Platelet Parameters in First-Episode Patients with Schizophrenia and Bipolar Disorder

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ABSTRACT

Background: Measurement of platelet parameters, especially mean platelet volume (MPV), in mental disorders has been gaining importance. MPV is an indicator of platelet activity, and increased MPV is considered a risk factor for cardiovascular disease. Cardiovascular diseases and associated mortality are more common in patients with schizophrenia (SZ) and bipolar disorder (BD) than in the general population. We aimed to evaluate platelet parameters, including MPV, platelet count (PLT), platelet distribution volume (PDW), and plateletcrit (PCT) level, in first-episode patients with SZ and BD before disease progression and the effect of antipsychotic drugs caused changes in their lives.
Methods: In this retrospective cohort study, we compared the platelet parameters in 72 patients with SZ at the time of their first psychotic episode and 63 patients with BD at the time of their first manic episode with 64 healthy controls.
Results: SZ group had significantly lower MPV and PCT values than the control group ($P=.003$ and $P = .03$, respectively). BD group had significantly lower MPV and PCT values than the control group ($P=.001$ and $P=.02$, respectively).
Conclusion: This is the first study to compare the platelet parameters between first-episode patients with SZ and BD and healthy controls. Although a few studies have reported an increase or decrease in platelet parameters in SZ and BD, our results are valuable in terms of evaluating platelet parameters in first-episode patients who have not started drugs.

INTRODUCTION

Platelets in plasma also affect serotonin production, release, and reuptake, similar to platelets in the central nervous system.[1] Platelet 5-HT-2A receptor may be an acceptable peripheral marker of central nervous system 5-HT-2A receptors.[2] Mean platelet volume (MPV), a pointer of platelet size, is an indicator of platelet activity.[3] Larger platelets have more granules and, after all, have more prothrombic and vasoactive factors.[4] Increased MPV is considered an independent risk factor for cardiovascular disease.[5, 6] The importance of measuring platelet parameters such as MPV is gaining importance, and platelet parameters are routinely measured in many laboratories. Although some reports have stated that MPV is associated with inflammation, reduced MPV was found in some inflammatory diseases, and no direct relationship was observed between MPV and inflammation in the acute phase.[7]

Schizophrenia (SZ) and bipolar disorder (BD) may have some common pathogenetic mechanisms. These two disorders share some common features. For example, cardiovascular risk factors, cardiovascular diseases, and associated mortality rates are high in both patient groups,[8] which may at least partly be due to the antipsychotic drug intake in these patients.[9] Some studies have stated that cardiovascular risk factors occur in the first episode before medications are initiated.[10-12] Recently, studies on the relationship between psychiatric diseases and platelets have gained importance. Changes in platelet activity have previously been reported in many psychiatric illnesses, such as major depression, BD, and SZ.[13-15] However, no study has compared platelet parameters in patients with episodes of SZ and BD with healthy controls. This study evaluated platelet parameters—MPV, platelet count (PLT), platelet distribution volume (PDW), and plateletcrit (PCT)—in patients with the first psychotic episode of SZ and the first manic episode of BD and compared them with healthy controls to explore the diagnostic value of platelet parameters in SZ and BD.

METHODS

Subjects

This study was designed as a retrospective cohort study. Our study included patients from the psychiatric clinic of a university-affiliated training and research hospital between August 1, 2015, and August 1, 2020, and they were followed up at this hospital for at least 6 months. We recorded MPV, PLT, PDW, and PCT levels of 72 patients with SZ at the time of their first psychotic episode and 63 patients with BD at the time of their first manic episode and compared them with the data of 64 age- and sex-matched healthy individuals. Patients with risk factors (diabetes mellitus, cardiovascular disease, hypertension, hyperlipidemia, cancer, pregnancy, alcohol, drug, and substance use) that may have an effect on platelet parameters were excluded. Patients with mental disorder comorbidities and unclear diagnoses were also excluded.

SZ and BD were diagnosed according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

Procedure

This study was approved by the Ethics Committee of Adıyaman University (no. 2020/7-25 dated July 21, 2020). Blood samples were taken from the antecubital vein of all study participants between 9 AM and 10 AM after at least 8 h of starvation. Blood samples were centrifuged for 1 h. Then serum samples were examined the same day in the biochemistry laboratory of our university-affiliated training and research hospital with a CELL-DYN 3700 SL analyzer (Abbott Diagnostics, Chicago, IL, USA). The reference intervals were assumed as 142-424 10^3/μL for PLT, 6.8-10.8 fL for MPV, 0-1000 fL for PDW, 0-1000% for PCT.

Statistical Analysis

IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp. Armonk, NY: USA.) was used for all statistical analyses. Descriptive parameters are expressed as mean ± standard deviation or number (percentage). The chi-square test was used to compare categorical data. Normality of distribution was tested with Levene's test and homogeneity tests. The difference between the groups was examined using one-way ANOVA and Bonferroni tests, a post hoc test, for normally distributed data, and non-normally distributed data were

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MAIN POINTS

- Mean platelet volume (MPV) and plateletcrit (PCT) values in first-episode patients with schizophrenia (SZ) and bipolar disorder (BD) were significantly lower than healthy controls.
- Decreased MPV and PCT can be used as supportive data for the diagnosis of SZ and BD.
- Because first-episode patients have not started medication yet and have not experienced changes in life due to chronic disease, it indicates a specific change of the disease making this finding a valuable one.
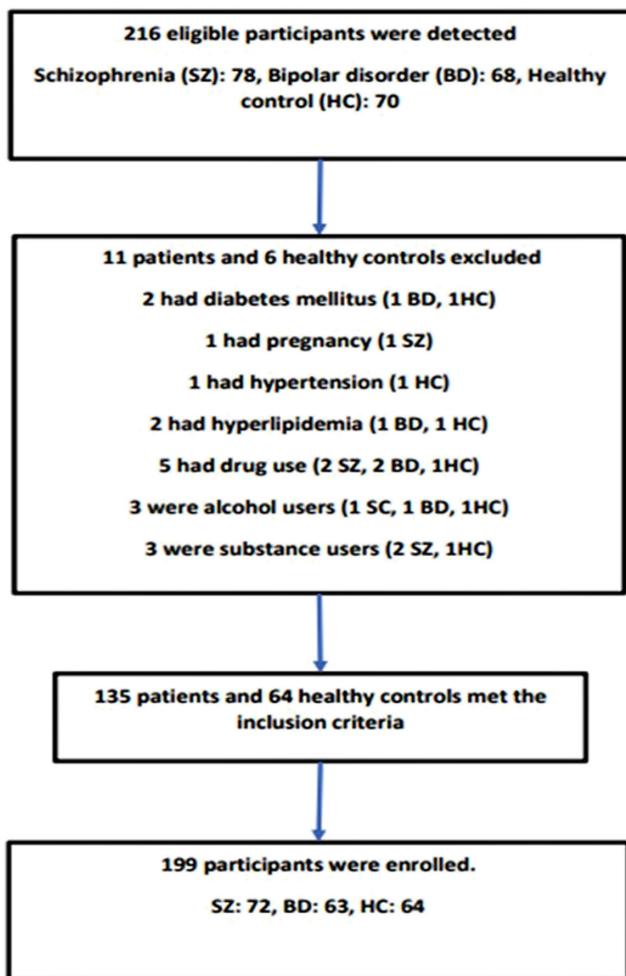
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evaluated using the Kruskal–Wallis test. A P value of <.05 was accepted statistically significant. Receiver operating characteristic (ROC) curve analysis was performed to examine the diagnostic value of platelet parameters.

RESULTS

A total of 199 individuals were included: 72 patients with SZ (mean age: 30.35 ± 9.09), 63 patients with BD (mean age: 27.92 ± 8.33), and 64 healthy controls (mean age: 31.23 ± 10.62). The SZ group comprised 28 (38.9%) women and 44 (61.1%) men. The BD group comprised 32 (50.8%) women and 31 (49.2%) men. The control group comprised 35 (54.7%) women and 29 (45.3%) men. No significant difference was detected in age and gender between the 3 groups (P = .122 and P = .155, respectively).

There was a significant difference between the 3 groups in terms of MPV and PCT (P < .001 and P = .012, respectively). There was no significant difference between the 3 groups in terms of PLT and PDW. Comparison of MPV, PCT, PDW, and platelet counts of groups is shown in Table 1.

No significant difference was detected between the SZ and BD groups in MPV and PCT in the Bonferroni test conducted to find in which group among the 3 groups the difference originated from (P > .99); however, significant differences were noted between the SZ group and control group (P = .003 and P = .03, respectively) and between the BD group and control group (P = .001 and P = .02, respectively).

Because both the SZ and BD groups had significantly lower MPV and PCT values than the control group, ROC curve analysis was applied to examine the diagnostic value of platelet parameters.

ROC curve analysis for the SZ group is illustrated in Figure 1. The area under the ROC curve (AUC) of MPV levels for SZ was 0.675 (95% CI: 0.585-0.766, P < .001).

Table 1. Comparison of Mean Platelet Volume, Platelectrit, Platelet Distribution Width and Platelet Counts of Groups

Parameters	Schizophrenia	Bipolar Disorder	Control	P
MPV (fL)	7.87 ± 1.50	7.76 ± 1.83	8.83 ± 1.62	<.001[a]**
PCT (%)	0.18 ± 0.04	0.18 ± 0.05	0.20 ± 0.04	.012[a]*
PDW (fL)	18.81 ± 1.92	18.34 ± 1.76	18.33 ± 2.72	.269[b]
PLT (10³/uL)	247.71 ± 58.40	250.58 ± 63.11	241.91 ± 46.75	.679[a]

The significant results are presented in bold.
[a]One way ANOVA.
[b]Kruskall–Wallis test.
*P < .05.
**P < .001.
MPV, mean platelet volume; PCT, platelectrit; PDW, platelet distribution width; PLT, platelet.

Figure 1. Flow-chart of the study enrollment protocol

Figure 2. ROC curve analysis for schizophrenia group

The optimal cutoff value for the MPV level was 8.17 fL, and its sensitivity and specificity for the diagnosis of SZ were 68 and 64%, respectively. The AUC of PCT levels for SZ was 0.632 (95% CI: 0.538-0.725, $P = .008$). The optimal cutoff value for the PCT level was 0.20 fL, and its sensitivity and specificity for the diagnosis of SZ were 69 and 52%, respectively.

ROC curve analysis for the BD group is illustrated in Figure 2. The AUC of MPV levels for BD was 0.702 (95% CI: 0.610-0.794, $P < .001$). The optimal cutoff value for MPV level was 7.91 fL, and its sensitivity and specificity for the diagnosis of BD were 67 and 66%, respectively. The AUC of PCT levels for BD was 0.653 (95% CI: 0.557-0.749, $P = .003$). The optimal cutoff value for PCT level was 0.19 fL, and its sensitivity and specificity for the diagnosis of BD were 62 and 67%, respectively.

DISCUSSION

In this study, we evaluated the platelet parameters of patients with SZ in the first psychotic episode and patients with BD in the first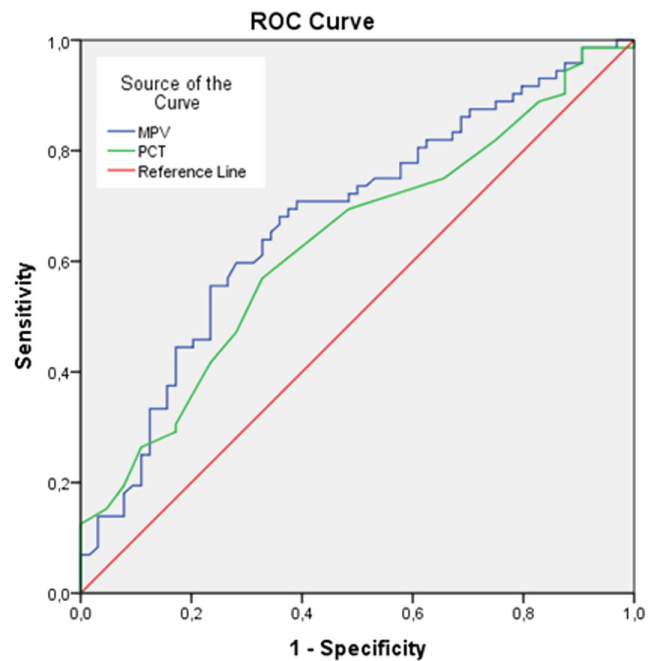 manic episode and compared them with the parameters of healthy controls. Although platelet parameters have been examined in patients with SZ and BD in the past, this is the first study to compare the platelet parameters between first-episode patients and healthy controls.

Notably, MPV and PCT values in first-episode patients with SZ and BD were significantly lower than healthy controls. Because first-episode patients have not started medication yet and have not experienced life changes due to chronic disease, it indicates a specific change of the disease, making this finding a valuable one. Antipsychotics for SZ and BD have shown to be an independent risk factor for increased MPV.[16]

One study compared platelet parameters in patients with SZ, BD, and unipolar depression.[15] The authors found higher MPV levels in the SZ and BD groups, but their study did not have a control group. In addition, the groups were not age- and sex-matched, and data on patients' medication use were not available.

Another study reported increased MPV in patients with SZ, but the cohort was not first-episode patients and included the ones taking antipsychotics.[17] Therefore, this result may be thought to be due to the effect of antipsychotics. In another retrospective study, increased MPV and PCT were found in first-episode SZ patients.[18] However, we are confident in the accuracy of our results because the patients in our study were followed up in our clinic with the same diagnosis.

In a study, higher MPV and PCT values were determined in patients with BD than in healthy controls, which is inconsistent with our results.[19] This discrepancy may be because we included first-episode manic patients. Similar to our study, another study found that MPV levels were

lower in manic patients than in the control group.[20] Again, in another study conducted by Inanli et al.[21] on patients with BD, high MPV values were found in both depressive and manic episodes, but the patients were not first-episode patients and were already using medications.[21] One study demonstrated no difference between MPV in patients with mixed and manic episodes and the control group.[22] This study included patients who had taken medication at the time of admission but not for the last 1 month. Considering the different results and confounding factors in all these studies, we think that our data clearly demonstrate that MPV values are decreased at the time of the first manic episode in BD patients who have not started antipsychotic drugs.

Although platelet parameters are routinely measured, their clinical significance has not been fully elucidated, thus limiting their diagnostic use. We found that MPV and PCT had a sensitivity of 67% and 62%, respectively, and specificity of 66% and 67%, respectively, for BD diagnosis and a sensitivity of 68% and 69%, respectively, and a specificity of 64% and 52%, respectively, for SZ diagnosis. These findings indicate that decreased MPV and PCT can be used as supportive data for the diagnosis of SZ and BD. However, more research is required to demonstrate the utility of these findings for diagnosis.

Increased MPV is a risk factor for cardiovascular disease.[5,6] Cardiovascular disease and associated mortality rates are high in patients with SZ and BD.[8] Therefore, high MPV levels can be expected in patients with SZ and BD. However, in first-episode patients, lower MPV values may be seen, as indicated by our findings. This implies that the side effects of antipsychotic drugs and behavioral patterns
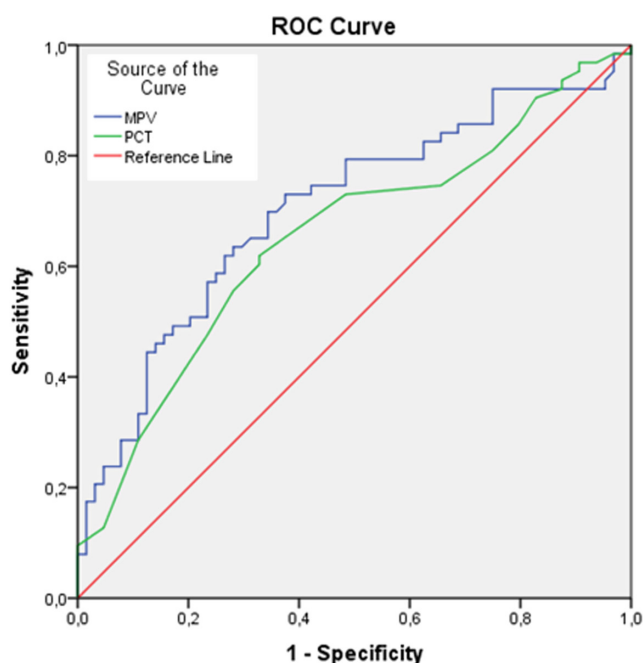
such as overeating, sedentary life, and inadequate medical care contribute to the etiopathogenesis of medical comorbidities in patients with SZ and BD.[23-27]

Our study had some limitations. The relationship between MPV level and disease severity could not be searched because this study was performed retrospectively, and we could not reach any scale showing disease severity. Nevertheless, this study is valuable in terms of evaluating the platelet parameters of the first-episodes patients with SZ and BD. Finally, our results showed that the first-episodes patients with SZ and BD had significantly lower MPV and PCT values than the healthy subjects.

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Figure 3. ROC curve analysis for bipolar disorder

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