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Review of Standard Laboratory Blood Parameters in Patients with Schizophrenia and Bipolar Disorder

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ABSTRACT

Introduction: Symptomatic and etiopathologic heterogeneity of schizophrenia (SCH) and bipolar disorder (BD) can be adequately addressed using a dimensional approach to psychopathology, as well as interpreting physiological properties and markers as predictors of disease onset and relapse. Risk factors, genetic and environmental, are likely to modify the neurobiological processes characteristic of certain physiological processes that manifest to a greater degree of overlapping symptoms. One of the most common laboratory tests in psychiatric patients is a standard laboratory blood test. It gives us an insight into the general somatic condition of the patient. It assesses the ability to transport oxygen to tissues and carbon dioxide back to the lungs via erythrocytes (RBC) and hemoglobin (HGB) as their most important constituents, and is also an indicator of iron status and blood oxygenation. **Aim:** Schizophrenia (SCH) and bipolar disorder (BD) are psychiatric disorders whose complex etiology and pathogenesis are still far from known. A correlation between red blood cell abnormalities and these diseases has been recognized in some studies. One of the most common laboratory tests in psychiatric patients is a standard laboratory blood test. However, so far there is a small number of published papers that relate to the relationship between laboratory parameters of blood and the aim of this paper is to reveal more light in this subject. **Methods:** The research was done as an observational prospective clinical study that has evaluated different physiological and pathological parameters in patients with BD and SCH over a two-year period. A total of 159 patients with schizophrenia, 61 patients diagnosed with bipolar disorder and 82 healthy subjects participated in this study. **Results:** At baseline, BD compared to SCH patients had higher mean lymphocyte count (2,6±0,7 vs. 2,0±0,6x10^9; p=0,006) and haemoglobin concentration (146,8±12,2 vs. 140,2±14,7 g/L; p=0,03), and significantly lower red cell distribution width (13,6±2,2 vs. 14,7±1,8%; p=0,008). In both BD and SCH patients there was a significant number of patients with low red blood cells count and low haemoglobin concentration, and high MCH and MCHC at baseline and at 3 and 6 months of follow up. **Conclusions:** The finding that SCH as well as BD differed from controls with respect to red blood cells, hemoglobin, lymphocytes, and average platelet count was consistent with previous findings and could be understood as a qualitative measure in the evaluation of this sample. The fact that no association with other parameters was found, as well as an association with the diagnosis, does not exclude that these associations can be found in larger samples.

Key words: Schizophrenia, Bipolar disorder, Blood cells

1. INTRODUCTION

Symptomatic and etiopathologic heterogeneity of schizophrenia (SCH) and bipolar disorder (BD) can be adequately addressed using a dimensional approach to psychopathology, as well as interpreting physiological properties and markers as predictors of disease onset and relapse. Risk factors, genetic and environmental, are likely to modify the neurobiological processes characteristic of certain physiological processes that manifest to a greater degree of overlapping symptoms. Several parallel studies on the endophenotype of SCH and BD have investigated the genotype-endophenotype relationship (1, 2), which is a sufficiently informative explanation of the extent to which these two diseases share etiopathophysiology (3). There are many different aspects that can be discussed in these disorders, and one of them is the physiological characteristics of the red blood cell. A correlation between red blood cell abnormalities and these diseases has been recognized in previous studies. (4-6).

One of the most common laboratory tests in psychiatric patients is a standard laboratory blood test. It gives us an insight into the general somatic

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condition of the patient. It assesses the ability to transport oxygen to tissues and carbon dioxide back to the lungs via erythrocytes (RBC) and hemoglobin (HGB) as their most important constituents, and is also an indicator of iron status and blood oxygenation (7, 8). Hematocrit (HCT) is the volume of erythrocytes in a unit of whole blood. Erythrocyte constants are calculated from the number of erythrocytes, the concentration of HGB and HCT and give information about the quality of erythrocytes. MCV (mean cell volume) is the average volume of erythrocytes, and provides information about the size of erythrocytes. MCHC (mean cell hemoglobin concentration) represents the average hemoglobin concentration per liter of erythrocytes. RDW (red cell distribution width) refers to a measure of RBC size variability, and specifically indicates the existence of one or more erythrocyte populations, and is also an important prognostic indicator of treatment efficacy. Changes in the values of individual RBC constants are diagnostically significant in the classification of individual hematological diseases and are always observed in correlation with the obtained values of RBC count and HGB concentration. Leukocytes (WBC), are formed in the bone marrow and participate in the immune response. There are five different types of white blood cells; they are all part of the body's defenses. Neutrophilic granulocytes are the most abundant and defend with their phagocytic activity. Monocytes are immature cells, precursors of macrophages, high defense capabilities within tissues. Eosinophilic granulocytes participate in the body's defense against allergic agents and parasitic infections. Lymphocytes participate in humoral and cellular immunity with their T and B subpopulations. Basophilic granulocytes participate in the allergic response. There are already few well known hypothesis about correlation of SCH and immune blood parameters. One of them suggest that cytokines that are produced by chronically activated macrophages and T-lymphocytes are the key indicators or mediators of schizophrenia (9). Second one postulates that shift from Th1 in Th2 immune responses is major feature in SCH (10). And there is an observation that activated CNS microglia release pro-inflammatory cytokines and free radicals that cause abnormal neurogenesis, neuronal degradation, and white matter abnormalities contributing to the pathophysiology of schizophrenia (11). However, so far there is a small number of published papers that relate to the relationship between laboratory parameters of blood and the aim of this paper is to reveal more light in this subject.

2. AIM

Schizophrenia (SCH) and bipolar disorder (BD) are psychiatric disorders whose complex etiology and pathogenesis are still far from known. A correlation between red blood cell abnormalities and these diseases has been recognized in some studies. One of the most common laboratory tests in psychiatric patients is a standard laboratory blood test. However, so far there is a small number of published papers that relate to the relationship between laboratory parameters of blood and the aim of this paper is to reveal more light in this subject.

3. METHODS

The research was done as an observational prospective clinical study that has evaluated different physiological and pathological parameters in patients with BD and SCH over a two-year period. Implementation, examination and determination of clinical, test and laboratory parameters were performed together with all other routine procedures within the treatment and monitoring of patients during hospitalization at the Psychiatric Clinic, Clinical Center University of Sarajevo (CCUS), so that ethical principles of working with patients were not violated.

Symptoms of SCH and BD were determined using validated instruments to assess the most reliable psychiatric diagnosis. A total of 159 patients with SCH, 61 patients diagnosed with BD and 82 healthy subjects (HC) participated in this study. In a period of two years, 77 patients with SCH in hospital and 82 patients with SCH in outpatient treatment, 38 patients with BD in hospital and 23 patients with BD in outpatient, at the Psychiatric Clinic, CCUS and 82 HC, were included. Patients on hospital treatment were included from consecutive admissions. The lifetime best diagnosis assessment with assessment of all episodes during life was awarded according to DSM-IV criteria, using information from multiple sources. The study included: Patients diagnosed with SCH and BD diagnosed according to DSM-IV criteria and HC who do not have any of the psychiatric disorders, as well as negative heredity and patients older than 18 years and younger than 65. The study did not include: Patients who refuse to participate in studies, patients with somatic diseases that affect the change in blood count, as well as patients who are unable to give their oral and written informed consent.

	Bipolar disorder (N=31)	Schizophrenia (N=58)	p-value
WBC (x109)	8.0±2.0	8.4±2.6	0.6
NEU (x109)	4.6±1.7	5.7±2.1	0.09
LYM (x109)	2.6±0.7	2.0±0.6	0.006
MONO (x109)	0.6±0.2	0.5±0.2	0.6
EOS (x109)	0.15±0.1	0.15±0.1	0.9
BASO (x109)	0.07±0.02	0.07±0.02	0.4
RBC (x1012)	4.7±0.4	4.6±0.5	0.2
HGB (g/L)	146.8±12.2	140.2±14.7	0.03
HCT (%)	42.5±3.4	41.0±4.1	0.09
MCV (fL)	90.1±3.7	89.2±4.8	0.4
MCH (pg)	31.1±1.4	30.5±1.9	0.1
MCHC (g/L)	345.8±11.8	342.3±11.4	0.2
RDW (%)	13.6±2.2	14.7±1.8	0.008
PLT (x106)	270.1±57.6	276.8±65.9	0.6
MPV (fL)	7.8±1.5	7.4±0.95	0.1

Table 1. Complete blood count in patients with bipolar disorder and schizophrenia at baseline

	Bipolar disorder (N=31)	Schizophrenia (N=58)	p-value
WBC (x109)	7.3±2.0	7.4±2.1	0.9
NEU (x109)	4.6±1.8	4.9±1.5	0.7
LYM (x109)	2.2±0.5	2.0±0.6	0.2
MONO (x109)	0.5±0.2	0.5±0.2	0.9
EOS (x109)	0.14±0.2	0.15±0.2	0.8
BASO (x109)	0.06±0.04	0.06±0.03	0.5
RBC (x1012)	4.8±0.6	4.8±0.5	0.98
HGB (g/L)	148.4±15.7	144.4±15.0	0.2
HCT (%)	43.3±4.2	42.3±4.2	0.3
MCV (fL)	90.9±4.1	88.6±4.4	0.02
MCH (pg)	31.2±1.5	30.3±1.8	0.02
MCHC (g/L)	342.7±8.5	341.6±11.0	0.6
RDW (%)	13.9±2.2	14.1±2.8	0.7
PLT (x106)	255.2±58.1	261.4±55.7	0.6
MPV (fL)	8.3±2.1	7.3±1.3	0.008

Table 2. Complete blood count in patients with bipolar disorder and schizophrenia 3 months after follow-up

	Bipolar disorder (N=31)	Schizophrenia (N=58)	p-value
WBC (x109)	8.1±2.4	7.2±2.5	0.2
NEU (x109)	5.1±2.2	4.1±1.4	0.04
LYM (x109)	2.6±0.7	2.1±0.7	0.024
MONO (x109)	0.6±0.1	0.4±0.2	0.003
EOS (x109)	0.13±0.1	0.15±0.1	0.52
BASO (x109)	0.07±0.04	0.05±0.04	0.2
RBC (x1012)	4.8±0.4	4.7±0.4	0.5
HGB (g/L)	146.8±11.8	143.0±13.9	0.2
HCT (%)	43.2±3.0	42.2±3.6	0.2
MCV (fL)	90.5±3.6	89.4±4.0	0.25
MCH (pg)	30.7±1.4	30.3±1.8	0.4
MCHC (g/L)	339.1±8.9	339.4±12.6	0.9
RDW (%)	12.9±1.8	14.2±2.4	0.02
PLT (x106)	262.9±71.0	273.1±66.2	0.5
MPV (fL)	7.8±1.3	7.4±1.5	0.25

Table 3. Complete blood count in patients with bipolar disorder and schizophrenia 6 months at follow-up

4. RESULTS

During the two-year period, the study included 77 patients with SCH in hospital and 82 SCH patients in outpatient treatment, 38 patients with BD in hospital, and 23 patients with BD in outpatient treatment at the Psychiatric Clinic, CCUS as well as 82 HC.

Mean age in patients with BD was 42.5±10.1 years and was not significantly different compared to mean age in SCH patients (39.1±10.4 years; p=0.15). Most of the BD patients were in the age group 45-54 years (45,2% patients), while SCH patients were more prevalent in younger age groups.

At baseline, BD compared to SCH patients had higher mean lymphocyte count (2.6±0.7 vs. 2.0±0.6x10^9; p=0.006) and haemoglobin concentration (146.8±12.2 vs. 140.2±14.7 g/L; p=0.03), and significantly lower red cell distribution width (13.6±2.2 vs. 14.7±1.8%; p=0.008) (Table 1).

At 3 months follow-up, BD patients compared to SCH patients had significantly higher mean corpuscular volume (90.9±4,1 vs. 88.6±4.4 fL; p=0.02), haemoglobin concentration (31.2±1.5 vs. 30.3±1.8 pg; p=0.02) and mean platelets volume (8.3±2.1 vs. 7.3±1.3 fL; p=0.008) (Table 2).

At 6 months follow-up, BD patients compared to SCH patients had significantly higher neutrophil (5.1±2.2 vs. 4.1±1.4 x10^9; p=0.04), lymphocyte (2.6±0.7 vs. 2.1±0.7 x10^9; p=0.024) and monocyte count (0.6±0.1 vs. 0.4±0.2 x10^9; p=0.003)(Table 3).

Red cell distribution width was significantly lower in BD compared to SCH patients (12.9±1.8 vs. 14.2±2.4%; p=0,02). Mean white blood cells, neutrophil, lymphocyte, eosinophil, basophil and platelets count were within referral values in both BD and SCH patients at baseline, 3 and 6 months of follow up. However, in both BD and SCH patients mean monocyte count was significantly lower compared to referral values. Low monocyte count (<0.8x10^9) was found in 94.1% of BD and in 95.5% of SCH patients at baseline and at 3 and 6 months follow-up. In both BD and SCH patients there was a significant number of patients with low red blood cells count and low haemoglobin concentration, and high MCH and MCHC at baseline and at 3 and 6 months of follow up (Table 4).

Distribution of patients with BD and SCH with low and hight red cells distribution width at baseline and 3 and 6 months of follow-up is shown in Figure 2. There was a significantly higher number of BD patients with low red cells distribution width (29.0%) compared to SCH patients (8.6%) at baseline (X^2=6.5 ; p=0.039). Low mean platelets volume was prevalent in both BD and SCH patients at baseline and on follow-up. Analyzing the changes in blood count from baseline to 6 months follow up, there was a significant decrease in MCHC values in patients with BD. Mean MCHC significantly decreased from baseline to 6 months follow-up (345.8±11.8 vs. 339.1±8.9g/L; p=0.049) (Table 5).

	BD (N=31)			SCH (N=58)		
	Baseline	3 mo(s) follow-up	6 mo(s) follow-up	Baseline	3 mo(s) follow-up	6 mo(s) follow-up
Low RBC	6 (19.4%)	5 (16.1%)	4 (12.9%)	13 (22.4%)	9 (15.5%)	7 (12.1%)
Low HGB	9 (29.0%)	7 (22.6%)	5 (16.1%)	24 (41.4%)	16 (27.6%)	21 (36.2%)
Low HCT	12 (38.7%)	8 (25.8%)	5 (16.1%)	29 (50%)	18 (31.0%)	17 (29.3%)
Low MCV	3 (9.7%)	5 (16.1%)	2 (6.4%)	15 (25.9%)	13 (22.4%)	12 (20.7%)
High MCH	15 (48.4%)	14 (45.2%)	10 (32.3%)	20 (34.5%)	17 (29.3%)	16 (27.6%)
High MCHC	10 (32.3%)	6 (19.4%)	1 (3.2%)	17 (29.3%)	12 (20.7%)	7 (12.1%)

Table 4. Red blood cells parameters in patients with bipolar disorder and schizophrenia at baseline and 3 and 6 months of follow-up.

	Baseline	3 months follow-up	6 months follow-up	p-value
WBC (x109)	8.0±2.0	7.3±2.0	8.1±2.4	0.3
NEU (x109)	4.6±1.7	4.6±1.8	5.1±2.2	0.6
LYM (x109)	2.6±0.7	2.2±0.5	2.6±0.7	0.2
MONO (x109)	0.6±0.2	0.5±0.2	0.6±0.1	0.9
EOS (x109)	0.15±0.1	0.14±0.2	0.13±0.1	0.9
BASO (x109)	0.07±0.02	0.06±0.04	0.07±0.04	0.4
RBC (x1012)	4.7±0.4	4.8±0.6	4.8±0.4	0.9
HGB (g/L)	146.8±12.2	148.4±15.7	146.8±11.8	0.9
HCT (%)	42.5±3.4	43.3±4.2	43.2±3.0	0.6
MCV (fL)	90.1±3.7	90.9±4.1	90.5±3.6	0.7
MCH (pg)	31.1±1.4	31.2±1.5	30.7±1.4	0.4
MCHC (g/L)	345.8±11.8	342.7±8.5	339.1±8.9	0.049
RDW (%)	13.6±2.2	13.9±2.2	12.9±1.8	0.2
PLT (x106)	270.1±57.6	255.2±58.1	262.9±71.0	0.6
MPV (fL)	7.8±1.5	8.3±2.1	7.8±1.3	0.4

Table 5. Complete blood count in patients with bipolar disorder at baseline and during follow-up

	Baseline	3 months follow-up	6 months follow-up	p-value
WBC (x109)	8.4±2.6	7.4±2.1	7.2±2.5	0.02
NEU (x109)	5.7±2.1	4.9±1.5	4.1±1.4	0.004
LYM (x109)	2.0±0.6	2.0±0.6	2.1±0.7	0.9
MONO (x109)	0.5±0.2	0.5±0.2	0.4±0.2	0.02
EOS (x109)	0.15±0.1	0.15±0.2	0.15±0.1	0.4
BASO (x109)	0.07±0.02	0.06±0.03	0.05±0.04	0.2
RBC (x1012)	4.6±0.5	4.8±0.5	4.7±0.4	0.9
HGB (g/L)	140.2±14.7	144.4±15.0	143.0±13.9	1.0
HCT (%)	41.0±4.1	42.3±4.2	42.2±3.6	0.7
MCV (fL)	89.2±4.8	88.6±4.4	89.4±4.0	0.5
MCH (pg)	30.5±1.9	30.3±1.8	30.3±1.8	0.95
MCHC (g/L)	342.3±11.4	341.6±11.0	339.4±12.6	0.9
RDW (%)	14.7±1.8	14.1±2.8	14.2±2.4	0.007
PLT (x106)	276.8±65.9	261.4±55.7	273.1±66.2	0.35
MPV (fL)	7.4±0.95	7.3±1.3	7.4±1.5	0.037

Table 6. Complete blood count in patients with schizophrenia at baseline and during follow-up

In SCH patients, mean white blood cells count significantly decreased from baseline to 6 months follow-up (8.4±2.6 vs. 7.2±2.5x10^9; p=0,02), as well as neutrophils (5.7±2.1 vs. 4.1±1.4x10^9; p=0,004), monocytes (0.5±0.2 vs. 0.4±0.2 x10^9; p=0.02) and red cells distribution width (14.7±1.8 vs. 14.2±2.4%; p=0.007) (Table 6).

5. DISCUSSION

The aim of this study was to investigate the differences in red and white blood cell parameters in a sample of patients with SCH and BD. The study confirmed that there are differences for some of the analyzed parameters. Upon admission, patients with BD had higher mean lymphocyte counts and HGB concentrations compared to patients with SCH and a significantly lower width of red blood cell distribution. In our study, patients with BD had higher hemoglobin concentrations compared with patients with SCH, in contrast to the results of the study by Wysokinski and Szczeposka (2018) who found that patients with SCH had a higher mean HGB and erythrocyte count. In the given study, patients with BD had reduced red blood cell parameters, which is in line with many studies that support the hypothesis that low values of red blood cell parameters may contribute to the risk of developing of some psychiatric disorder as depression (12). Patients with SCH had significantly higher HCT values compared with patients with BD, which is consistent with previous research showing the same results due to dehydration that occurs due to acute psychosis (13). Inflammatory processes are thought to play a significant role in the etiopathogenesis of BD and there are some suggestions that inflammatory cytokines in the systemic circulation suppress erythropoesis, resulting in inflammatory anemia, known as chronic anemia. The results of our study, which included an assessment of the values of blood parameters within the red line of patients with BD, are consistent with the results of a study conducted by a group of authors (14). This indicates that the values of RBC, HCT and the average concentration of HGB in the blood in patients diagnosed with BD were reduced in comparison with the control group of subjects. By comparing the values of hemograms in patients with BD and HC in the control group, it was shown that the ratios of inflammatory cells changed during manic episodes, which actually supports the hypothesis of activation of inflammatory processes during this episode.

Also, patients with BD have the highest values of MCV and MCH, and at the same time the lowest mean values of RBC. The most common occurrence of erythrocyte values below the lower limit was found in a patient diagnosed with BD. Interestingly, it has not been confirmed by previous observations indicating that there are differences in hematological parameters with respect to the type of episode within BD. Hochman et al. observed that patients had elevated HGB and HCT values during a depressive episode and decreased HGB and HCT values during a manic episode (15). Compared with patients with SCH, there was a significantly higher percentage of subjects with evident anemia or impaired values of erythrocyte parameters who were diagnosed with affective disorders. In most of these parameters, male patients in whom it was increased. In most epidemiological studies, as well as in ours, the values of most red blood cell parameters were elevated in male subjects (16). By cross-section of clinical groups, age was negatively correlated with most parameters. In the examined group of patients with SCH, the majority were male, younger age and these two discrepancies resulted in a better hematological status of this group. The study indicated that there are differences in red line parameters when comparing groups of patients with diagnoses of SCH, unipolar depression, and BD (both manic and depressive episodes). In patients with unipolar or BD, the appearance of anemia or deviations in the values of red line parameters when compared with patients with SCH is evident. A positive correlation between age and MCV as well as erythrocyte values, and negative correlations of age and other parameters, were found in all examined groups. Many psychiatric patients have an increased risk

of developing cardiovascular diseases caused by atherosclerotic disorders, obesity and smoking, monitoring of impaired redness is necessary.

During the 3-month follow-up, patients with BD had significantly higher average erythrocyte volume compared to patients with SCH, which is consistent with the Wysokinski and Szczeposka (2018) study (12). Patients suffering from SCH and BD had significantly lower red blood cell and HGB values at the beginning of treatment, as well as after three and six months, which is consistent with many studies (17). This is supported by the fact that SCH is a serious and complex multifactorial disorder of unknown etiology that significantly impairs the quality of life and that people with this disease also suffer from other somatic diseases that are unrecognized and untreated in as many as 50% of cases. Significant risk factors are smoking, obesity, inadequate diet, reduced physical activity (18). They are more likely to have various somatic diseases that are often neglected and untreated. Cardiovascular, cerebrovascular and malignant diseases are the most common. Red blood cell parameters may also be due to other factors such as drugs, which we did not include in this study which may be considered a drawback of the study. On the other hand, the findings were accompanied by a significant reduction in MCHC in patients with BD, compatible with other studies, suggesting inflammation as a possible cause of elevated RDW and PDW (19, 20). Studies have shown that serotonin metabolism disorders result in increased levels of oxidative stress. Thus, it can affect the membrane of erythrocytes and platelets. Due to damage to the antioxidant defense system, ROS can damage the endothelium and activate platelets that cause cardiovascular disease (21). The evaluation of MPV, RDW and PDW regarding the development of laboratory methods in the sciences of clinical hematology has become routine. However, they are not commonly used in diagnosis and monitoring (22). In our study, there was a significantly higher number of patients with BD with a low red cell width (29.0%) compared to patients with SCH (8.6%) at baseline (X^2 = 6.5; p = 0.039) (Figure 2). Low mean platelet counts were also present in patients with BD and SCH in the initial phase and after follow-up (Figure 3). Certain studies have shown an association between platelet counts and serotonin transporters, which are later associated with an increased risk of cardiovascular disease in people with depression and anxiety (23).

A low average platelet count, in our study, was also present in patients with SCH and BD during hospitalization, as well as 3 and 6 months after outpatient treatment. Platelet volume depends on increased platelet activation or production and on the presence of immature platelets in the peripheral blood. Platelet activation and its release from granules leads to a reduction in platelet volume, which is associated with a decrease in peripheral platelets, so bone marrow activity and the presence of immature platelets in the blood is inevitable, leading to an increase in PDW (24, 25). Studies of platelet disorders in people with anxiety indicate damage to the serotonin transporter. In this study, a significant reduction in MPV indicates a possible disorder of serotonin metabolism and its transporters, which could be a possible therapeutic guide in these patients. A study by Atagun et al (2016) demonstrated a characteristic improvement in this parameter for lithium users (26). Circulating blood cells can be disturbed both qualitatively and quantitatively in psychiatric disorders. Previous studies have reported changes in blood cell number and function in psychiatric disorders. The changes may be related to different etiologies in different psychiatric disorders but also to medications. If the findings are replicated in relation to drugs it will help to resolve the different biological pathways in SCH and BD.

Hochman et al. (15) found that patients during a depressive episode have higher levels of HGB and HCT and lower levels of HGB and HCT during episodes of mania (15). For most parameters, male gender was associated with reduced risk below normal values, while age was associated with increased risk. As shown in larger epidemiological studies, men have higher values of most red blood cell parameters (16). Also, age was negatively associated with most parameters in all clinical groups. In the study group, patients with schizophrenia were significantly younger. This deviation may result in better hematologic parameters in patients with SCH. In our study, there is no difference in gender representation among the examined groups.

Our study showed that patients with BD had a significantly higher number of total lymphocyte patients compared to patients with SCH, which is consistent with a study conducted by Selzuck et al in 2017 (27). Also, the total number of neutrophilic lymphocytes was significantly higher at the beginning of the study in relation to the period after three months of follow-up in patients with both BD and SCH, which correlates with a study conducted by Catak et al. 2018. Patients with BD had a higher number of lymphocytes during the psychotic phase of the disease, while the number of lymphocytes was reduced during the clinical remission of the disease (30). The same speaks in favor of the previously established theory of inflammatory activation that occurs in affective disorders. Based on these changes in the immune system, it can be assumed that other therapeutic strategies for affective disorders are possible, such as the application of anti-inflammatory and monoclonal antibody therapy. Analysis of white blood cell count and reactive protein C value in patients with psychotic disorders may indicate the severity of the clinical picture within the psychotic illness, as well as the therapeutic response. The study, conducted by Johann Steiner and colleagues, included the analysis of blood samples from 253 hospitalized patients diagnosed with a psychotic disorder (29). Subjects were divided into two groups n = 129 with a diagnosis of the first psychotic episode and n = 124 with a diagnosis of schizophrenia who were not taking antipsychotics. White blood cell counts and CRP values were compared in patients with psychotic disorder and healthy subjects (n = 294). Neutrophil, monocyte, and CRP values were found to be significantly elevated in patients compared to the healthy group

at the beginning of the study, while eosinophils were decreased at the beginning of the study in the group of patients. Patients who had elevated neutrophil counts at the beginning of the study had positive symptoms present on the PANSS-P scale.

In our study we have found that more significant blood lymphocyte parameters are present in patients with SCH in comparison with controls from BD, so our research can support earlier given hypothesis. In addition to this finds we are in similar observations with previous research that total number of lymphocytes is not related to antipsychotic treatment itself. CRP values at baseline correlated with PANSS-P scale values in the group of patients with the first psychotic episode, but not in the group diagnosed with SCH. Antipsychotic therapy was then included in all psychotic subjects (n = 163) for a period of 6 weeks. Neutrophil and CRP values decreased during this period, remaining elevated in the healthy group. In contrast, eosinophil values were elevated in psychotic subjects that the values did not differ from the control group over a period of six weeks. The degree of improvement in positive symptoms after antipsychotic treatment correlated with changes in neutrophil concentration, CRP, and eosinophil levels. Decreased neutrophil or CRP values and elevated eosinophil values at baseline and during the study should be considered as markers of the therapeutic response, as these changes correlate with improvement on the PANSS-P scale.

Also, research conducted by Christian Núñez et al. in 2019 included an assessment of whether white blood cell values were related to brain mass volume and/or clinical picture. It is known that neuroradiological research has confirmed changes in the brain mass of patients with psychotic disorders, which is confirmed by the above. A total of 218 subjects were included (n = 137 with a diagnosis of the first psychotic episode and n = 81 of the healthy population). It was found that in the group of subjects with the first psychotic episode, the neutrophil value was associated with a reduced volume of gray matter and an increased volume of cerebrospinal fluid (CT analysis). The neutrophil value was associated with the overall PANSS score, including the scoring of the presence of perceptual delusions and avolition (31). The mentioned research indicated that the loss of brain tissue is associated with the concentration of neutrophils within a psychotic disorder, which supports the hypothesis of dysregulation of the immune system. Elevated neutrophil counts are associated with a more severe clinical picture, which is a promising indicator in assessing the clinical picture of SCH and possibly developing new therapeutic approaches.

Further research is needed to better investigate inflammatory relationships. First, it would be useful to investigate a comparison between the acute phase and the remission phase to understand whether inflammatory changes can be considered a feature or a feature of a specific psychiatric disorder. Secondly, it is necessary to study the effect of psychopharmacological treatment on inflammatory characteristics.

6. CONCLUSIONS

This is a study that compared the parameters of red, white blood cells and platelets on inpatient and outpatient treatment. The finding that SCH as well as BD differed from controls with respect to red blood cells, hemoglobin, lymphocytes, and average platelet count was consistent with previous findings and could be understood as a qualitative measure in the evaluation of this sample. The fact that no association with other parameters was found, as well as an association with the diagnosis, does not exclude that these associations can be found in larger samples. On the other hand, this finding could also indicate that certain blood parameters are independent of diagnosis and associated with other biological measures. In this case, research into the biological difference between SCH and BD requires replication in independent studies. Further examination of the SCH and BD subgroups is needed to determine whether biologically valid subgroups can be identified by these clear levels of blood parameters. If the findings are replicated this will help to resolve the different biological pathways in SCH and BD.

- **Patients Consent Statement**: The first author confirms that patients consent to enroll in the study was obtained. The authors certify that they have obtained all appropriate patient consent
- **Authors contribution**: All authors were included in all steps of preparation this letter and made final proof reading.
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