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Evaluation of Inflammatory Markers in Patients with Fibromyalgia Syndrome in King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia: A Cross-Sectional Study

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Abstract

Objectives: The goal of this study was to examine various markers in patients with FMS, including the neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), platelet distribution width (PDW), and mean platelet volume (MPV).

Methods: This was a cross-sectional, retrospective study conducted at King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia, involving the examination of inflammatory markers, such as PDW, NLR, and MPV. The results were evaluated with IBM SPSS version 25, and a *P*-value of <0.05 was used to reject the null hypothesis.

Results: In total, 396 participants were included in this study: 235 in the FMS group and 161 in the control group. MPV, PDW and NLR values are 10.31 ± 1.6 fL, 124.57 ± 70.0, 2.30 ± 3.2, respectively. The PDW in the control group (12.47 ± 2.5) was significantly higher than that in the FMS group (11.84 ± 2.4) ($P = 0.003$). Erythrocyte sedimentation rate and Vitamin D levels ($P = 0.001$) were significantly higher in the control group than in the FMS group, with values of 31.71 and 24.2 and 75.60 and 39.4, respectively. No significant differences were found in MPV and NLR values between the FMS and control groups.

Conclusion: The findings in this study suggest that PDW and PLR are important inflammatory markers that may be beneficial in FMS diagnosis.

Keywords: Fibromyalgia syndrome, neutrophil/lymphocyte ratio, platelet distribution width, mean platelet volume

Introduction

Fibromyalgia syndrome (FMS) is a condition that causes chronic widespread musculoskeletal and soft tissue pain that is accompanied by systemic symptoms, including debilitating fatigue, cognitive disturbances, and mood disorders.[1,2] Although evidence regarding the definitive etiology of this disease is scarce, disturbances in the brain's ability to process pain have been described as the most likely culprit.[3,4] Patients are often hypersensitive to the perception of pain due to an increase in the levels of excitatory neurotransmitters such as glutamate and substance P. There is also a prolonged enhancement of the sensation of pain that has been found to be associated with dopamine dysregulation. This constant hypervigilance of pain eventually leads to crippling psychological manifestations, including depression and anxiety.[5]

FMS can also be primary or secondary to systemic diseases such as rheumatoid arthritis. The diagnosis was based on the American College of Rheumatology (ACR) criteria published in 1990.[6] Globally, the prevalence of FMS was found to be approximately 2.7%. It is more prevalent in women and individuals older than 50 years. This seems to affect people with low educational and/or socioeconomic status who live in rural areas. Obese women were also found to be more afflicted.[7] However, the prevalence of FMS in Saudi Arabia remains unclear.

The neutrophil/lymphocyte ratio (NLR) is an inexpensive and easily available marker for measuring systemic inflammation.[8-10] While the mean platelet volume (MPV) is a measure of platelet size and a marker and indicator of platelet function,[11] a correlation has also been found between the MPV and inflammatory conditions.[12,13] The platelet distribution width (PDW) is another inflammatory marker that increases during platelet activation. It measures platelet size variability and is considered a more specific indicator of platelet reactivity than the mean platelet volume (MPV) because it remains unaffected by single platelet distention caused by platelet swelling. The fraction of larger platelets that are enzymatically and metabolically active is usually detected based on PDW.[14]

A study was conducted to measure the NLR, MPV, and PDW of a total of 197 patients with FMS while comparing them with a control group. The NLR and MPV were found to be significantly higher and the PDW significantly lower than those in the control group. This study concluded that these inflammatory markers could add value to the diagnosis of FMS. In the receiver operating characteristic curve analysis, blood PDW had ≥90.4% sensitivity and 90% specificity in predicting fibromyalgia.[15]

Ongoing research suggests that inflammatory processes play a role in the etiology of FMS.[16] In FMS, there are no blood tests that can confirm the diagnosis or predict the existence of the disease. In our study, we aimed to investigate the NLR, platelet/lymphocyte ratio (PLR), PDW, and MPV, among other markers, in patients with FMS.

Methodology

This cross-sectional, retrospective study was conducted at King Abdulaziz University Hospital (KAUH) in Jeddah, Saudi Arabia and included patients who were ≥18 years old and diagnosed with FMS based on the 1990 American College of Rheumatology criteria. The study was conducted with adherence to the Declaration of Helsinki guidelines. This study included 396 participants (235 and 161 in the FMS and control groups, respectively). Patients aged < 18 years with endocrine problems (hypo and hyperthyroidism), malignancies, psychological illnesses, or a known chronic pain condition were excluded from the study. The hospital's Institutional Board approved this study.

Data were collected from electronic records, including demographics (age, sex, ethnicity, and body mass index [BMI]) and past medical history, such as the presence of comorbidities, history of hypothyroidism, depression, and sleep disturbances. Further data consisted of the patients' laboratory panels, which included complete blood count components (hemoglobin level, red blood cell count, neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio, platelet count, mean platelet volume, platelet distribution width, and platelet/lymphocyte ratio), kidney function tests (creatinine and urea), Vitamin D, and thyroid stimulating hormone levels. Inflammatory markers, including the erythrocyte sedimentation rate and C-reactive protein, ferritin, prothrombin, and fibrinogen levels, were also evaluated.

The results were analyzed using IBM SPSS version 25 (IBM Corp., Armonk, N.Y., USA), with a margin of error of 5% and confidence interval of 95%. To establish a relationship between categorical variables, we used the chi-square test. An independent t-test was used to compare two groups. These tests were performed under the assumption of a normal distribution. Welch's t-test for the two-group means was performed as an alternative test. Dependent variables yielded binary results. To evaluate the important predictors of any given dependent study variable with 95% confidence intervals, a Binary Logistic Regression Model (BLRM) with Backward Conditional Elimination and Enter Criteria = 0.05 and Elimination = 0.10 was utilized. Finally, a standard *P*-value of 0.05 was used to reject the null hypothesis.

Results

This study included 396 participants, with 235 patients with FMS and 161 in the control group. A majority of the participants were female (68.2%), Saudi Arabian (79.1%), and unemployed (93.1%). In terms of their BMI, 34.7% were overweight, 34.1% were obese, and 28.8% had normal BMI. When asked if they were smoking, 97.5% answered no, and 56.5% were taking medications, as shown in Table 1.

Table 2 summarizes the comorbidities and medical histories of the study participants. The majority of the participants (22.5%) had depression, followed by hypertension (17.2%) and diabetes (15.9%). Figure 1 shows the comorbidities of patients in the FMS and control groups. Patients with FMS (35.3%) had higher rates of depression (3.7%). The control group, on the other hand, had a higher percentage of patients with hypertension (27.1%) and diabetes (17.4%).

The mean MPV, PDW, NLR, and other markers of the participants are presented in Table 3. The mean MPV, PDW and NLR were 10.31 ± 1.6 fL, 124.57 ± 70.0, 2.30 ± 3.2, respectively. The mean levels of inflammatory markers are shown in Table 3.

Using the chi-square test at <0.05 level, significant differences were found between the frequency of normal and abnormal levels of MPV ($P = 0.041$), lymphocyte count ($P = 0.009$), CRP ($P < 0.001$) and Vitamin D level ($P < 0.001$). The results further showed that most participants in both the FMS and control groups had normal levels of MPV, PDW, and NLR (Table 4).

The mean levels of MPV, PDW, NLR, and other markers in the FMS and control groups are presented in Table 4. On using the independent t-test at <0.05 level, findings revealed that the MPV of the FMS group was somewhat similar to that of the control group (10.22 ± 1.1 fL and 10.45 ± 2.0 fL, respectively). No statistically significant difference was found in MPV between the two groups. In contrast, the PDW, platelet/lymphocyte ratio, ESR, and Vitamin D levels were significantly different between the two groups. The PDW value of the control group (12.47 ± 2.5) was significantly higher than that of the FMS group (11.84 ± 2.4) ($P = 0.003$). The ESR ($P = 0.017$) and Vitamin D levels of the control group ($P = 0.001$) were significantly higher as well: 31.71 ± 24.2 and 75.60 ± 39.4, respectively. In contrast, the platelet/lymphocyte ratio of the FMS group (133.45 ± 69.7) was significantly higher than that of the control group (107.57 ± 67.7) ($P = 0.037$). No significant difference was found between the two groups in NLR (Table 5).

Discussion

In this study, we investigated the MPV, PDW, and NLR of patients with FMS treated in the King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. FMS is a typical rheumatic disorder involving the bones and muscles, but not the joints. However, the etiology of FMS remains unknown. It is not recognized as a form of inflammatory disorder. However, Bote et al. showed that anti-inflammatory therapies enhance and modify neutrophil function in patients with FMS, suggesting a role for inflammatory processes in the development of FMS.[17] NLR, PLR, MPV, and PDW are widely accepted markers of inflammatory reactions.[18]

In the present study, the PDW of the FMS group was significantly lower than that of the control group, which is similar to the results of previous studies in Turkey.[15,19] According to the current research, there may be an association between platelet count, PDW, MPV, and inflammation.[20] The PDW is low in patients with rheumatoid arthritis (Isik et al., 2014). MPV has been positively and negatively associated with inflammation.[21,22]

The PLR and NLR of individuals were also assessed in the current study. The findings demonstrated that The PLR in the FMS group was significantly higher than that in the control group; however, the NLR showed no statistical difference.

Table 1. **Demographic characteristics of 396 study samples**

Demographics		N	Min	Max	Mean	SD
Age (regroup)		396	16	90	43.45	14.4
BMI		340	15.63	56.49	28.62	6.5
			Count		%	
Total			396		100.0	
Case/Control	Case		235		59.3	
	Control		161		40.7	
Sex	Male		126		31.8	
	Female		270		68.2	
Ethnicity	Saudi		186		79.1	
	Non-Saudi		49		20.9	
	Missing		161			
BMI	Underweight		8		2.4	
	Normal		98		28.8	
	Overweight		118		34.7	
	Obese		116		34.1	
	Missing		56			
Occupation	Unemployed		148		93.1	
	Employed		11		6.9	
	Missing		237			
Smoking	Yes		4		2.5	
	No		155		97.5	
	Missing		237			
Medications	Yes		91		56.5	
	No		70		43.5	
	Missing		235			

Table 2. **Comorbidities of the study participants**

Comorbidities	Count	%
Diabetes	63	15.9
Hypertension	68	17.2
Hypothyroidism	35	8.8
Cancer	6	1.5
Depression	89	22.5
Sleep disturbance	12	3.0
Viral infection	6	1.5

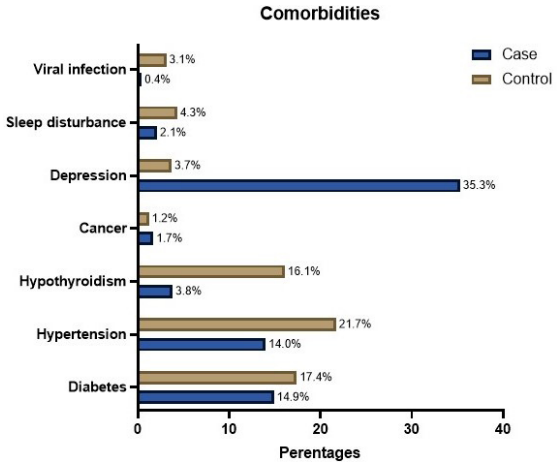

Fig. 1 **Comorbidities of the 396 study participants.**

These results were similar to those reported by Ilgun et al. In a study by Kilic et al., the NLR and PLR were statistically significantly higher in patients with FMS than in the control group.

A similar finding was obtained in a study by Karabas and Atar et al., who found no significant differences among control, FMS, and knee osteoarthritis groups. Molina et al., on the other hand, discovered that PDW levels were higher and MPV values were lower in patients with FMS.[23] Al-Nimer et al. reported a significant increase in the MPV and PDW in women.[24] Karlıbel et al. also showed that PDW values were significantly higher, while MPV values were significantly lower in patients with FMS.[25] These contradictory results may be due to the differences in the characteristics of the groups involved.

This study also found that the FMS and control groups had significantly different levels of vitamin D and ESR.

Table 3. **Mean values of inflammatory markers obtained from 396 study participants**

Variables	N	Min	Max	Mean	SD
WBC (4.5–11.0)	130	2.96	38.71	7.95	3.8
Hemoglobin level (Male = 14–17, Female = 12–16)	315	6.90	39.30	12.72	2.6
Platelet count (150–350 mm)	314	10.00	812.00	283.30	86.1
Mean platelet volume (7.2–11.7 fL)	302	1.20	24.00	10.31	1.6
Platelet distribution width (8.3%–56.6%)	281	3.20	21.70	12.09	2.5
Platelet/lymphocyte ratio (90–210)	277	3.33	485.00	124.57	70.0
Neutrophil count (1.56–6.13 x 109/L)	277	0.30	77.00	6.05	9.7
Lymphocyte count (1.00–4.80 x 109/L)	278	0.40	61.20	3.80	7.1
Neutrophil/lymphocyte ratio (0.78–3.53)	277	0.02	35.55	2.30	3.2
ESR (0–20)	138	0.29	121.00	27.76	23.6
CRP (<3.3 mg/dL)	148	0.028	177.000	8.24	21.8
Vitamin D level (N >75 ng/dL)	180	4.80	253.60	63.30	40.9
RBC count (4.2–5.9 x 10/L)	185	2.17	7.53	4.70	0.9
Prothrombin time (11–13 S)	124	10.10	27.80	12.06	2.0
Creatinine (61.9–115 µmol/L)	175	3.00	700.00	81.91	74.3
Urea (2.9–7.1 mmol/L)	173	1.70	105.00	6.00	10.1
TSH (0.5–5.0 mU/L)	113	0.01	25.01	2.41	3.0
Fibrinogen 200–400 mg/ dL	15	195.00	995.00	477.97	196.1
Ferritin (15–200 µg/L)	48	3.34	2081.05	245.43	461.0

Table 4. **Frequency of normal and abnormal levels of inflammatory markers in the FMS and control groups**

Variables		Total	Case/Control		*P*-value
			Case	Control	
Hemoglobin Level (Male = 14–17, Female = 12–16)	Normal	184	101(54.6%)	83(63.8%)	0.101
	Abnormal	131	84(45.4%)	47(36.2%)	
Platelet count (150–350 mm)	Normal	241	142(77.2%)	99(76.2%)	0.833
	Abnormal	73	42(22.8%)	31(23.8%)	
Mean platelet volume (7.2–11.7 fL)	Normal	269	164(92.1%)	105(84.7%)	0.041[a]
	Abnormal	33	14(7.9%)	19(15.3%)	
Platelet distribution width (8.3%–56.6%)	Normal	279	168(99.4%)	111(99.1%)	0.769
	Abnormal	2	1(0.6%)	1(0.9%)	
Platelet/lymphocyte ratio (90–210)	Normal	170	117(64.3%)	53(55.8%)	0.168
	Abnormal	107	65(35.7%)	42(44.2%)	
Neutrophil count (1.56–6.13 x 109/L)	Normal	214	140(76.5%)	74(78.7%)	0.676
	Abnormal	63	43(23.5%)	20(21.3%)	
Lymphocyte count (1.00–4.80 x 109/L)	Normal	245	168(91.8%)	77(81.1%)	0.009[a]
	Abnormal	33	15(8.2%)	18(18.9%)	
Neutrophil/lymphocyte ratio (0.78–3.53)	Normal	212	139(76.0%)	73(77.7%)	0.751
	Abnormal	65	44(24.0%)	21(22.3%)	
ESR (0–20)	Normal	66	32(57.1%)	34(41.5%)	0.070
	Abnormal	72	24(42.9%)	48(58.5%)	
CRP (<3.3 mg/dL)	Normal	106	38(50.7%)	68(93.2%)	<0.001[a]
	Abnormal	42	37(49.3%)	5(6.8%)	
Vitamin D level (N >75 ng/dL)	Normal	57	23(21.1%)	34(47.9%)	<0.001[a]
	Abnormal	123	86(78.9%)	37(52.1%)	

[a]significant using the chi-square test at <0.05 level. [b]No statistics are computed because variable is a constant.

Table 5. **Comparison of mean values of inflammatory markers of FMS and control groups**

Variables	Total	Case	Control	*P*-value
Hemoglobin level (Male = 14–17, Female = 12–16)	315	12.72 ± 2.3	12.71 ± 2.9	0.956
Platelet count (150–350 mm)	314	284.36 ± 86.8	281.80 ± 85.5	0.796
Mean platelet volume (7.2–11.7 fL)	302	10.22 ± 1.1	10.45 ± 2.0	0.250
Platelet distribution width. (8.3%–56.6%)	281	11.84 ± 2.4	12.47 ± 2.5	0.037[a]
Platelet/lymphocyte ratio (90–210)	277	133.45 ± 69.7	107.57 ± 67.7	0.003[a]
Neutrophil count (1.56–6.13 x 109/L)	277	5.14 ± 7.5	7.83 ± 12.9	0.064
Lymphocyte count (1.00–4.80 x 109/L)	278	3.16 ± 5.7	5.02 ± 9.0	0.069
Neutrophil/lymphocyte ratio. (0.78–3.53)	277	2.28 ± 2.6	2.34 ± 4.0	0.883
ESR (0–20)	138	21.97 ± 21.5	31.71 ± 24.2	0.017[a]
CRP (<3.3 mg/dL)	148	14.81 ± 28.7	1.49 ± 5.7	<0.001[b]
Vitamin D level (N >75 ng/dL)	180	55.29 ± 40.1	75.60 ± 39.4	0.001[a]

[a]significant using the Independent t-test at <0.05 level. [b]significant using Welch's t-test at <0.05 level.

Chronic pain and tiredness are indications of vitamin D deficiency, which usually coincide with FMS symptoms. Similar to vitamin D deficiency, FMS exerts its effects through inflammatory pathways and neurotransmitters, which is similar to how vitamin D deficiency occurs.[26] Our study found that the Vitamin D levels in the FMS group were significantly lower than those in the control group. Several studies have also discovered a significant decrease in Vitamin D levels in patients with FMS.[27,28] In most patients with fibromyalgia, the ESR is normal, but obese people may have a somewhat higher ESR. A high ESR could indicate an inflammatory condition or an undiscovered malignancy.[29]

The current study has some limitations. Most study participants had comorbidities, high BMIs, and were taking medications that may influence variables that affect inflammatory markers. Furthermore, because the study was cross-sectional and retrospective, it was difficult to determine causal correlations. Nonetheless, a large sample size may help generalize the findings. Our findings suggest that inflammatory indicators, such as PDW, ESR, and Vitamin D levels, may be relevant in FMS diagnosis and treatment planning.

Conclusion

The MPV, NLR, PLR, and PDW values of patients with FMS and controls were assessed in this cross-sectional retrospective investigation. Our findings revealed that the PDW of the FMS group was much lower than that of the control group, whereas the PLR of the FMS group was significantly higher than that of the control group. Furthermore, ESR and Vitamin D levels in the FMS group were much lower than those in the control group. These indicators can be obtained using a complete blood test, which is rapid and inexpensive. The findings of this study may be relevant for the diagnosis and treatment of FMS.

Statements and Declarations

Authorship

All the authors contributed to the conception and design of this study. The materials were prepared, data were gathered, and an analysis was performed by Yasser Bawazir, Mohammad Attiyah, Bushra Almusally, and Rola Hassan. The first draft of the paper was written by Yasser Bawazir and earlier drafts were reviewed by all authors. All authors examined and approved the final draft of the manuscript.

Ethical Part & Confidentiality

Ethical approval was obtained from King Abdulaziz University Hospital, with the IRB Approval number, in accordance with the Helsinki Declaration for human subjects.

Consent to Participate

Informed consent was obtained from the participants after explaining the study objectives and health benefits, and stressing the anonymity of the collected data.

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Competing Interest

The authors declare no conflicts of interest in relation to this study, which was self-funded.

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Availability of Data and Material

The datasets generated and analyzed during the current study are not publicly available because the data are contained within our hospital's electronic medical records, but are available from the corresponding author upon reasonable request.

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