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Evaluation of complete blood count values in individuals diagnosed with anxiety disorders

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Abstract

Anxiety disorders are an increasingly common psychiatric disorder. The most common subtypes are generalized anxiety disorder (GAD), panic disorder (PD), and social phobia(SP). This study aimed to investigate the relationship between anxiety disorders and complete blood count (CBC) and calculated inflammation ratios. 85 patients (GAD = 34, PD = 34, SP = 17) and 50 healthy controls admitted to the psychiatry outpatient clinic of a tertiary care hospital were included in the study. The relationship between anxiety and subtypes, gender, age group and CBC were evaluated. In our study, while a significant lower level was observed in hemoglobin, hematocrit, MCV, and MCH values in the patient group ($p < 0.05$), no significant difference was found in other parameters ($p > 0.05$). This lower level was observed to may associated with GAD and female gender. No significant differences in inflammation ratios (NLR, MLR, PLR and others) were found between the patient and control groups. We believe that CBC in patients with anxiety disorders should be examined in detail and studies with larger populations should be conducted. These findings highlight the potential value of routine hemogram analysis in psychiatric evaluations and underscore the need for further multidisciplinary studies to explore underlying pathophysiological mechanisms.

Keywords: Anxiety disorders, complete blood count, hematocrit, inflammation

Introduction

One of the earliest uses is based on the Greek word "anxsietas," meaning "anxiety" or "fear" [1]. Anxiety is the body's response of restlessness to the excessive worry generated by the mind in response to an uncertain or potential threat [2]. Anxiety disorders are characterized by symptoms that include worry, social and performance fears, unexpected and/or triggered panic attacks, anticipatory anxiety, physical symptoms and avoidance behaviors. Generalized anxiety disorder (GAD), panic disorder (PD), social phobia (SP) are common anxiety disorders seen in primary care [3]. Others include agoraphobia, specific phobia, separation anxiety disorder, selective mutism, and substance-induced anxiety disorder, which are less common [4]. According to large population-based surveys, up to 33.7% of the population are affected by an anxiety disorders during their lifetime and an estimated 301 million people worldwide, representing 4.05% of the total global population [5,6]. GAD is characterised by a persistent, excessive and unrealistic sense of worry, fear and overwhelm regarding everyday events. This worry may relate to economic, family, health and future concerns and has been affecting daily life for the past 6 months. PD is characterised by recurrent, unexpected and sudden panic attacks, as well as a fear of having further attacks, the development of phobic avoidance behaviour, or physical symptoms associated with the attacks. Patients usually present with complaints of having a heart attack or difficulty breathing, and fear is the predominant emotion. SP, on the other hand, is characterised by intense anxiety and fear in social situations where the person fears they will be judged negatively. Its main feature is the fear of being judged, rejected or humiliated, which leads to avoidance of situations such as meeting new people, giving presentations, or going shopping [7].

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Several studies have been conducted in recent years on complete blood count (CBC) parameters in psychiatric disorders [8-10]. Blood biomarkers are commonly utilized to investigate inflammatory processes in psychiatry; however, many are expensive or challenging to collect on a regular basis. The neutrophil/lymphocyte ratio (NLR), initially introduced as a straightforward measure of systemic inflammation in critically ill patients, has recently been employed to evaluate systemic inflammation in psychiatric populations. Since NLR can be derived from a complete blood count, it represents a more cost-effective and accessible alternative to cytokine assays. Given that it reflects components of both the innate (neutrophil) and adaptive (lymphocyte) immune system, it may be less susceptible to confounding factors such as physical activity. NLR has consistently demonstrated prognostic significance across various physical health conditions, highlighting a strong correlation between systemic inflammation and adverse clinical outcomes [11]. The monocyte/lymphocyte ratio (MLR) and the platelet/lymphocyte ratio (PLR) are other commonly used parameters. They are signs of systemic inflammation in the body, as well as indicators of infection, the state of the immune system and the course of diseases [10,12]. A number of other studies provide evidence that changes in platelet parameters, particularly platelet distribution width (PDW) and mean platelet volume (MPV), may result from underlying systemic inflammation. Platelets represent the largest storage site for serotonin, an important neurotransmitter in the pathophysiology of depression, and have many similar properties to neurons; therefore, many studies have examined the relationship between emotional disorders and platelet parameters. Increased MPV has been closely associated with anxiety and depression disorders in cardiovascular diseases such as myocardial infarction and ischemic heart disease. Higher MPV was found in patients with PD, depression disorder and anxiety disorder compared to the control group. Increased PDW has been observed in PD and in patients with treatment-resistant relapsing depression. Furthermore, in a large Italian cohort study, a significant positive association was found between depressive symptoms and PDW, which persisted after adjustment for various socio-demographic characteristics [13,14].

In this study, we aimed to examine anxiety disorders from an alternative perspective and explore the association between hemogram parameters, demographic characteristics, and diagnosis to assess their physiological underpinnings.

Material and Methods

The study employed a retrospective, cross-sectional design. It was conducted between January 1, 2023, and December 1, 2023 at a tertiary care hospital in Türkiye.

Ethical Approval Statement

This study, with application date 28 December 2022 and application number 63650, was approved by the Ethics Committee of the Rectorate of Siirt University on 30 January 2023 with decision number 2023/01/01/01. This study was conducted in accordance with the Declaration of Helsinki, as revised in 2013.

Study Design and Participants

The study included 85 participants diagnosed with an anxiety disorders (34 with GAD, 34 with PD and 17 with SP) according to Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and 50 healthy controls. In the study, patients with anxiety disorders were compared with a control group in terms of hemogram parameters. In addition, comparisons were made in terms of gender and age range.

Inclusion Criteria:

The patient group was determined based on the following criteria.

1. Participants diagnosed by a psychiatrist with GAD, PD or SP in according with the DSM-5 diagnostic criteria,
2. Participants with no history of psychiatric medication use in the past 1 (one) year,
3. No psychiatric disorders other than GAD, PD or SP,
4. Aged between 18 and 75, regardless of gender,
5. No additional medical disease/acute or systemic infection/ medication,
6. No tobacco/alcohol/substance use.

The control group was determined based on the following criteria.

1. According to DSM-5 diagnostic criteria, with no diagnosis of any psychiatric disorder
2. Aged between 18 and 75, regardless of gender,
3. No additional medical disease/acute or systemic infection/ medication,
4. No tobacco/alcohol/substance use.

Those who did not meet the inclusion criteria were excluded from the study.

Data Collection and Laboratory Measurements

Hemogram data, sociodemographic data and disease anxiety subtypes of all participants were analyzed retrospectively. All participants provided peripheral venous blood samples from the antecubital vein using sterile techniques. Blood samples were collected in ethylenediaminetetraacetic acid (EDTA) tubes for haematological analysis and processed within 2 hours.

Hematological parameters were measured using an automated hematology analyzer and included: White Blood Cell Count (WBC), Red Blood Cell Count (RBC), Hemoglobin (HGB), Hematocrit (HCT), Platelet Count (PLT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH),

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Mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW-CV, RDW-SD), MPV, Plateletcrit (PCT), PDW, Platelet Large Cell Count (P-LCC), Platelet Large Cell Ratio (P-LCR), Percentage of Neutrophil and Neutrophil Count (NEU% and NEU#), Percentage of Lymphocyte and Lymphocyte Count (LYM% and LYM#), Percentage of Monocyte and Monocyte Count (MON% and MON#), Percentage of Eosinophil and Eosinophil Count (EOS% and EOS#), Percentage of Basophil and Basophil Count (BAS% and BAS#). Inflammatory indices derived from hematological parameters were calculated: NLR, Eosinophil/Lymphocyte Ratio (ELR), Basophil/Lymphocyte Ratio (BLR), MLR, Neutrophil/Monocyte Ratio (NMR), PLR, Platelet/Neutrophil Ratio (PNR), WBC/(Neu+Lymph), MPV/PLT, HGB/HCT, HGB/MCV and RDW-CV/PLT.

Statistical Analysis: In this study, data from a total of 135 participants were analysed; the cases were classified into patient and control groups, with the patient group further subdivided into GAD, PD and SP subgroups, and the control group. Firstly, the distribution of the sample across groups, subgroups, age and gender was described using frequency and percentage values; the central tendency and dispersion characteristics of the data were presented in detail, including the mean ± standard deviation (parametric distribution), median-interquartile range (not parametric distribution) for continuous variables. In comparing CBC parameters between two independent groups, the independent samples t-test was used for variables meeting the parametric distribution, and the Mann–Whitney U test was used for variables not meeting the parametric distribution. In comparisons between the four groups, one-way analysis of variance (ANOVA) was used for data showing a normal (parametric) distribution, and the Kruskal–Wallis H test was used for data not following a normal distribution; in cases of significant results requiring multiple comparisons, post-hoc analyses were performed using the Tukey test following parametric analyses and the Dunn test following non-parametric analyses. The age variable was categorised into the patient groups as 18–27, 28–37, 38–47 and 48 years and over, and an analysis was performed to determine whether hemogram parameters differed according to age groups. Finally, the groups were analysed by gender, distinguishing between female and male groups. In all comparisons, a p-value of < 0.05 was considered statistically significant; the sizes of the differences identified were interpreted by reporting not only the p-values but also the effect sizes The SPSS 27.0 program was used to perform the analyses.

Results

The study included a total of 135 participants. 62.96% of the participants (n = 85) were in the patient group, whilst 37.04% (n = 50) were in the control group. When the distribution of anxiety disorder subtypes was examined, it was observed that 25.19% of the participants (n = 34) were in the GAD group, 25.19% (n = 34) in the PD group, 12.59% (n = 17) in the SP group, and 37.04% (n = 50) in the control group. The distribution by age group was assessed, 35.56% of participants (n = 48) were in the 18–27 age group, 32.59% (n = 44) in the 28–37 age group, 20.00% (n = 27) in the 38–47 age group, and 11.85% (n = 16) were aged 48 and over. With regard to gender distribution, it was determined that 57,04 % of participants (n = 77) were female and 42.96% (n = 58) were male. These findings indicate that the sample exhibits a balanced distribution in terms of age and gender and that adequate representation is ensured between the patient and control groups (Table 1).

Comparing the blood parameters of the patient and control groups, and examining the parameters showing statistically significant differences, it was determined that HGB levels were 13.84 ± 1.54 in the patient group and 14.54 ± 1.83 in the control group, and that this difference was statistically significant ($p = 0.020$; effect size = -0.421). This finding indicates that the control group's HGB levels were moderately higher than those of the patient group. Similarly, it was found that the HCT values were 42.50 ± 4.03 in the patient group and 44.63 ± 4.97 in the control group, and that the difference between the groups was significant ($p = 0.012$; effect size = -0.486). This result indicates that HCT levels in the control group were higher, with an effect size close to moderate. MCV values were 87.63 ± 6.98 in the patient group and 90.30 ± 4.04 in the control group, with a significant difference between the groups ($p = 0.015$; effect size = -0.441). This indicates that MCV was higher in the control group. Regarding MCH values, the patient group had a mean of 28.55 ± 2.69 and the control group 29.39 ± 1.66, and this difference was found to be statistically significant ($p = 0.027$; effect size = −0.356). This result indicates that the MCH levels in the control group were higher than those in the patient group and that the effect size was small to moderate. In contrast, no statistically significant difference was found between the patient and control groups in terms of the remaining hemogram parameters (t-test or Mann-Whitney U test, $p > 0.05$). The effect sizes calculated for these parameters were generally very small or small, supporting the finding that there was no clinically significant difference between the groups (Table 2).

Comparing the blood parameters of the anxiety subtypes and the control group, and examining the parameters showing statistically significant differences, it was determined that HGB levels differed significantly between the groups (ANOVA, $p = 0.040$); according to the Tukey post-hoc analysis, this difference was observed between the GAD group and the control group. Accordingly, the HGB level in the GAD group (13.50 ± 1.31) was lower than that in the control group (14.54 ± 1.83), with a small effect size. Similarly, a significant difference was detected between the groups in terms of HCT levels ($p = 0.024$), and the post-hoc analysis revealed that the

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difference was again between the GAD and control groups; it was observed that the control group's HCT levels (44.63 ± 4.97) were higher than those of the GAD group (41.69 ± 3.17), and the effect size was small. MCV values also showed a significant difference (p = 0.029), and it was determined that the GAD group's MCV level (86.66 ± 6.40) was lower than that of the control group (90.30 ± 4.04). A significant difference was also found between the groups in terms of MCH (p = 0.047), and it was determined that the MCH values of the GAD group (28.07 ± 2.41) were lower than those of the control group (29.39 ± 1.66). Furthermore, the Kruskal-Wallis test conducted for ELR revealed a significant difference between the groups (p = 0.034), and according to the Dunn post-hoc analysis, the ELR level in the PD group was found to be lower than that of both the control group and the GAD group; however, the effect size of this difference was quite low. However, no statistically significant differences were found between the groups with regard to the remaining haemogram parameters (ANOVA or Kruskal-Wallis, p > 0.05) The fact that the effect sizes calculated for these variables were very low supports the conclusion that there were no clinically significant differences between the groups (Table 3).

Comparing hemogram parameters by age group, statistically significant differences were observed in the RDW-SD, PCT, Neu# and PNR variables. RDW-SD levels differ significantly by age group; according to the post-hoc test, RDW-SD levels in the 28–37 age group are higher than those in the 18–27 age group. PCT levels differ significantly across age groups; PCT levels in those aged 48 and over are lower than in the 18–27 age group. The Neu# level shows a significant difference across age groups; post-hoc analysis revealed that the neutrophil count in those aged 48 and over is higher than in the 18–27 age group. The PNR level also shows significant differences across age groups; it was found that the PNR ratio in those aged 48 and over is significantly lower than in both the 18–27 age group and the 38–47 age group. In contrast, no statistically significant differences were found in the remaining hemogram parameters when comparing age groups (ANOVA or Kruskal-Wallis H, p > 0.05). The very low effect sizes calculated for these variables support the conclusion that there is no clinically significant difference between the groups (Table 4).

Comparing blood parameters by gender, and evaluating those parameters that showed statistically significant differences; it was determined that RBC levels were significantly higher in males (5.23 ± 0.39) than in females (4.64 ± 0.35) (p = 0.001; effect size = -1.625), and this difference was found to be very large. Similarly, HGB levels were found to be significantly higher in males (15.47 ± 1.17) compared to females (13.04 ± 1.16) (p = 0.001; effect size = -2.091), and the effect size was found to be very large. HCT values were also found to be significantly higher in males (46.69 ± 3.55) compared to females (40.64 ± 3.20) (p = 0.001; effect size = -1.802), and this difference was also found to be very large. PLT levels, however, were found to be significantly higher in females (283.87 ± 68.60) compared to males (259.07 ± 58.56) (p = 0.028; effect size = 0.385), and the effect size was determined to be small to moderate. MCH and MCHC values were found to be significantly higher in males than in females (MCH: p = 0.001; effect size = -0.657; MCHC: p = 0.001; effect size = -0.992), and these differences were observed to range from moderate to large. It was determined that RDW-CV and RDW-SD values were significantly higher in females than in males (RDW-CV: p = 0.001; effect size = 0.711; RDW-SD: p = 0.009; effect size = 0.481), and the effect sizes were found to be of moderate strength. PCT levels were found to be significantly higher in females than in males (p = 0.012; effect size = -0.311), and the effect size was small to moderate. Monocyte count (Mon#) was found to be significantly higher in males than in females (p = 0.011; effect size = -0.170), although the effect size was small. Furthermore, significant differences between the genders were found for PLR (p = 0.031; effect size = 0.010) and PNR (p = 0.042; effect size = 0.120), although the effect sizes of these differences were found to be quite low. Furthermore, it was determined that the HGB/HCT and HGB/MCV ratios were significantly higher in males than in females (p = 0.001; effect size≈0.255–0.256), and the effect sizes were found to be small to moderate. In contrast, no statistically significant difference was found between the females and males for the remaining haemogram parameters (t-test or Mann-Whitney U, p > 0.05). The fact that the effect sizes calculated for these variables were generally very low or small indicates that gender has no significant effect on these parameters (Table 5).

Table 1. Sociodemographic data and distribution by diagnostic group

Category	n	%
Anxiety		
Patient	85	62.96
Control	50	37.04
Anxiety subtypes		
GAD	34	25.19
PD	34	25.19
SP	17	12.59
Control	50	37.04
Age		
18-27	48	35.56
28-37	44	32.59
38-47	27	20.00
48+	16	11.85
Gender		
Female	77	57.04
Male	58	42.96

GAD: Generalized anxiety disorder, PD: panic disorder, SP: social phobia

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Table 2. Comparison of CBC parameters between patient and control groups

Variable	Group		p	Effect size
	Patient (n = 85)	Control (n = 50)		
	(Mean ± SD)[t] or (Median-IQR)[u]	(Mean ± SD)[t] or (Median-IQR)[u]		
WBC	7.89 ± 2.27	7.53 ± 1.50	0.309[t]	0.182
RBC	4.86 ± 0.43	4.94 ± 0.52	0.335[t]	-0.172
HGB	13.84 ± 1.54	14.54 ± 1.83	**0.020*[t]**	-0.421
HCT	42.50 ± 4.03	44.63 ± 4.97	**0.012*[t]**	-0.486
PLT	266.59 ± 63.22	283.98 ± 68.07	0.136[t]	-0.267
MCV	87.63 ± 6.98	90.30 ± 4.04	**0.015*[t]**	-0.441
MCH	28.55 ± 2.69	29.39 ± 1.66	**0.027*[t]**	-0.356
MCHC	32.56 ± 1.33	32.55 ± 1.09	0.948[t]	0.012
RDW-CV	13.20 – 1.60	13.10 – 0.80	0.351[u]	0.231
RDW-SD	43.20 – 3.90	44.30 – 2.70	0.218[u]	-0.211
MPV	9.80 – 1.50	10.15 – 1.20	0.534[u]	-0.020
PCT	0.27 – 0.09	0.28 – 0.07	0.329[u]	0.310
PDW	16.10 – 0.40	16.20 – 0.40	0.254[u]	-0.080
P-LCC	69.41 ± 22.26	74.76 ± 25.36	0.203[t]	-0.228
P-LCR	26.56 ± 8.52	26.56 ± 7.03	0.996[t]	0.001
Neu%	60.53 ± 10.96	61.39 ± 8.51	0.635[t]	-0.085
Neu#	4.88 ± 2.01	4.68 ± 1.40	0.634[t]	0.111
Lymph%	30.41 ± 10.26	29.86 ± 7.15	0.737[t]	0.061
Lymph#	2.19 – 0.98	2.23 – 0.71	0.637[u]	0.140
Eos%	1.50 – 1.50	1.65 – 1.80	0.538[u]	-0.240
Bas#	0.09 – 0.14	0.11 – 0.11	0.238[u]	0.320
Eos#	0.03 – 0.05	0.03 – 0.02	0.259[u]	0.170
Bas%	0.40 – 0.30	0.40 – 0.20	0.493[u]	-0.040
Mon%	6.40 – 1.90	6.20 – 1.70	0.629[u]	0.130
Mon#	0.45 – 0.20	0.45 – 0.12	0.438[u]	0.180
NLR	1.96 – 1.59	1.95 – 0.92	0.765[u]	0.160
ELR	0.05 – 0.06	0.05 – 0.07	0.597[u]	-0.170
BLR	0.01 – 0.01	0.01 – 0.01	0.942[u]	0.400
MLR	0.19 – 0.12	0.21 – 0.07	0.761[u]	0.150
NMR	9.59 – 4.14	9.91 – 3.49	0.599[u]	0.010
WBC/(Neu+Lymph)	1.09 – 0.03	1.10 – 0.03	0.765[u]	0.080
PLR	117.77 – 61.67	122.03 – 52.32	0.158[u]	0.080
PNR	60.11 – 36.04	65.40 – 34.01	0.475[u]	-0.090
MPV/PLT	0.04 ± 0.02	0.04 ± 0.01	0.611[t]	-0.091
HGB/HCT	0.33 – 0.01	0.33 – 0.01	0.716[u]	0.010
HGB/MCV	0.16 – 0.02	0.16 – 0.03	0.327[u]	0.020
RDW-CV/PLT	0.05 – 0.02	0.05 – 0.02	0.217[u]	0.030

*p < 0.05; t: t test, u: Mann Whitney u test, SD: standat deviation, IQR: interquartile range, WBC: white blood cell count, RBC: red blood cell count, HGB: hemoglobin, HCT: hematocrit, PLT: platelet count, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW-CV: red cell distribution width-coefficient of variation, RDW-SD: red cell distribution width-standard deviation, MPV: mean platelet volume, PCT: plateletcrit, PDW: platelet distribution width, P-LCC: platelet large cell count, P-LCR: platelet large cell ratio, Neu: neutrophil, Lymph: lymphocyte, Eos: eosinophil, Bas: basophil, Mon: monocyte, NLR: neutrophil-to-lymphocyte ratio, ELR: eosinophil-to-lymphocyte ratio, BLR: basophil-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, NMR: neutrophil-to-monocyte ratio, PLR: platelet-to-lymphocyte ratio, PNR: platelet-to-neutrophil ratio, #: absolute count, %: percentage

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Table 3. Distribution of CBC parameters according to anxiety disorders subtypes

Variable	Anxiety subtypes				p	Post hoc	Effect size
	GAD[(1)] (n = 34)	PD[(2)] (n = 34)	SP[(3)] (n = 17)	Control[(4)] (n = 50)			
	(Mean ± SD)[a] or (Median-IQR)[k]						
WBC	7.96 ± 2.32	7.78 ± 2.12	7.98 ± 2.58	7.53 ± 1.50	0.755[a]		0.009
RBC	4.83 ± 0.43	4.88 ± 0.50	4.91 ± 0.28	4.94 ± 0.52	0.734[a]		0.01
HGB	13.50 ± 1.31	14.19 ± 1.65	13.84 ± 1.68	14.54 ± 1.83	**0.040*[a]**	1 < 4[a']	0.061
HCT	41.69 ± 3.17	43.30 ± 4.42	42.51 ± 4.61	44.63 ± 4.97	**0.024*[a]**	1 < 4[a']	0.069
PLT	260.47 ± 66.29	273.50 ± 68.17	265.00 ± 46.36	283.98 ± 68.07	0.408[a]		0.022
MCV	86.66 ± 6.40	89.05 ± 6.90	86.72 ± 8.11	90.30 ± 4.04	**0.029*[a]**	1 < 4[a']	0.066
MCH	28.07 ± 2.41	29.17 ± 2.60	28.26 ± 3.26	29.39 ± 1.66	**0.047*[a]**	1 < 4[a']	0.059
MCHC	32.39 ± 1.34	32.74 ± 1.28	32.55 ± 1.43	32.55 ± 1.09	0.708[a]		0.011
RDW-CV	13.88 ± 1.26	13.23 ± 1.17	13.48 ± 1.05	13.29 ± 0.91	0.056[a]		0.056
RDW-SD	44.23 ± 3.16	43.51 ± 2.83	42.45 ± 2.04	44.18 ± 2.58	0.104[a]		0.046
MPV	9.76 ± 1.05	10.11 ± 1.32	10.28 ± 1.17	10.03 ± 1.00	0.412[a]		0.022
PCT	0.25 ± 0.06	0.27 ± 0.06	0.27 ± 0.06	0.28 ± 0.07	0.202[a]		0.034
PDW	16.04 ± 0.34	16.14 ± 0.41	16.20 ± 0.31	16.14 ± 0.35	0.416[a]		0.021
P-LCC	64.44 ± 19.13	70.88 ± 21.26	76.41 ± 28.36	74.76 ± 25.36	0.188[a]		0.036
P-LCR	24.85 ± 7.62	27.21 ± 9.27	28.71 ± 8.47	26.56 ± 7.03	0.391[a]		0.023
Neu%	59.66 ± 13.49	60.27 ± 9.25	62.79 ± 8.46	61.39 ± 8.51	0.722[a]		0.01
Neu#	4.91 ± 2.33	4.74 ± 1.64	5.09 ± 2.09	4.68 ± 1.40	0.843[a]		0.006
Lymph%	29.84 ± 12.77	31.81 ± 8.23	28.75 ± 8.27	29.86 ± 7.15	0.669[a]		0.012
Lymph#	2.21 – 1.13	2.20 – 0.98	2.12 – 0.70	2.23 – 0.71	0.747[k]		0.002
Eos%	1.95 – 2.10	1.30 – 1.10	1.60 – 1.40	1.65 – 1.80	0.115[k]		0.002
Bas#	0.12 – 0.16	0.07 – 0.11	0.10 – 0.10	0.11 – 0.11	0.353[k]		0.008
Eos#	0.03 – 0.05	0.03 – 0.05	0.03 – 0.03	0.03 – 0.02	0.715[k]		0.002
Bas%	0.30 – 0.30	0.40 – 0.20	0.40 – 0.20	0.40 – 0.20	0.386[k]		0.007
Mon%	6.45 – 1.90	5.90 – 1.90	6.40 – 1.70	6.20 – 1.70	0.739[k]		0.002
Mon#	0.44 – 0.17	0.46 – 0.19	0.45 – 0.18	0.45 – 0.12	0.849[k]		0.001
NLR	1.97 – 2.20	1.86 – 1.07	2.33 – 1.74	1.95 – 0.92	0.698[k]		0.003
ELR	0.07 – 0.05	0.03 – 0.04	0.06 – 0.03	0.05 – 0.07	**0.034*[k]**	2 < 4.2 < 1[k']	0.032
BLR	0.01 – 0.01	0.01 – 0.01	0.01 – 0.01	0.01 – 0.01	0.825[k]		0.001
MLR	0.20 – 0.19	0.18 – 0.08	0.21 – 0.13	0.21 – 0.07	0.286[k]		0.011
NMR	9.54 – 5.37	9.82 – 3.66	9.61 – 2.77	9.91 – 3.49	0.791[k]		0.002
WBC/(Neu+Lymph)	1.10 – 0.05	1.08 – 0.03	1.09 – 0.01	1.10 – 0.03	0.209[k]		0.013
PLR	128.66 – 72.11	114.12 – 54.87	131.86 – 43.16	122.03 – 52.32	0.336[k]		0.008
PNR	59.91 – 41.56	58.44 – 29.58	66.89 – 35.08	65.40 – 34.01	0.753[k]		0.002
MPV/PLT	0.04 – 0.01	0.04 – 0.01	0.04 – 0.02	0.04 – 0.01	0.756[k]		0.002
HGB/HCT	0.32 – 0.02	0.33 – 0.02	0.32 – 0.03	0.33 – 0.01	0.537[k]		0.004
HGB/MCV	0.16 – 0.03	0.16 – 0.03	0.16 – 0.01	0.16 – 0.03	0.634[k]		0.003
RDW-CV/PLT	0.05 – 0.02	0.05 – 0.02	0.05 – 0.01	0.05 – 0.02	0.141[k]		0.016

*p < 0.05; a: ANOVA test; a': Tukey test; k: Kruskal Wallis h test; k': Dunn test; SD: standat deviation, IQR: interquartile range, WBC: white blood cell count, RBC: red blood cell count, HGB: hemoglobin, HCT: hematocrit, PLT: platelet count, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW-CV: red cell distribution width-coefficient of variation, RDW-SD: red cell distribution width-standard deviation, MPV: mean platelet volume, PCT: plateletcrit, PDW: platelet distribution width, P-LCC: platelet large cell count, P-LCR: platelet large cell ratio, Neu: neutrophil, Lymph: lymphocyte, Eos: eosinophil, Bas: basophil, Mon: monocyte, NLR: neutrophil-to-lymphocyte ratio, ELR: eosinophil-to-lymphocyte ratio, BLR: basophil-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, NMR: neutrophil-to-monocyte ratio, PLR: platelet-to-lymphocyte ratio, PNR: platelet-to-neutrophil ratio, #: absolute count, %: percentage

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Table 4. Analysis of CBC parameters according to age groups

Variable	Age groups				p	Post hoc	Effect size
	18-27(1) (n = 48)	28-37(2) (n = 44)	38-47(3) (n = 27)	48+(4) (n = 16)			
	(Mean ± SD)[a] or (Median-IQR)[k]						
WBC	7.37 ± 1.70	7.78 ± 2.34	7.75 ± 1.99	8.86 ± 1.75	0.087[a]		0.143
RBC	4.87 ± 0.46	4.85 ± 0.45	5.01 ± 0.50	4.90 ± 0.48	0.531[a]		0.027
HGB	14.03 ± 1.67	14.03 ± 1.64	14.24 ± 1.88	14.29 ± 1.63	0.909[a]		0.198
HCT	43.13 ± 4.70	43.15 ± 4.42	43.74 ± 4.85	43.40 ± 3.82	0.945[a]		0.01
PLT	283.25 ± 67.17	268.00 ± 70.91	284.33 ± 58.77	237.13 ± 40.00	0.068[a]		0.084
MCV	88.64 ± 5.97	89.13 ± 5.71	87.60 ± 7.82	88.86 ± 5.18	0.789[a]		0.012
MCH	28.84 ± 2.41	28.98 ± 2.24	28.50 ± 2.90	29.22 ± 1.81	0.782[a]		0.176
MCHC	32.51 ± 1.16	32.51 ± 1.33	32.51 ± 1.14	32.91 ± 1.44	0.701[a]		0.055
RDW-CV	13.30 ± 1.20	13.64 ± 0.94	13.49 ± 1.32	13.28 ± 0.83	0.463[a]		0.098
RDW-SD	43.35 ± 3.03	44.86 ± 2.55	43.47 ± 2.27	42.85 ± 2.73	**0.01*[a]**	1 < 2[a']	0.003
MPV	10.06 ± 1.12	10.12 ± 1.24	9.95 ± 0.76	9.70 ± 1.31	0.618[a]		0.167
PCT	0.28 ± 0.07	0.27 ± 0.07	0.28 ± 0.05	0.23 ± 0.05	**0.03*[a]**	1 > 4[a']	0.072
PDW	16.14 ± 0.37	16.18 ± 0.36	16.05 ± 0.36	16.04 ± 0.31	0.378[a]		0.039
P-LCC	74.71 ± 26.51	71.75 ± 22.88	72.85 ± 16.71	58.00 ± 22.77	0.098[a]		0.12
P-LCR	26.99 ± 8.22	27.16 ± 8.79	26.02 ± 5.28	24.56 ± 8.92	0.683[a]		0.015
Neu%	60.21 ± 8.46	60.10 ± 10.90	59.61 ± 9.73	66.86 ± 11.75	0.88[a]		0.188
Neu#	4.47 ± 1.37	4.80 ± 2.10	4.67 ± 1.68	6.03 ± 1.94	**0.026*[a]**	1 < 4[a']	0.064
Lymph%	31.07 ± 7.70	30.22 ± 10.30	31.84 ± 8.65	24.81 ± 9.95	0.078[a]		0.098
Lymph#	2.26 ± 0.68	2.23 ± 0.78	2.42 ± 0.79	2.10 ± 0.65	0.546[a]		0.021
Eos%	2.05 ± 1.70	1.71 ± 1.60	2.00 ± 1.32	2.19 ± 1.75	0.663[a]		0.151
Bas#	0.13 ± 0.13	0.12 ± 0.13	0.15 ± 0.12	0.12 ± 0.12	0.781[a]		0.045
Eos#	0.03 – 0.03	0.03 – 0.04	0.03 – 0.03	0.03 – 0.06	0.588[k]		0.132
Bas%	0.43 ± 0.21	0.40 ± 0.24	0.44 ± 0.28	0.28 ± 0.17	0.136[a]		0.008
Mon%	6.24 ± 1.10	6.85 ± 3.57	6.10 ± 1.75	5.86 ± 1.79	0.392[a]		0.174
Mon#	0.46 – 0.17	0.45 – 0.16	0.45 – 0.18	0.44 – 0.23	0.431[k]		0.058
NLR	2.12 ± 0.79	2.95 ± 3.94	2.15 ± 1.16	3.29 ± 1.65	0.188[a]		0.109
ELR	0.06 – 0.07	0.04 – 0.04	0.05 – 0.05	0.07 – 0.06	0.268[k]		0.034
BLR	0.01 – 0.01	0.01 – 0.01	0.01 – 0.01	0.01 – 0.01	0.551[k]		0.186
MLR	0.21 ± 0.06	0.64 ± 2.73	0.20 ± 0.07	0.27 ± 0.13	0.536[a]		0.079
NMR	10.02 ± 2.69	10.11 ± 4.11	13.17 ± 16.55	13.75 ± 9.69	0.221[a]		0.141
WBC/ (Neu+Lymph)	1.10 ± 0.03	1.13 ± 0.21	1.09 ± 0.03	1.09 ± 0.03	0.621[a]		0.006
PLR	134.12 ± 45.15	171.27 ± 295.11	130.40 ± 53.53	120.43 ± 32.90	0.636[a]		0.165
PNR	69.44 ± 29.11	63.74 ± 26.64	66.05 ± 20.04	44.30 ± 19.22	**0.010*[a]**	4 < 1.4 < 3[a']	0.052
MPV/PLT	0.03 – 0.01	0.04 – 0.01	0.04 – 0.01	0.04 – 0.02	0.783[k]		0.117
HGB/HCT	0.33 ± 0.01	0.33 ± 0.01	0.32 ± 0.01	0.33 ± 0.01	0.738[a]		0.024
HGB/MCV	0.16 ± 0.02	0.16 ± 0.02	0.16 ± 0.02	0.16 ± 0.02	0.517[a]		0.193
RDW-CV/PLT	0.05 – 0.01	0.05 – 0.02	0.05 – 0.02	0.06 – 0.02	0.243[k]		0.068

*p < 0.05; a: ANOVA test; a': Tukey test; k: Kruskal Wallis h test; k': Dunn test; SD: standat deviation, IQR: interquartile range, WBC: white blood cell count, RBC: red blood cell count, HGB: hemoglobin, HCT: hematocrit, PLT: platelet count, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW-CV: red cell distribution width-coefficient of variation, RDW-SD: red cell distribution width-standard deviation, MPV: mean platelet volume, PCT: plateletcrit, PDW: platelet distribution width, P-LCC: platelet large cell count, P-LCR: platelet large cell ratio, Neu: neutrophil, Lymph: lymphocyte, Eos: eosinophil, Bas: basophil, Mon: monocyte, NLR: neutrophil-to-lymphocyte ratio, ELR: eosinophil-to-lymphocyte ratio, BLR: basophil-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, NMR: neutrophil-to-monocyte ratio, PLR: platelet-to-lymphocyte ratio, PNR: platelet-to-neutrophil ratio, #: absolute count, %: percentage

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Table 5. Analysis of CBC Parameters According to Gender Groups

Variable	Gender		p	Effect size
	Female (n = 77)	Male (n = 58)		
	(Mean ± SD)[t] or (Median-IQR)[u]	(Mean ± SD)[t] or (Median-IQR)[u]		
WBC	7.47 ± 1.83	8.13 ± 2.21	0.061[t]	-0.329
RBC	4.64 ± 0.35	5.23 ± 0.39	**0.001***[t]	-1.625
HGB	13.04 ± 1.16	15.47 ± 1.17	**0.001***[t]	-2.091
HCT	40.64 ± 3.20	46.69 ± 3.55	**0.001***[t]	-1.802
PLT	283.87 ± 68.60	259.07 ± 58.56	**0.028***[t]	0.385
MCV	87.90 ± 6.34	89.54 ± 5.88	0.126[t]	-0.267
MCH	28.21 ± 2.35	29.70 ± 2.18	**0.001***[t]	-0.657
MCHC	32.07 ± 1.07	33.18 ± 1.17	**0.001***[t]	-0.992
RDW-CV	13.40 – 1.75	13.00 – 0.70	**0.001***[u]	0.711
RDW-SD	44.30 – 4.20	43.10 – 3.10	**0.009***[u]	0.481
MPV	10.06 ± 1.04	9.95 ± 1.22	0.582[t]	0.096
PCT	0.28 ± 0.07	0.26 ± 0.06	**0.012***[t]	-0.311
PDW	16.07 ± 0.33	16.18 ± 0.39	0.076[t]	0.439
P-LCC	74.00 – 30.00	66.00 – 33.00	0.051[u]	0.371
P-LCR	26.95 ± 7.39	26.06 ± 8.70	0.523[t]	0.111
Neu%	60.25 – 14.05	59.50 – 13.50	0.945[u]	0.001
Neu#	4.37 – 2.28	4.44 – 2.02	0.403[u]	-0.222
Lymph%	30.86 ± 9.08	29.35 ± 9.37	0.346[t]	0.164
Lymph#	2.18 – 0.85	2.32 – 0.78	0.436[u]	-0.080
Eos%	1.50 – 1.60	1.60 – 1.50	0.523[u]	-0.100
Bas#	0.09 – 0.14	0.12 – 0.14	0.415[u]	-0.240
Eos#	0.03 – 0.02	0.03 – 0.05	0.158[u]	0.040
Bas%	0.40 – 0.20	0.30 – 0.30	0.366[u]	0.280
Mon%	6.20 – 1.80	6.40 – 1.70	0.173[u]	-0.180
Mon#	0.44 – 0.14	0.48 – 0.25	**0.011***[u]	-0.170
NLR	1.93 – 1.31	1.97 – 1.30	0.554[u]	-0.320
ELR	0.05 – 0.05	0.06 – 0.06	0.288[u]	-0.200
BLR	0.01 – 0.01	0.01 – 0.01	0.944[u]	-0.100
MLR	0.19 – 0.07	0.21 – 0.13	0.281[u]	-0.180
NMR	10.03 – 4.02	9.59 – 4.00	0.416[u]	-0.080
WBC/ (Neu+Lymph)	1.09 – 0.03	1.10 – 0.04	0.164[u]	0.370
PLR	132.00 – 70.61	113.69 – 44.33	**0.031***[u]	0.010
PNR	67.25 – 31.41	55.67 – 38.22	**0.042***[u]	0.120
MPV/PLT	0.04 – 0.01	0.04 – 0.02	0.256[u]	0.250
HGB/HCT	0.32 – 0.02	0.33 – 0.02	**0.001***[u]	0.255
HGB/MCV	0.15 – 0.02	0.17 – 0.02	**0.001***[u]	0.256
RDW-CV/PLT	0.05 – 0.02	0.05 – 0.02	0.408[u]	0.102

*p < 0.05; t: t test; u: Mann Whitney u test; SD: standat deviation, IQR: interquartile range, WBC: white blood cell count, RBC: red blood cell count, HGB: hemoglobin, HCT: hematocrit, PLT: platelet count, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, RDW-CV: red cell distribution width-coefficient of variation, RDW-SD: red cell distribution width-standard deviation, MPV: mean platelet volume, PCT: plateletcrit, PDW: platelet distribution width, P-LCC: platelet large cell count, P-LCR: platelet large cell ratio, Neu: neutrophil, Lymph: lymphocyte, Eos: eosinophil, Bas: basophil, Mon: monocyte, NLR: neutrophil-to-lymphocyte ratio, ELR: eosinophil-to-lymphocyte ratio, BLR: basophil-to-lymphocyte ratio, MLR: monocyte-to-lymphocyte ratio, NMR: neutrophil-to-monocyte ratio, PLR: platelet-to-lymphocyte ratio, PNR: platelet-to-neutrophil ratio, #: absolute count, %: percentage

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Discussion

Extensive research continues to be conducted into the etiology and effects of psychiatric disorders. Psychiatric disorders may have a similar pathophysiology to autoimmune diseases. Haematological manifestations seen in immune system disorders may also be seen in some psychiatric diagnoses. Research is ongoing into whether certain infections or immune system disorders can lead to psychiatric disorders, and whether psychiatric disorders can in turn cause inflammation.

NLR is most used as a prognostic marker in inflammation. In a review study, the consistent finding of elevated NLR values in the psychiatric patients examined suggests that an abnormal NLR is not specific to any particular disorder; rather, it may reflect a pathological brain process leading to impaired brain function, supporting the hypothesis that neuroinflammation plays a significant role in the aetiology of psychiatric disorders. It was noted that further research is required to elucidate the relationship between NLR and specific diagnostic/behavioural constructs in greater detail [15,16]. In our study, the NLR value was found to be within the normal range in patients with anxiety disorders and across all anxiety subtypes. Another ratio used is MLR. In a retrospective study published in 2020 by Örüm et al. comparing NLR and Monocyte/Lymphocyte ratio (MLR) values of patients diagnosed with GAD (n = 32) and healthy subjects (n = 35), Neutrophil count, Neutrophil percentage and NLR were found to be significantly higher in the patient group; Monocyte count, lymphocyte count, monocyte percentage and MLR were similar between the groups [9]. Another study examining patients with depression noted that MLR has not been sufficiently investigated and that large-scale replication studies are needed in the future [17]. In our study, the MLR value was found to be within the normal range in patients with anxiety disorders and across all anxiety subtypes. The PLR ratio has also come into widespread use. It has been studied particularly in patients with schizophrenia, depression and bipolar disorder. The PLR ratio has been found to be elevated in patients with hypomania or mania, whilst in patients with schizophrenia, it has been suggested that it may be associated with cognitive impairment [17-19]. ELR, BLR, NMR and PLR ratios, however, have been studied more extensively in medical conditions. They have not been investigated much in psychiatric disorders. In our study, no significant differences were found in terms of BLR, NMR, PLR, and other ratios between the anxiety disorders and the control group.

Other than the calculated ratios, the blood parameters examined include white blood cells, red blood cells, haemoglobin, platelets, and their distribution and volumes. In a study published by Yurteri et al. in 2020, HGB, RDW, PLT, MPV, PDW, PCT, WBC, neutrophil, lymphocyte and monocyte counts, and NLR values were compared in paediatric and adolescent patients with GAD (n = 48) and a control group (n = 46). In this retrospective study, MLR and PLR values also were examined, and it was found that MPV levels were significantly higher, whilst PLT and PDW levels were significantly lower in patients with GAD; No statistically significant difference was found between the case and control groups in terms of HGB, RDW, PCT, WBC, neutrophil, lymphocyte and monocyte counts, or NLR, MLR and PLR values [20]. Bölükbaşı et al. conducted a cross-sectional study in 2021 comparing anxiety and depression levels, platelet count, MPV and NLR values in patients with essential thrombocytosis (n = 46) and a healthy control group (n = 46). While significant differences were observed between the groups in terms of depression and anxiety levels, platelet count and NLR levels, no significant difference was observed in MPV values. It was noted that platelet count may be a predictive factor for depressive symptoms in patients [21]. 500 patients with chronic psychiatric conditions – 174 (34.8%) with schizophrenia, 105 (21.0%) with generalised anxiety disorder, 72 (14.4%) with bipolar affective disorder, 70 (14.0%) with major depressive disorder, 36 (7.2%) with adjustment disorder, 21 (4.2%) with schizoaffective disorder and 18 (3.6%) with other psychiatric disorders—and 100 healthy control participants in a cross-sectional study, compared HGB, PLT, monocytes, PDW, NLR, PLR, RDW, RDW-CV, RDW-SD, lymphocytes, eosinophils, basophils and MPV values. No significant differences were found in HGB, PLT, monocyte, PCT or RDW-CV values; however, lymphocyte, eosinophil, basophil, MPV and RDW-SD values were significantly higher in the patient group, whilst NLR and PLR values were significantly lower compared to the healthy control group [22]. In our study, HGB, HCT, MCV and MCH values were found to be significantly lower in patients with anxiety disorders compared to the control group. No differences were observed in other parameters.

A literature overview shows that, among studies on CBC in anxiety disorders and subtypes, GAD has been studied more frequently, whereas the number of studies on PD and SP is relatively smaller. A study investigating the prevalence of anaemia in psychiatric disorders examined HGB, HCT, MCV, RBC and RDW values. While anemia was most common in patients with psychotic disorders, it was found to be the second most common in patients with GAD [23]. In one study on GAD patients, published by Mutka et al. in 2021 who were investigating coagulation, the PLT, MPV, PDW and PCT values of GAD patients (n = 72) and a healthy control group (n = 72) were compared; whilst MPV was found to be associated with higher levels, PDW and PCT values were also found to be higher in the patient group compared to the control group [24]. In our study, we also observed low levels of HGB, HCT, MCV, and MCH in patients with GAD. However, no changes were observed in the PLT, PCT, MPV, PDW, PCT, and other inflation rates. A study conducted on patients with PD demonstrated a significant increase in MPV, PDW, RDW and MCHC values compared to healthy controls. A high MPV value has been considered a haematological marker for patients with PD [25]. In another study examining CBC parameters in 40 patients diagnosed with PD, the following parameters were analyzed: RBC, HGB, HCT, MCV, MCH, PLT, and WBC parameters. The results of the study revealed elevated eosinophil and basophil

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counts and a low lymphocyte count compared to the control group [26]. In our study, no significant changes were observed in the absolute counts of eosinophils, basophils, lymphocytes and other parameters in patients with PD. Conversely, only the ELR was found to be lower. ELR was found to be lower in PD patients compared to the control group and GAD. However, this effect size was small. Regarding the prevalence of ELR in relation to allergic reactions, it may be higher in patients with asthma and urticaria [27,28]. In our study, the low ELR rate in PD patients—due to the small effect size and limited sample size—should not be interpreted as indicating that allergic reactions are less common. Studies on CBC in patients with SP also are limited. A study conducted on patients with sickle cell anemia and low HGB reported higher levels of social anxiety [29]. In our study, no significant values were identified regarding SP. Our findings on anxiety subtypes led us to conclude that GAD may be more affected than PD and SP.

There are studies on anxiety disorders that have examined gender and age. In a study by Cemali et al., consisting of 3006 urban and rural youth aged 15 to 35 years, RDW and NLR values were significantly associated with MDD in men, while HCT, RDW and MPV values were significantly associated with GAD in women. Additionally, NLR values and lymphocyte percentages were associated with GAD in males [30]. In another study, HGB levels were found to be lower in females than in males; however, no significant differences were observed between the genders in terms of HCT, RBC, and RDW [23]. Although our study obtained similar results (HGB, HCT, MCV, MCHC) regarding gender, analyses should be conducted in smaller study groups with similar demographic characteristics. Our study focused on the adult age group and found no significant difference.

A strength of our study is that it simultaneously examines the three most common anxiety subtypes and most inflammation markers derived from a CBC. The limitations of our study include the small sample size for anxiety subtypes and the use of single blood samples.

Conclusion

In present study, lower levels of HGB, HCT, MCV, and MCH were observed in patients with anxiety disorders. Additionally, it was observed that this lower level may associated with the GAD anxiety subtype and female gender. Contrary to studies in the literature, no significant differences were found in NLR, MLR, PLR, and other inflammation ratios. However, more comprehensive studies that include other parameters indicating inflammation biochemically should be conducted.

Ethical Approval
Ethics committee approval was received for this study from the Ethics Committee of Rectorate of Siirt University (Date: December 28, 2022, Number: 63650).

Patient Consent
Since the study was designed retrospectively, written and/or verbal consent was not obtained from the participants.

Conflict of Interest
The authors confirm the absence of any conflicts associated with this work.

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