complete blood count values, comorbidities accompanying MDD, and different results are obtained in studies, it is crucial that clinical studies investigating BCPI in the child and adolescent age group increase gradually. The role of inflammation in the etiology of depression may occur through different pathways. Therefore, it may be useful to continue to evaluate the role of BCPI in MDD development with clinical studies. Since the introduction of inflammatory biomarkers in pediatric diseases, there has been increased interest in studies examining the changes of markers in neuropsychiatric disorders.[1] The fact that it contains parameters that can provide predictions about the diagnosis can also make the complete blood count a vital source for the prognosis of adolescent depression.[3]

In this study, it was aimed to investigate the BCPI NLR, PLR, and MPV levels in children and adolescents diagnosed with MDD by comparing them with healthy controls. It is assumed that defining the inflammatory-immune system's role in the etiopathogenesis of depression and monitoring inflammatory parameters during the treatment follow-up process may play an essential role in developing algorithms on this subject. Monitoring the BCPI level in the clinic of MDD may allow the development of new follow-up algorithms that will accelerate treatment. The primary purpose of the study is to discover biomarker(s) that can help in the management of MDD. In addition, a cut-off value for the marker was determined in this study. Our hypothesis is one-sided; NLR, PLR, and MPV levels, which are thought to be inflammatory parameters, are expected to be higher in children and adolescents with a diagnosis of the depressive disorder compared to healthy controls.

MAIN POINTS

- Platelet-to-lymphocyte ratio (PLR) values were found to be significantly higher in the depression group compared to healthy controls.
- No significant difference was found between the depression and control groups in terms of neutrophil-to-lymphocyte ratio (NLR) and mean platelet volume (MPV) values.
- When the depression group was compared with the healthy control group regarding NLR, PLR, and MPV values as suicidal and non-suicidal groups, a significant difference was found in the non-suicidal depression group in PLR value.
- Suicide and depression may have developed through different inflammatory pathways.
- No significant relationship was found between inflammation parameters and Children's Depression Inventory Scale score.
- The PLR value may be an essential parameter in the clinical follow-up of major depressive disorder.
- The PRL cut-off estimates and the corresponding (sensitivity and specificity) values were determined as 112.5 (70% and 63%) which had the highest positive likelihood ratio.

METHODS

Subjects

The study is a case–control study, and our sample consisted of the patients aged 9-16 years who referred to Dr. Behçet Uz Children's Diseases and Surgery Training and Research Hospital Child and Adolescent Psychiatry Clinic and the pediatrics outpatient clinic for the first time between 01.07.2019 and 01.07.2020 and was diagnosed with depressive disorder according to *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (*DSM 5*) diagnostic criteria, and healthy children and adolescents matched at a ratio of 1 to 2.

The sample size with the aid of the G-power program was calculated as 148, when alpha was taken as 0.05, power value as 0.80, and effect size as 0.60.[9] Fifty-eight individuals for the patient group and 90 individuals for the control group were included in the study. For the psychiatric evaluation of the control group, the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime, Turkish Version (K-SADS-PL-T) was used, and healthy children without any medical or psychiatric diagnosis were determined as the control group.[10,11]

All participants were screened for comorbidities using K-SADS-PL-T. The diagnosis of MDD was made as per the *DSM-5*.[12]

Children with an acute or chronic disease (neurological, immunological, genetic, endocrine, oncological, or any other inflammatory), as factors that may cause inflammation, a history of any chronic drug use (e.g., antibiotic, anti-inflammatory, steroid, immune modulator, immune suppressor), psychotropic drug use in the last 3 months, intellectual disability, obesity, smoking and children with another comorbid psychiatric disorder were not included in the case group. The same exclusion criteria were applied to the control group, and children and adolescents with physical and comorbid mental disorders and parental depression were not included in the control group. Seven children with a chronic disease accompanying MDD, 4 children with psychotropic drug use history in the last 3 months, and 2 children whose parents did not approve the inclusion in the study were excluded. After reaching 58 cases, interviews were completed with healthy control cases.

This study was approved by the Ethics Committee of University of Health Sciences, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital (decree number: 2020/17-20). Written informed consent was obtained from all participants' parents and legally responsible individuals for this study.

Measurements

Descriptive information about age, gender, and the presence of depression in the parents was analyzed using the Descriptive Information Form; depression scale scores were analyzed by Children's Depression Inventory (CDI), the psychiatric diagnosis was made according to *DSM-5* criteria, screening for comorbid mental disorders was done by K-SADS-PL-T, and laboratory analysis of data on hemogram parameters was used to collect research data.

Data Collection Tools

Children's Depression Inventory: It is a 27-item self-report scale developed by Kovacs[13] that can be applied to children aged 6-17. Its validity and reliability in Turkish were made by Öy[14], and the pathological cut-off point was determined as 19 points.

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime, Turkish Version: It is a semi-structured interview form developed by Kaufman et al[10] in 1997 to screen psychopathology in children and adolescents aged between 6 and 18 years as per DSM-III-R, DSM-IV, and DSM-5 diagnostic criteria. The validity and reliability of the new Turkish form adapted according to *DSM-5* were made by Ünal et al[11] in 2016. With this semi-structured interview, many psychiatric disorders are evaluated, except for specific learning disabilities, autism spectrum disorders, and schizophrenia with negative symptoms.

Statistical Analysis

The Statistical Package for the Social Sciences software version 25.0 (IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY, USA) was used for statistical analysis. The Kolmogorov–Smirnov test was used to evaluate whether the distribution of continuous variables was normal. As continuous variables were normally distributed, descriptive analyses were presented as means±standard deviations. The Student's *t*-test was used to compare NLR, PLR, MPV, and hemogram values between age- and gender-matched groups, and the one-way analysis of variance (ANOVA) test was used to analyze the differences between more than 2 groups. Levene's test was used to assess the homogeneity of variances. Post hoc Tukey's test was performed to determine the significance of pairwise differences using the Bonferroni correction to adjust for multiple comparisons. Multivariate ANOVA (MANOVA) statistics were performed to determine the blood count parameter values between 3 groups (suicidal MDD group, non-suicidal MDD group, and healthy group) analysis. A chi-square test was used to compare intergroup categorical data. The relationship between the Children's Depression Inventory, numerical variables of sociodemographic data obtained from the interview, and BCPI with hemogram data were evaluated with Pearson's correlation analysis. A 5% type 1 error level was used to infer statistical significance. Our hypothesis is that the BCPI levels will be higher in children and adolescents diagnosed with MDD than healthy controls. Moreover, receiver operating characteristic (ROC) analysis was performed, and a threshold value was determined for the PLR that had the potential of serving as a diagnostic biomarker of depressive disorders of children.

RESULTS

The mean age of the patient group was 13.97±1.98 years, the mean age of the control group was 14.29±1.67 years. In total, 75.9% of the patient group (n=44) and 66.7% (n=60) of the control group consisted of girls. Patient and control groups were similar in terms of age and gender distribution, parallel to 1-2 rates ($P > .05$).

It was determined that 25.9% (n=15) of the patient group had suicidal behavior. In the patient group, the history of MDD was present in 35 (60.3%) of 58 parents, and the distribution of these rates was 17 (29.3%) mothers, 3 (5.2%) fathers, and 15 (27.6%) in the form of both mother and father.

As presented in Table 1, PLR values were found to be significantly higher in the case group compared to healthy controls ($P=.005$). No significant difference was found between the patient and control groups regarding NLR and MPV values ($P > .05$). Besides, a statistically significant difference was found between the 2 groups in terms of hemoglobin (Hb), hematocrit (Htc), neutrophil, platelet, and red cell distribution width (RDW) counts ($P < .05$) (Table 1).

When the case group was examined regarding BCPI values in female and male genders, no significant difference was found between them ($P > .05$). When it was compared with regards to Hb and Htc levels in the case group, it was found that the boys had significantly higher Hb and Htc values compared to girls ($P < .001$).

According to MANOVA analysis using Pillai's trace, there was a significant effect on having depressive disorder on PLR, Hb, Htc, platelet, and RDW values (V: 0.33, F: 2.74 and $P < .001$). Separate univariate ANOVAs on the outcome variables revealed a significant impact as well. When the depression group was compared in terms of NLR, PLR, and MPV values as those who committed suicide and those who did not, a significant difference ($P=.018$) was found between the 3 groups in PLR values, while no significant difference was found in NLR and MPV values ($P > .05$). One-way ANOVA test was used since all 3 groups were suitable for normal distribution regarding PLR. The intergroup difference in PLR was found to be between the depression

Table 1. Comparison of the Patient and Control Groups in Terms of NLR, MPV, and PLR and Complete Blood Count Parameters

	Patient Group, Mean±SD	Control Group, Mean±SD	*t*	*P*
NLR	1.94±1.11	1.65±0.66	1.78	.780
MPV	10.35±0.83	10.16±0.78	1.41	.160
PLR	133.95±41.65	114.44±40.53	2.82	**.005***
Hb	12.88±1.62	13.83±1.21	-3.842	**<.001***
Htc	39.11±3.84	41.61±3.31	-4.199	**<.001***
WBC	7.96±1.99	7.44±1.58	1.732	.085
Neutrophil	4.53±1.54	4.03±1.18	2.133	**.035***
Lymphocyte	2.56±0.83	2.60±0.71	-0.371	.711
Platelet	315.86±63.43	281.47±54.89	3.498	**<.001***
RDW	13.45±1.56	12.84±0.93	2.968	**.004***

NLR, neutrophil to lymphocyte ratio; MPV, mean platelet volume; PLR, platelet to lymphocyte ratio; Hb, hemoglobin; Htc, hematocrit; WBC, white blood cell; RDW, red cell distribution width.
*$P < .05$. *t*, Student's t-test.

group without suicide and the control group ($P < .01$). It was determined that the PLR level in the depression group was higher than in the control group.

Besides, when comparing all 3 groups with regards to complete blood count values, the platelet count was found to be significantly higher in the case group than in the healthy control group ($P = .003$). In contrast, Hb and Htc levels were found to be significantly lower in the depression group with suicide than in the depression group ($P < .001$), and RDW level was found to be significantly high ($P < .01$) (Table 2). Platelet lymphocyte ratio values between suicidal MDD group, non-suicidal MDD group, and healthy group is presented in Figure 1. When the CDI scale score variable, which was thought to be associated with BCPI values in the case group, was examined with Pearson's correlation analysis, no significant relationship was found between inflammation parameters and CDI scale score ($P > .05$) (Table 3).

For predicting children with depressive disorders, cut-off estimates and the corresponding (sensitivity and specificity) values for the PLR were determined from the curve in Figure 2 as 112.5 (70% and 63%) which had the highest positive likelihood ratio (area under the curve = 0.661, $P < .001$) (Figure 2).

DISCUSSION

In this study, which was conducted to define the role of the inflammatory-immune system in the etiopathogenesis of depression, it was found that PLR levels, one of the inflammatory parameters, in children and adolescents diagnosed with MDD were higher in patients with depression than in healthy controls. When depression cases with suicides were also included in the study, it was determined that the higher PLR levels of the group diagnosed with depression without suicide were more critical in terms of making the difference. It was also determined that Hb and Htc levels among the complete BCPI were lower in depressive cases with suicide and higher RDW levels

Table 2. Comparison of Depression, Depression Accompanied by Suicide, and Healthy Control Groups in Terms of NLR, MPV, and PLR Mean Values

	a Depression Group (Mean±SD) (N=43)	b Depression + Suicide Group (Mean±SD) (N=15)	c Healthy Control Group (Mean±SD) (N=90)	*F*	*P*
Parameter					
NLR	1.93±1.21	1.97±0.79	1.65±0.66	1.963	.144
MPV	10.29±0.87	10.54±0.70	10.16±0.78	1.565	.213
PLR	135.72±37.89	128.90±52.13	114.44±40.53	4.132	**.018***
Hb	13.1±1.51	12.00±1.66	13.83±1.21	13.01	**<.001****
Htc	39.73±3.62	37.34±4.02	41.61±3.31	11.68	**<.001****
WBC	7.88±1.92	8.17±2.23	7.44±1.58	1.64	.197
Neutrophil	4.51±1.58	4.61±1.48	4.03±1.18	2.55	.081
Lymphocyte	2.46±0.68	2.84±1.15	2.60±0.71	1.43	.243
Platelet	315.48±65.78	316.93±58.28	281.47±54.89	6.08	**.003***
RDW	13.23±1.37	14.08±1.94	12.84±0.93	7.30	**<.001****

NLR, neutrophil-to-lymphocyte ratio; MPV, mean platelet volume; PLR, platelet-to-lymphocyte ratio; Hb, hemoglobin; Htc, hematocrit; WBC, white blood cell; RDW, red cell distribution width; ANOVA, analysis of variance (One-way ANOVA test was used since all 3 groups were suitable for normal distribution in terms of PLR).
*One-way ANOVA: significant between groups a and c.
**One-way ANOVA: significant between groups b and c.

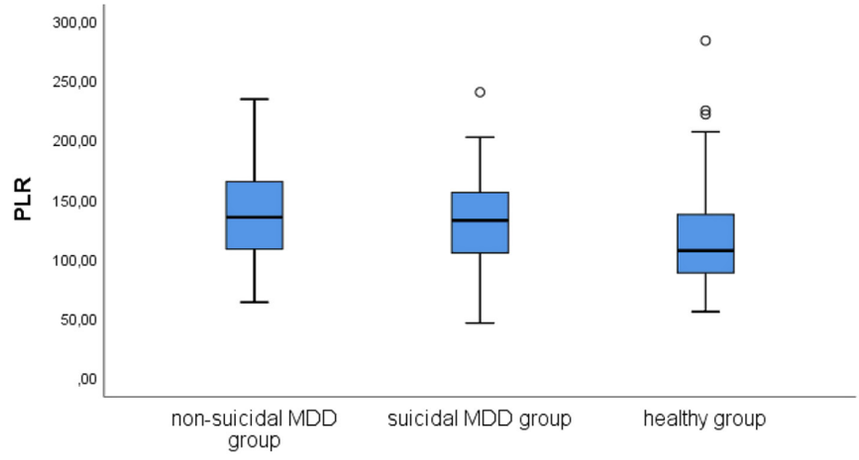

Figure 1. PLR values between suicidal MDD group, non-suicidal MDD group, and healthy group. MDD, major depressive disorder; PLR, platelet-to-lymphocyte ratio.

than healthy controls. Platelet levels were higher in the patient group with depression without suicide than healthy controls. There was no significant relationship between the childhood depression scale and inflammatory parameters.

Since the presence of mental or physical comorbidity might have affected the study results, cases with comorbidities were not included in the study. The correlation of each diagnostic group with inflammation should be evaluated within a framework that excludes confounding factors. Otherwise, it will not be possible to generalize the results of the study to a single diagnosis group.

Different results were obtained in studies conducted on inflammation in psychiatric disorders. Some studies found high MPV and platelet levels in schizophrenic patients, low MPV levels in bipolar depression, high NLR levels in acute mania similar to depression, and low MPV levels.[15] Since comorbid psychiatric diagnosis groups affect the results regarding inflammation parameters, patients with comorbid diagnosis were not included in our study. This exclusion criterion is thought to be one of the strengths of our study.

In studies conducted with adult depression patients, NLR, PLR,[8] and MPV levels[2] defined as inflammatory markers were found to be significantly higher in depressive patients[16-18] compared to healthy controls. Besides, it was stated that the white blood cell and neutrophil count increased and lymphocyte levels decreased,[17] and RDW levels were found to be significantly higher than the control group.[2,16]

Table 3. The Correlation of NLR, MPV, and PLR Values with CDI, Parental Depression, and Suicide Attempt

	NLR		MPV		PLR	
	r	*P*	*r*	*P*	*r*	*P*
CDI	0.140	.295	0.033	.806	0.123	.359

CDI, Children's Depression Inventory; NLR, neutrophil-to-lymphocyte ratio; MPV, mean platelet volume; PLR, platelet-to-lymphocyte ratio; *r*, Pearson correlation.

In addition to studies that found much higher levels of NLR in children and adolescents with MDD compared to healthy controls and did not detect a significant difference in PLR,[3,9] there were also studies that found the BCPI and monocyte-to-lymphocyte ratio significantly higher than the control group.[3,19] Adolescent MDD patients receiving inpatient treatment were found to have higher NLR and PLR ratios than healthy controls.[20] Bahrami et al[21] found higher PLR and RDW platelet ratio values in adolescents diagnosed with depression than healthy adolescents. Depression subtypes were not studied in our study, and the fact that it was performed in outpatients may have led to no significant difference in NLR level. In newly diagnosed depressive adolescents, PLR level may have increased first, but the expected level in inflammation in terms of NLR and MPV may not be reached yet. In our study, it is understood that the higher platelet counts in depressive adolescents compared to healthy controls were consistent with these meta-analysis results and other studies conducted in adolescents. However, unlike other studies, although lymphocyte level in the case group was lower than the healthy control group, no statistically significant lymphopenia was found. The lack of difference in inflammatory parameters other than PLR may be related to the absence of depression subtypes. The fact that NLR levels were found to be higher in the psychotic feature subtype than in other subtypes in adult MDD patients receiving inpatient treatment[22] suggests that examining BCPI in large sample groups in outpatients and inpatients in the adolescent age group will yield important results.

Parameters such as platelet count and MPV have been suggested as inflammatory markers and were investigated in various psychiatric disorders. It was found that MPV is higher in adult MDD patients than in healthy ones.[23] In a study evaluating PLR and chronic illness and depression, platelet counts were found to be higher in depressive adolescents with suicidal tendencies than

inpatients and without suicidal patients.[24] In our study, platelet levels were found to be significantly higher in the case group than in the control group. This finding is in parallel with other studies in the literature. In the triple group comparison made with the healthy control group based on whether they contain suicide or not, it was found that the platelet level of the group with only depression (without suicide) was found to be significantly higher than the controls, and there was no difference in this direction between the group containing suicides and the control group. This result suggests that suicide and depression may have developed through different inflammatory pathways. The data we have obtained are insufficient to comment on these pathways, and it will be possible to reach more robust analyses in the presence of studies evaluating cytokine and kynurenine pathways simultaneously with BCPI. No significant difference was found between the 2 groups in terms of MPV. Specifically, recent researches conducted in other areas report that PLR is better than NLR in determining the severity of inflammation.[24] The results of our study also support this forecasting.

It has been identified that MPV, PLR, and NLR are associated with suicide risk in adult depression cases. Ragolsky et al[25] identified significantly higher platelet counts in suicidal patients than non-suicidal patients.[25-27] It is especially hard to make a strong argument for PLR to reflect disease activity without compelling evidence that indicates the biological roles of total platelets or lymphocytes in MDD pathogenesis. However, it was concluded that the number of studies investigating large sample groups and depression subtypes should be increased. In light of the information obtained from our study and other studies, it was thought that MPV could be an inflammatory marker for suicidality rather than depression, and it would be important to focus on studies involving large sample groups in this direction.

Considering other hematological parameters, Hb and Htc levels were found to be significantly lower in the case group than in the healthy control group of our study, and platelet and RDW levels were found to be significantly higher in the case group, in line with the studies conducted in both adolescents and adults. Complete blood count findings, except lymphocyte results, are parallel to studies conducted in adult and adolescent cases. It was suggested that inflammation may cause a decrease in lymphocyte production as a result of apoptosis and an increase in the number and activity of neutrophils and platelets.[6,26,27] The fact that Hb and Htc levels are lower in MDD cases with suicidality than healthy controls suggests that it is a candidate to be one of the parameters that should be examined in studies to be conducted with larger sample groups. While there was no difference between male and female gender in terms of BCPI in the case group, Hb and Htc values were found to be significantly higher in boys than girls. It has been defined that the detection of lower levels of Hb and Htc in girls than in boys, although not at the level of anemia, is an expected finding and may

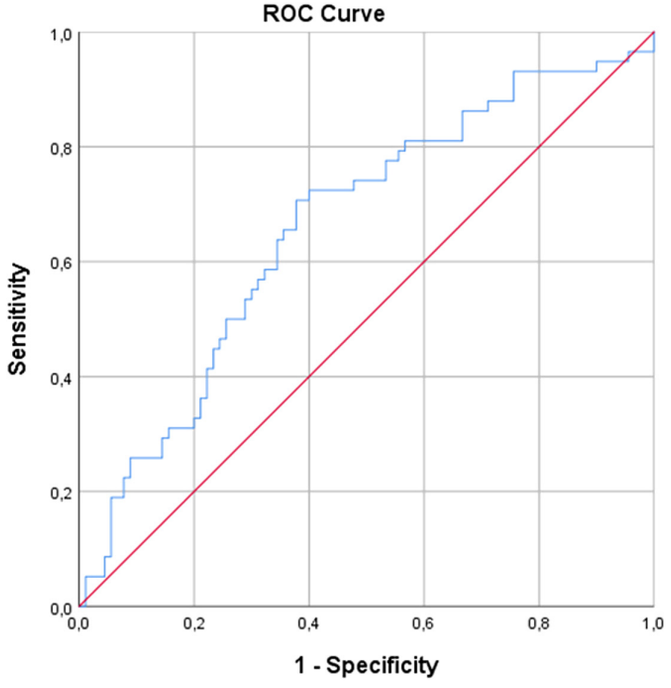

Figure 2. ROC predicting the criterion values of PLR measurements. ROC, receiver operating curve; PLR, platelet-to-lymphocyte ratio.

be associated with menstrual bleeding, and menstruation may be associated with the risk of developing anemia and depression in girls.[28,29]

In studies investigating the relationship between depression rating scales and inflammation parameters, some studies do not find a correlation between BCPI and depression scale scores in adult patients with depression,[2,5,17,30] as well as some studies that found that NLR was higher in patients with depression and assumed that it was a predictor of severe depression.[14,16] Studies reporting a relationship between severe depression and immunosuppression state that the severity of depression is associated with immunological changes, and as the severity of depression increases, lymphocyte response decreases.[31] In a study conducted with adults, it was suggested that PLR is more related to the severity of depression.[22] A study conducted in the child adolescent age group found a positive correlation between the severity of depression and NLR and PLR in depressed adolescents.[9] No significant relationship was found between BCPI levels and depression scale scores in our study. This result may be related to the fact that our study included only an outpatient sample group. Besides, unlike adult age group studies, one of the reasons for the lack of difference in terms of NLR and MPV may be that the number of depressive episodes in children is lower than that in adult patients. It is thought that it will be important to continue these studies in both a larger sample group representing the whole society and in sample groups, including inpatients.

We determined a cut-off value of 112.5 for the PLR (sensitivity as 70% and specificity as 63%). One of the most critical findings of this study is that a threshold value for PLR was determined as a depression marker in children and adolescents with MDD by performing ROC analysis. It was observed that the only study that reported a cut-off value for MDD made a recommendation on behalf of the NLR.[32] Studies indicating a cut-off value for PLR are associated with acute ischemic stroke,[33] diabetes mellitus, and myocardial infarction.[34] This study is the first to determine a cut-off value for PLR in MDD. It is thought to be essential to continue determining the threshold values for biomarkers in both childhood and adult MDD studies, and studies on this subject should be promoted.

In our study, the relationship with medical treatment was not a parameter for investigation. However, in studies conducted with adults, it was found that NLR and RDW levels[16] decreased after SSRI (selective serotonine reuptake inhibitors) treatment, and MPV and NLR values[16] decreased after inpatient treatment. It was described that MPV levels, which were initially high in MDD patients, decreased after 8 weeks of escitalopram treatment.[5,23] Conducting studies in which these obtained data will also be defined in the adolescent age group may provide important results regarding the role of inflammation in the etiopathogenesis of depression.

Limitations

This study had some limitations. The small sample size, not evaluating depression subgroups (such as those with atypical or melancholic features), case–control study design, and the inability to perform cytokine analyses accompanying inflammatory parameters are the limitations of our study. It was reported that inflammatory cytokine profiles differ according to the depression subtype.[18] It will be essential to repeat studies that will also examine depression subtypes in larger sample groups and their future analysis. It may also be possible that both the changes in the investigated biomarker values and MDD result from a common etiology, but the BCPI changes do not have a causal relationship with MDD development. Our study's strength is that it is a study conducted on BCPI in the child adolescent age group and contributes to the literature in this area and that comorbid psychiatric diagnosis groups were not included. In addition, the determination of a cut-off value for the PLR level is one of the strengths of our study. Our study presents PLR as a critical inflammatory parameter in adolescent MDD. For future studies to be conducted on suicidality in adolescent MDD, we present MPV, Hb, and Htc levels as a parameter recommendation to be examined.

CONCLUSION

This study aimed to create original material to understand the etiopathogenesis of child–adolescent depression and determine the treatment algorithms. Defining the inflammatory-immune system's role in the etiopathogenesis of depression may make inflammatory parameters a part of the algorithms in the treatment follow-up process. Interviews with the patient and surveys are primarily used in the evaluation of diagnosis and treatment processes. It is tough to make a strong argument for PLR to reflect disease activity in the absence of compelling evidence that indicates the biological roles of total platelets or lymphocytes in MDD pathogenesis, but biomarkers appear to be a promising option in psychiatry to diagnose psychiatric disorders, predict treatment response, prevent onset or relapse of major depression, and determine its severity. Biomarkers can provide a monitorable observation opportunity to determine treatment efficacy in evaluating response to treatment. Platelet lymphocyte ratio value may be an essential parameter in the clinical follow-up of MDD.

In this study, which was conducted to define the role of the inflammatory-immune system in the etiopathogenesis of depression, it was found that PLR levels, one of the inflammatory parameters, in children and adolescents diagnosed with MDD were higher in patients with depression than in healthy controls. It is thought that the inclusion of inflammatory parameter level monitoring in the clinical follow-up of MDD will allow the development of new follow-up algorithms to accelerate the treatment.

Ethics Committee Approval: Ethics committee approval was received from the Dr. Behcet Uz Children's Diseases and Surgery Training and Research Hospital (2020/17-20).

Informed Consent: Written informed consent was obtained from all participants' parents and legally responsible individuals for this study.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept - Ö. Ö.; Design - Ö.Ö., H.E., Ö.B., F.A.; Supervision - F.A.; Resource - Ö.Ö.; Materials - Ö.Ö., H.E.; Data Collection and/or Processing - Ö.Ö., Ö.B.; Analysis and/or Interpretation - Ö.Ö., F.A.; Literature Search - Ö.Ö., H.E.; Writing - Ö.Ö.; Critical Reviews - Ö.Ö., H.E., Ö.B., F.A.

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