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Original Research

A Comparative Assessment of the Inflammatory Markers in Patients with Fibromyalgia under Duloxetine Treatment

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Abstract

Background: This study was carried out to compare the levels of inflammatory markers in the complete blood count before and after they began receiving duloxetine in patients with fibromyalgia syndrome (FMS). **Methods**: The patient and control groups were composed of 40 patients diagnosed with FMS in accordance with the 2016 American College of Rheumatology (ACR) criteria and 40 healthy volunteers, respectively. The data collection tools comprised the sociodemographic information form, the fibromyalgia impact questionnaire (FIQ), and the sleep hygiene index (SHI), which were used to assess patients' sociodemographic characteristics, FMS disease activity, and sleep quality, respectively. The inflammatory markers of the patient group were assessed by complete blood count before and after the duloxetine treatment and compared with those of the control group. **Results**: The white blood cell (WBC), neutrophil, and lymphocyte counts were significantly higher in the patient group than in the control group ($p < 0.001$, $p = 0.036$ and $p = 0.004$, respectively). Moreover, platelet distribution width (PDW) was significantly lower, whereas mean platelet volume (MPV) was significantly higher in the patient group than in the control group ($p < 0.001$ for both cases). In addition to patients' platelet-to-lymphocyte ratio (PLR) values, C-reactive protein (CRP) levels, and white blood cell (WBC) counts decreasing but not significantly ($p = 0.083$, $p = 0.068$, and $p = 0.065$, respectively), their neutrophil-to-lymphocyte ratio (NLR), hemoglobin (Hgb), and hematocrit (Hct) values declined substantially after commencing duloxetine treatment ($p = 0.001$, $p = 0.008$, and $p = 0.001$, respectively). **Conclusions**: The significant reduction in NLR, Hgb, and Hct levels following duloxetine treatment may indicate that these parameters can be utilized as biomarkers in determining the efficacy of treatment and in the follow-up of the treatment in FMS patients.

Keywords: fibromyalgia; duloxetine; neutrophil-to-lymphocyte ratio; platelet-to-lymphocyte ratio; mean platelet volume

1. Introduction

Fibromyalgia syndrome (FMS) typically presents as a chronic, widespread musculoskeletal pain syndrome and is often accompanied by fatigue, insomnia, cognitive impairment, and multiple somatic symptoms [1]. Although the etiology of FMS is not fully known, it has been suggested that changes in sleep stages, hormonal and biochemical changes, mood disorders, and dysfunction of the central nervous system play a role in the etiological process [2]. In parallel, it has been suggested that various cytokines, including tumor necrosis factor (TNF) and interleukin 8 (IL-8), contribute to the disease's inflammatory phase [3]. On the other hand, the role of non-traditional hematological markers in determining systemic inflammation has been increasingly investigated in recent years. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are indices that correlate with the prognosis of systemic inflammatory diseases, including inflammatory arthritis, diabetes mellitus, coronary artery diseases, ulcerative colitis, and some cancers (ovarian and colorectal cancer) [4]. Mean platelet volume (MPV) is an indicator of platelet function and activity, which is thought to play a role in immunological and inflammatory processes [5]. Immunological and inflammatory events are associated with the pathogenesis of FMS, as demonstrated by a number of investigations [4,6,7]. NLR, PLR, and MPV are the most commonly researched hematological markers, and their high levels indicate underlying inflammation. To the best of our knowledge, there are no published reports about how these indicators changed following treatment for patients with FMS. The purpose of this study is to investigate the relationship between duloxetine treatment and hematological factors such as MPV, NLR, and PLR, which are assumed to be involved in inflammatory processes in FMS patients.

2. Material and Methods

This was a prospective observational clinical study conducted between March 2022 and November 2022. The population of the study consisted of patients between the ages of 18 and 50 who applied to our pain clinic and were diagnosed with FMS according to the 2016 edition of the 2010/11 American College of Rheumatology (ACR) criteria. Written informed consent was obtained from each participant. The study was approved by the ethics committee of Mustafa Kemal University (08/14.04.2022) and conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria for the Patient group were defined as being 18–50 years of age, having been diagnosed with FMS for the first time, not having received FMS treatment, not having any systemic disease other than FMS, and not having been using any medication for any reason in the last three weeks. On the other hand, the study exclusion for the Patient group was defined as having any inflammatory autoimmune disease, history of malignancy, cardiovascular, neurological, renal, metabolic, and endocrine problems, abnormal uterine bleeding (hypermenorrhea, hypomenorrhea...), being pregnant or breastfeeding. In addition to the exclusion criteria defined for the patient group, the exclusion criteria for the control group also included an FMS diagnosis and chronic pain. Accordingly, the control group was selected from patients who applied to our pain clinic with localized joint pain. A complete blood count and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values were routinely measured at the time of the initial diagnosis of patients with FMS in order to exclude inflammatory diseases and also in the control group to exclude other inflammatory joint diseases. Subsequently, duloxetine 30 mg once a day was initiated in patients diagnosed with FMS. A complete blood count and ESR and CRP values were re-checked at the third-month follow-up while the FMS patients were on medical treatment. The demographic characteristics of the participants were recorded, and the body mass index (BMI) (kg/m^2) values were calculated for each participant. The revised fibromyalgia impact questionnaire (FIQ), the most recently approved self-report composite assessment tool developed to assess the impact of FMS symptoms and functional impairment, was used to assess FMS severity. The Sleep Hygiene Index (SHI) is designed to evaluate the presence of behaviors that are thought to impair sleep quality. Complete blood count measurements of the patients were carried out using the Sysmex XN-9000 series (Sysmexi Kobe, Japan) brand complete blood count device. Neutrophil, lymphocyte, and platelet counts and other hematological parameters were measured per manufacturers' instructions. The NLR was calculated by dividing the neutrophil count by the lymphocyte count, and the PLR was calculated by dividing the platelet count by the lymphocyte count. Clinical and laboratory assessments of the patients were performed within the scope of the same follow-up visit.

2.1 Power Analysis

G*Power (G*Power Ver. 3.1.9.2, Franz Faul, Universität Kiel, Germany) software package was used to determine the effective sample size for the study. With reference to the study conducted by Sargin *et al.* [8], based on a mean Neutrophil-to-lymphocyte ratio 3.4 $\pm$ 1.3, α = 0.05 type I error, r = 0.3 effect size, and 80% power, the minimum sample size was calculated as 44. Therefore, the minimum number of patients should be 22.

2.2 Statistical Analysis

The research data were analyzed using the SPSS 21.0 (Statistical Product and Service Solutions for Windows, Version 21.0, IBM Corp., Armonk, NY, USA, 2012) software package. The descriptive statistics obtained from the research data were expressed using mean and standard deviation, median, minimum and maximum, frequency, and percentage values. The normal distribution characteristics of the variables were analyzed using the Shapiro–Wilk test. Comparisons between the groups were made using the student's *t*-test, Mann–Whitney U test, paired *t*-test, and Wilcoxon test. The relationships among categorical variables were analyzed using chi-squared tests. Probability (p) statistics of $\leq$0.05 were deemed to indicate statistical significance.

3. Results

The study sample consisted of 80 individuals: 40 (50%) FMS patients and 40 (50%) control subjects. The mean ages of the patient and control groups were 36.9 $\pm$ 7.9 and 28.4 $\pm$ 4.2 years, respectively (p = 0.014). There was no significant difference between the groups in terms of BMI values (p = 0.233). Sixty-two percent of FMS patients were housewives, and 60% lived in the district. In contrast, 60% were housewives, and 62.5% lived in a city center in the control group (Table 1). The distribution of the complete blood count inflammatory markers by the groups shown in Table 2 indicates that WBC, neutrophil, and lymphocyte counts were significantly higher in the patient group than in the control group ($p < 0.001$, p = 0.036, and p = 0.004, respectively). In addition, platelet distribution width (PDW) was significantly lower, whereas MPV was significantly higher in the patient group than in the control group ($p < 0.001$ for both cases). A comparison of patients' pre- and post-treatment conditions is shown in Table 3, and also a comparison of complete blood count parameters before and after duloxetine treatment is shown in Table 4. As a result, in addition to the patients' PLR values, CRP levels and WBC counts decreased, albeit not significantly (p = 0.083, p = 0.068, and p = 0.065, respectively), after they were started on duloxetine treatment, their NLR, hemoglobin (Hgb), and hematocrit (Hct) values decreased significantly (p = 0.001, p = 0.008, and p = 0.001, respectively). In patients with FMS, when FIQ and SHI scores were compared before and after duloxetine treatment, a statistically significant difference was found ($p < 0.001$ and p = 0.017, respectively) (Fig. 1).

4. Discussion

This prospective research disclosed the change of inflammatory parameters that may be used as biomarkers over time while patients with FMS are under duloxetine treatment.

The comparison of FMS patients with control subjects did not reveal any significant difference between the two

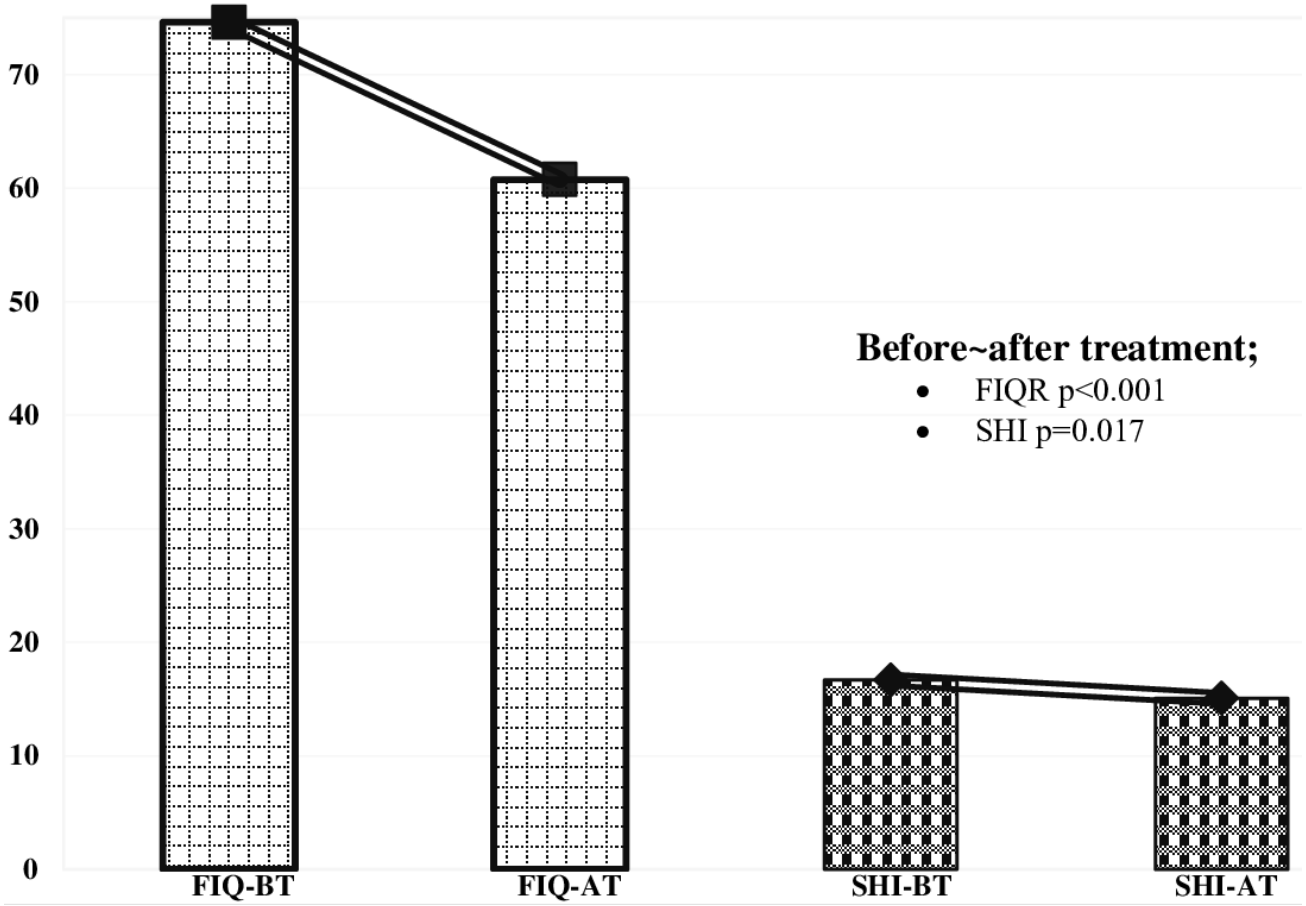

Fig. 1. Variation of FIQ and SHI according to treatment. FIQ, Fibromyalgia Impact Questionnaire; SHI, Sleep Hygiene Index; BT, Before Treatment; AT, After Treatment.

Table 1. Distribution of sociodemographics and clinical characteristics by the groups.

Variables	Categories	Patient group	Control group	*p*-value
Age		36.9 ± 7.9	28.4 ± 4.2	0.014
BMI		28.8 ± 4.6	27.3 ± 3.76	0.233
Gender	Female	32 (80)	30 (75)	0.225
	Male	8 (20)	10 (25)	
Marital status	Married	38 (95)	31 (77.5)	0.031
	Single	2 (5)	6 (15)	
	Widowed	0 (0)	3 (7.5)	
Educational level	Illiterate	2 (5)	3 (7.5)	0.17
	Literate	1 (2.5)	5 (12.5)	
	Primary education	18 (45)	12 (30)	
	Secondary education	8 (20)	13 (32.5)	
	Post-secondary education	11 (27.5)	7 (17.5)	
Occupation	Homemaker	25 (62.5)	24 (60)	0.45
	Government official	9 (22.5)	6 (15)	
	Laborer	5 (12.5)	6 (15)	
	Other	1 (2.5)	4 (10)	
Place of residence	City center	16 (40)	25 (62.5)	0.044
	District	24 (60)	15 (37.5)	

Table 2. Distribution of the values of complete blood count inflammatory markers by the groups.

Variables	Patient group			Control group			*p*-value
	Mean ± SD	Median	Min–Max	Mean ± SD	Median	Min–Max	
ESR	12.5 ± 6.1	13	2–34	14.5 ± 8.7	14	3–28	0.174
CRP	2.4 ± 2	1.8	0.4–7.8	2.7 ± 2.1	1.7	1–5.1	0.197
WBC COUNT × 10^3 (mm^3)	8.1 ± 2	7.8	5–13.5	6.7 ± 1.5	6.6	4.3–10.5	<0.001
Hgb g/dL	12.8 ± 1.4	12.8	9.7–16.2	12.8 ± 1.2	12.8	10.1–15.5	0.899
MCV (fL)	84.8 ± 5.7	85.7	71.1–97.7	86.4 ± 6.4	87.5	62.8–95.7	0.119
PLT COUNT × 10^3 (mm^3)	281.2 ± 67.4	269.5	179–488	277.8 ± 61.9	267.5	173–411	0.813
NEUTROPHIL COUNT × 10^3 (mm^3)	4.5 ± 1.3	4.5	2.4–7.8	3.9 ± 1.2	3.7	2–7.3	0.036
LYMPHOCYTE COUNT × 10^3 (mm^3)	2.6 ± 0.8	2.3	1.1–4.9	2.1 ± 0.5	2.1	1.4–3.3	0.004
NLR	1.9 ± 0.5	1.9	0.9–3.1	1.9 ± 0.6	1.8	0.9–3.4	0.651
PLR	120.6 ± 46.3	111.9	50.8–282.2	136.3 ± 32.8	132.9	84.1–207.6	0.082
PDW	13 ± 5.1	11.9	9.5–42.3	19.6 ± 22.8	16	12.7–160	<0.001
HTC	39.4 ± 3.7	39.4	32.2–50.1	38.6 ± 3.1	38.9	31.7–45.1	0.3
MPV (fL)	10.4 ± 0.9	10.3	9.2–12.3	9.6 ± 0.9	9.6	7.2–12.2	<0.001

ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; WBC, White blood cell; MCV, Mean corpuscular volume; hgb, Hemoglobin; Htc, hematocrit; Plt, platelet; PDW, Platelet distribution width; MPV, Mean platelet volume; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; g/dL, gram/deciliter; fL, femtoliter.

Table 3. Changes in the complete blood count inflammatory markers with the duloxetine treatment.

Variables	pre- or post-treatment	Mean ± SD	Median	Min–Max	*p*-value
ESR	Before	12.5 ± 6.1	13	2–39	0.515
	After	11.5 ± 5.6	11.5	2–25	
CRP	Before	2.4 ± 2	1.8	0.4–7.8	0.068
	After	2.2 ± 1.8	1.5	0.4–7.6	
WBC × 10^3 (mm^3)	Before	8.1 ± 2	7.8	5–13.5	0.065
	After	7.7 ± 1.8	7.6	4.8–13.8	
Hgb (g/dL)	Before	12.8 ± 1.4	12.8	9.7–16.2	0.008
	After	12.5 ± 1.6	12.8	9–15.9	
MCV (fL)	Before	84.8 ± 5.7	85.7	71.1–97.7	0.149
	After	83.7 ± 7	86.3	64.7–94.4	
PLT COUNT × 10^3 (mm^3)	Before	281.2 ± 67.4	269.5	179–488	0.064
	After	272.2 ± 63.3	265.5	185–460	
NEUTROPHIL COUNT × 10^3 (mm^3)	Before	4.5 ± 1.3	4.5	2.4–7.8	0.116
	After	4.2 ± 1.2	4	2.4–7.5	
LYMPHOCYTE COUNT × 10^3 (mm^3)	Before	2.6 ± 0.8	2.3	1.1–4.9	0.817
	After	2.6 ± 0.7	2.6	1.4–4.5	
NLR	Before	1.9 ± 0.5	1.9	0.9–3.1	0.044
	After	1.7 ± 0.4	1.7	0.8–2.5	
PLR	Before	120.6 ± 46.3	111.9	50.8–282.2	0.083
	After	111.8 ± 37.4	101.4	69.1–232.7	
PDW	Before	13 ± 5.1	11.9	9.5–42.3	0.95
	After	12.5 ± 2.2	12.2	9.1–17.4	
Htc	Before	39.4 ± 3.7	39.4	32.2–50.1	<0.001
	After	37.4 ± 5.7	38.6	12.2–47.1	
MPV (fL)	Before	10.4 ± 0.9	10.3	9.2–12.3	0.185
	After	10.5 ± 0.9	10.4	9.1–12.6	

ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; WBC, White blood cell; MCV, Mean corpuscular volume; hgb, Hemoglobin; Htc, hematocrit; Plt, platelet; PDW, Platelet distribution width; MPV, Mean platelet volume; PLR, platelet-to- lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; g/dL, gram/deciliter; fL, femtoliter.

Table 4. Complete blood count parameters before and after duloxetine treatment by BMI groups.

Variables	pre- or post-treatment	Normal (18.5–24.99)			Over-weight (24.99–29.99)			Obese (30+)		
		N	Mean ± SD/Median (Min–Max)	*p*-value	N	Mean ± SD/Median (Min–Max)	*p*-value	N	Mean ± SD/Median (Min–Max)	*p*-value
ESR	Before	11	13 (4–16)	0.95	16	13.50 (2–39)	0.80	13	14 (3–20)	0.194
	After	11	12.5 (4.10–19)		16	11 (2–25)		13	11 (3–18)	
CRP	Before	11	0.87 (0.35–2.37)	0.17	16	1.95 (0.67–5.30)	0.13	13	2.90 (0.43–7.81)	0.07
	After	11	1.25 (0.55–2.50)		16	1.37 (0.59–4.20)		13	2.86 (0.43–7.59)	
WBC × 10^3 (mm^3)	Before	11	7.85 ± 2.10	0.79	16	8.06 (5.60–10.76)	0.06	13	8.04 (5.59–13.51)	0.723
	After	11	7.74 ± 1.44		16	7.63 (5.75–8.77)		13	7.78 (4.76–13.84)	
Hgb (g/dL)	Before	11	13.05 (9.70–14.80)	0.01	16	12.70 (10.6–16.2)	0.24	13	12.67 ± 1.46	0.142
	After	11	12.50 (9–14.40)		16	13.20 (9.9–15.9)		13	12.35 ± 1.56	
MCV (fL)	Before	11	84.66 ± 6.67	0.31	16	87.68 ± 4.21	0.06	13	82 (72.9–90.7)	0.7
	After	11	84.08 ± 6.22		16	85.64 ± 690		13	85 (64.72–91.20)	
PLT COUNT × 10^3 (mm^3)	Before	1	282 (215–488)	0.09	16	265.5 (186–357)	0.44	13	265.40 (179–437)	0.544
	After	11	273 (200–460)		16	252.5 (185–338)		13	272 (193–427)	
NEUTROPHIL COUNT × 10^3 (mm^3)	Before	11	4.35 ± 1.60	0.64	16	4.55 (2.49–6.04)	0.07	13	4.71 ± 1.49	0.812
	After	11	4.17 ± 0.75		16	3.99 (2.44–5.16)		13	4.78 ± 1.71	
LYMPHOCYTE COUNT × 10^3 (mm^3)	Before	11	2.33 (1.84–3.31)	0.34	16	2.37 (1.12–4.94)	0.99	13	2.6 ± 0.88	0.923
	After	11	2.32 (1.80–4.53)		16	2.69 (1.67–3.53)		13	2.62 ± 0.71	
NLR	Before	11	1.77 (0.91–3.12)	0.66	16	1.82 (0.94–3.02)	0.03	13	1.90 (1.43–2.25)	0.857
	After	11	1.70 (0.79–2.54)		16	1.47 (1.06–2.35)		13	1.83 (1.02–2.51)	
PLR	Before	11	114.5 (89.72–201.09)	0.11	16	109.76 (50.81–171.8)	0.32	13	108.86 (62.74–282.2)	0.382
	After	11	112.21 (69.09–203.89)		16	91.33 (70.48–197.6)		13	108.53 (77.81–232.65)	
PDW	Before	11	14.67 ± 9.89	0.68	16	11.75 (9.8–16.4)	0.43	13	12 (10.40–15.50)	0.631
	After	11	12.11 ± 2.64		16	12.20 (9.5–16.9)		13	12.90 (10.05–15.50)	
Htc	Before	11	39.3 (32.9–45.1)	0.07	16	39.87 ± 4.19	0.08	13	39.10 (33.40–47.5)	0.032
	After	11	37.15 (12.2–41)		16	38.76 ± 4.61		13	39 (31.40–45.80)	
MPV (fL)	Before	11	9.95 (9.20–12.10)	0.24	16	10.40 (9.2–12.3)	0.95	13	10.54 ± 0.84	0.068
	After	11	10.25 (9.30–12.60)		16	10.25 (9.1–12.2)		13	10.78 ± 0.76	

ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein; WBC, White blood cell; MCV, Mean corpuscular volume; hgb, Hemoglobin; Htc, hematocrit; Plt, platelet; PDW, Platelet distribution width; MPV, Mean platelet volume; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; g/dL, gram/deciliter; fL, femtoliter.

groups in terms of ESR, CRP, NLR, and PLR values. However, there was a significant difference between the two groups in MPV and PDW values. In addition, in this first study to date on the comparative analysis of the whole blood count biochemical markers of FMS patients who were treated with duloxetine, significant changes were observed between pre- and post-treatment NLR, Hgb, and Hct values.

The mechanisms of the symptoms that develop on an inflammatory background and accompany FMS, such as morning stiffness and irritable bowel syndrome, have not been fully clarified. In fact, it is still a matter of debate whether FMS is an inflammatory disease or not. Furthermore, the literature data on the changes in ESR and CRP values in the context of FMS are contradictory [9–12]. The majority of studies revealed no change in ESR, whereas a large-scale investigation found a positive link between CRP and FMS, which was, however, diminished when BMI and comorbidities were ruled out as confounding variables [13]. Similar to this research, our study demonstrated no significant difference between the patient and control groups in terms of ESR and CRP. Several studies have demonstrated that cytokines such as interleukin 6 (IL-6), IL-8, and tumor necrosis factor-alpha (TNF- α), as well as neurotransmitters such as substance P (SP), are involved in the pathogenesis of FMS [13–15]. Due to their high cost, these biomarkers have limited utility in clinical practice. On the other hand, a complete blood count is a more routinely performed laboratory test. There are noteworthy studies on the systemic inflammatory markers in peripheral blood, such as NLR and PLR, which can be easily measured via hemogram. Studies have reported that high NLR and PLR values indicate increased inflammation and are associated with impaired renal function in diabetic patients, increased cardiovascular risk in some malignancies, and increased mortality [16–19]. Neutrophils function as mediators of inflammation. There is some evidence that neutrophil counts are higher in FMS patients than in the healthy population [20]. Lymphocytes play a role in chronic inflammation, and low lymphocyte counts have an impact on morbidity and mortality [21]. Platelets are positive acute-phase reactants that are produced in large amounts in response to inflammatory conditions. These findings suggest that NLR and PLR may be considered indicators of inflammation [10,22].

Otherwise, the mean neutrophil and lymphocyte counts were found to be significantly higher in FMS patients than in the control subjects included in this study. However, there was no significant difference between the groups in NLR and PLR values. Nevertheless, even though there was no significant difference between the groups in PLR, the fact that the respective *p*-value was 0.082 may suggest that the said difference between the groups in PLR may gain significance in a larger sample. Similarly, in another study, no significant difference was found between the FMS patients and control subjects in NLR and PLR [23]. IL-8 and IL-6 are associated with platelet hyperactivity, and cytokines may lead to lower MPV values centrally due to peripheral activation of platelets in the nervous system in the event of FMS. Other studies on excessive systemic inflammatory diseases, such as rheumatoid arthritis, lupus, *etc*., demonstrated that low MPV values indicate an active and/or chronic inflammatory state in the body [24]. Literature data suggest that there may be a relationship between platelet indices (platelet count, PDW, and MPV) and inflammation [25]. In fact, PDW, a negative acute phase reactant, has been reportedly low in patients with rheumatoid arthritis [26]. In addition, it has been stated that MPV levels may elevate in the event of inflammatory diseases [27]. In comparison, the mean PDW and MPV values were lower and higher, albeit not significantly, in the patient group than in the control group, respectively. In fact, some studies did not find any significant difference between the FMS patients and control subjects in MPV values [23,28,29]. MPV, a determinant of platelet activation, is an emerging independent risk factor for cardiovascular disease. It was demonstrated that MPV, a marker of early atherosclerosis, is elevated in FMS patients [30,31], indicating that platelet activation is increased and hence the risk of future cardiovascular disease is higher. The pathophysiology of FMS is still not completely clear. Functional changes in the context of FMS include altered sensory processing in the brain referred to as "central sensitization", decreased reactivity of the hypothalamic-pituitary-adrenal (HPA) axis against stress, increased pro-inflammatory and reduced anti-inflammatory cytokine profiles, disturbances in neurotransmitters such as dopamine and serotonin, and small nerve fiber pathology [32,33]. Serotonin and norepinephrine reuptake inhibitors are recommended treatment options for FMS. Duloxetine, which is used in the treatment of a variety of neuropathic and chronic pain conditions, functions by increasing the activity of noradrenergic and serotonergic neurons in the descending spinal tract in the dorsal horn. These descending neurons inhibit the activity of dorsal horn neurons, preventing excess input from reaching the brain [34].

Researchers have also focused on the anti-inflammatory potential of duloxetine through pathways associated with serotonin and noradrenaline [35]. It has been suggested that duloxetine exerts its therapeutic effect in part by targeting glial activation and thus inhibiting neuroinflammation. Furthermore, duloxetine has been shown to reduce ventricular lactate, which acts as a surrogate for central inflammation [36]. The lack of laboratory parameters that can be used in the follow-up of FMS treatment and the subjective evaluation of symptoms depending on various questionnaires cause difficulties in the follow-up of FMS treatment [37,38]. A statistically significant decrease was observed in the FIQR and SHI scores and the NLR, Hgb, and Hct values of FMS patients after they were started on duloxetine, suggesting that NLR, Hgb, and Hct may be used as indicators to predict the effectiveness of treatment in FMS patients. Even though

the findings of this study do not establish NLR, Hgb, and Hct as inflammatory markers, they may be used to evaluate treatment efficacy.

The fact that the *p*-value for the difference between the pre-treatment and post-treatment PLR values was 0.082 may indicate that the difference between the groups in PLR may become statistically significant with a larger sample size. It is not clear whether the changes occurring in blood parameters after the use of duloxetine are caused by the effect of duloxetine on the unknown etiology of FMS or the inflammatory parameters in the complete blood count. Further studies are needed to shed more light on the subject.

A higher BMI is negatively correlated with a positive outcome in fibromyalgia patients, according to a systematic review by Migliorini *et al*. [39]. Contrary to this study, we found no significant differences between the BMI groups.

Contrary to the previous studies on inflammatory markers in the etiopathogenesis of FMS, different parameters, such as the presence of comorbidities (especially high BMIs), medication use, and symptom patterns, were taken into account in the inclusion criteria of this study. Therefore, by excluding patients with comorbidities, it was possible to minimize the influence of confounding variables that can alter a complete blood count and inflammatory markers. This study is unique in demonstrating treatment response in FMS patients with objective parameters. In addition to the strengths highlighted, this study also had several limitations. The inability to examine the impact of duloxetine medication on inflammatory markers due to the lack of a randomized controlled design and the limited sample size were the main limitations of this investigation.

5. Conclusions

The findings of this study suggest that MPV and PDW may be used as inflammatory markers to aid in the diagnosis of FMS and that NLR, Hgb, and Hct values may be used as biomarkers in the follow-up of FMS treatment. In conclusion, there is a need for more research into these objective tests in order to assist in the diagnosis of FMS and guide treatment follow-up.

Availability of Data and Materials

The underlying datasets related to the results of the research paper can be shared as needed.

Author Contributions

FE contributed to implementation of the research and to the writing of the manuscript. RI conceived the original project and supervised the project. Both authors contributed to editorial changes in the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of Mustafa Kemal University (08/14.04.2022) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare no conflict of interest.

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