

## Assessment of Inflammatory Hematological Indices in Iraqi Patients with Fibromyalgia: A Case–Control Study

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**Abstract | Background:** Fibromyalgia syndrome is characterized by chronic widespread pain accompanied by physical and psychological symptoms, often without a clearly defined pathological cause. Inflammatory markers derived from routine hematological parameters, such as the Neutrophil-to-Lymphocyte Ratio (NLR), Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW), have been proposed as indicators of systemic inflammation. **Objective:** To evaluate NLR, MPV and PDW as inflammatory markers in patients with fibromyalgia. **Patients and Methods:** This case–control study was conducted at the Rheumatology Unit of Baghdad Teaching Hospital between July and November 2017. A total of 100 patients diagnosed with fibromyalgia according to the 2012 Canadian Guidelines and 50 healthy controls were included. Data collection involved structured questionnaires, clinical interviews and laboratory investigations. Hematological parameters, including MPV and PDW, were measured, while NLR was calculated manually from complete blood count data. **Results:** The neutrophil-to-lymphocyte ratio was significantly higher in patients with fibromyalgia (2.18) compared to healthy controls (1.92) ( $p = 0.033$ ). Mean platelet volume was also significantly elevated in patients (8.3) relative to controls (8.0) ( $p = 0.045$ ). In contrast, platelet distribution width was lower in patients (16.7) compared to controls (17.0), with a statistically significant difference ( $p = 0.01$ ). No significant differences were observed in demographic variables between the groups. However, Receiver Operating Characteristic (ROC) analysis demonstrated that none of these parameters reached sufficient diagnostic accuracy ( $AUC < 0.65$ ) to serve as reliable diagnostic markers for fibromyalgia. **Conclusion:** Patients with fibromyalgia exhibit elevated NLR and MPV alongside reduced PDW, suggesting a possible inflammatory component in the disease. However, these hematological indices lack adequate diagnostic performance and should not be used independently for the diagnosis of fibromyalgia.

**Key Words** Fibromyalgia Syndrome, Neutrophil-To-Lymphocyte Ratio, Mean Platelet Volume, Platelet Distribution Width, Inflammatory Biomarkers, Case–Control Study, Hematological Indices, Diagnostic Accuracy

### INTRODUCTION

#### Fibromyalgia

Fibromyalgia Syndrome (FMS) is a clinical designation employed to characterize the reduced life quality associated with caused by generalized body aches and psychological and physical symptoms, in the lack of a discernible pathological aetiology [1].

The absence of a definitive organic foundation for fibromyalgia, together with the elevated occurrence of affective disorders in individuals with fibromyalgia, prompted several observers to classified a psychosomatic illness or non-disease. In the 1980s, the word "fibrositis"

was replaced by "fibromyalgia" because all efforts to demonstrate that connective tissue and muscle were inflamed or had other problems had failed [2,3].

#### Epidemiology

Fibromyalgia Syndrome (FMS) exhibits a notable prevalence of females, with a female-to-male ratio ranging from 7 to 9:1. While its peak incidence occurs between the ages of 20 and 60, FMS has also been identified in individuals across various age groups, including adolescents, older adults and children. Consequently, FMS is recognized as a significant concern

within the realm of community health. Studies have reported its occurrence in 5% of patients attending general medical practices and up to 15% of patients seeking rheumatology care [4,9].

### Etiology

The etiology of FMS remains elusive [10].

- **Genetic:** The prevalence of fibromyalgia is greater among first-degree relatives, suggesting a genetic predisposition to the disease, as they have 8.5 times more risk to have FMS compared to the general population [2,11]
- **Environmental:** Fibromyalgia has been linked to the occurrence of various forms of physical trauma, infectious disorders and emotional trauma [6,12,13]

### Pathogenesis

Several mechanisms have been suggested including abnormal pain perception, sleep disturbance, abnormal circulating levels of central neurochemical substances and skeletal muscles abnormalities [14].

People with FMS also may have imbalances in any of the following brain chemicals: serotonin, melatonin, stress hormones, IGF-1 growth hormone all showed low level, while substance P shows high levels and there is abnormal pain perception [6,15].

### Clinical Feature

- **Pain:** The main presenting feature and dominant symptom is widespread pain lasting more than 3 months. According to the American College of Rheumatology (ACR), fibromyalgia is characterized as bilateral pain presented in regions both above and below the waist. Furthermore, the presence of pain in the axial skeleton (namely, the anterior chest, cervical spine, thoracic spine, or low back) is required. The condition often exhibits a lack of response to analgesic medications and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), while the use of physiotherapy frequently exacerbates the pain [16,17]
- **Fatigue:** Fatigue often exhibits a pattern of increased severity at awakening, gradual amelioration throughout the morning hours and subsequent exacerbation in the afternoon. The weariness encountered by patients is defined as quite debilitating. The evaluation and treatment of this symptom pose significant challenges because of potential factors such as depression, deconditioning, interrupted sleep, unpleasant effects of medication, or the presence of comorbid illnesses [18,19]
- **Nonrestorative Sleep:** Non-refreshing sleep is a prevalent characteristic seen in more than 90% of those diagnosed with fibromyalgia. The majority of patients have suboptimal sleep quality, which is characterized by feelings of fatigue, challenges in engaging in physical activities and impaired cognitive function [17]

- **Morning Stiffness:** Stiffness is generally present on arising in the morning; usually it improves during the day, but in some patients it lasts all day. This can be very debilitating; it was rated as the most troublesome symptom experienced by patient [18,20]
- **Anxiety and Depression:** Approximately 13–71 % of FMs patients have anxiety and 20–80 % have depression. Depression is often correlated with heightened weariness, decreased sleep quality and inadequate pain management. Conversely, individuals with anxiety commonly encounter symptoms such as palpitations, dizziness, perspiration and paresthesia [17,18]
- **Impaired Cognition:** Poor short-term memory as well as difficulty in learning a new task, processing information and problem solving are common complaints. It often described as brain fog [17]
- **Other Symptoms:** Individuals diagnosed with fibromyalgia may present with a range of symptoms that extend beyond the musculoskeletal system. These symptoms may manifest in various bodily systems, such as the gastrointestinal system, where patients may experience symptoms like vomiting, nausea, abdominal pain, diarrhea bloating and constipation. Additionally, urogynecologic symptoms, including frequency, incontinence, pelvic pain, urgency and dysmenorrhea, may also be reported. Furthermore, patients may exhibit neurologic symptoms such as paresthesia, vertigo, dizziness and tinnitus. Another common complaint among fibromyalgia patients is discomfort when touched, known as allodynia [16,17]

### Diagnosis

Diagnosis of FMS depends on clinical evaluation only since no laboratory tests, or radiographic studies have been established to reach the diagnosis [21].

In 1990 the ACR defined diagnostic criteria based on a history of widespread musculoskeletal pain present for at least three months and tenderness in at least 11 of 18 defined tender points with sensitivity of 88.4% and a specificity of 81.1 %. These criteria were modified in 2010, the new criteria do not require the presence of tender point but Symptoms are evaluated using the Widespread Pain Index (WPI) and the Symptom Severity Score (SSS) of symptoms (fatigue, waking unrefreshed and cognitive symptoms) [19,22,23].

In 2012, the Canadian Rheumatology Association introduced a criterion for the diagnosis of FMS depending on presence of generalized body pain for more than 3 months associated with 4 non-pain symptoms (fatigue, sleep disturbance, cognitive changes and mood changes and any one of the other associated somatic symptoms [24].

### Neutrophil-to-Lymphocyte Ratio (NLR)

Neutrophil-to-Lymphocyte Ratio (NLR) is a simple parameter to assess easily the inflammatory status of a

subject [25]. It has been used in combination with other inflammatory markers to determine inflammation in both auto- and non-autoimmune diseases [26]. NLR has been associated with some conditions such as chronic inflammation in cardiovascular diseases, malignancies, ulcerative colitis and hepatic cirrhosis [27]. It calculated as the neutrophil count divided by the lymphocyte count, may represent an easily measurable and inexpensive marker of systemic inflammation [28,29].

### Platelet Distribution Width (PDW)

Platelet Distribution Width (PDW) is a regular parameter in blood routine examination which reflects variation of platelet size distribution, measured by automatic hematology analyzer and calculated by measuring the width of the size distribution curve at the 20% level when the peak distribution curve is taken as 80% or 100%. There is always a morphological change when platelet is activated in the environment of inflammation. Thus, PDW can be utilized as a sign of activated platelet releasing in some inflammatory diseases. Studies have demonstrated that PDW level changes under specific conditions compared to healthy individuals [30,31]. Normal range of PDW 15-17%.

### Mean Platelet Volume (MPV)

Mean Platelet Volume (MPV) is a parameter generated by full blood count analyzers as part of the routine complete blood count test. It is an accurate measure of platelet size and considered a marker and determinant of platelet function [32]. MPV increases as the platelet production increases and giant platelets enter the circulation. It was reported that MPV increase in massive hemorrhage, leukemia, myeloproliferative neoplas, vasculitis, diabetes, stroke, hypertension and post splenectomy [33,34]. Many recent researches have also focused on whether MPV is increased in patients with rheumatic diseases [35]. Normal range of MPV (7-11 FL).

### The Relationship Between NLR, PDW and MPV with FMS

Fibromyalgia is a common disease whose etiology is not known precisely and its incidence is increasing. Recent studies indicate that inflammation may play a role in pathogenesis. In one study found that in the patient group, NLR and MPV were significantly higher and PDW was significantly lower compared to the control group. These markers can be inexpensively and easily evaluated in clinical practice and may help in the diagnosis [36].

### Study Design

This case-control study was conducted at the Rheumatology Unit of Baghdad Teaching Hospital from July 2017 to November 2017.

### Sample Selection

One hundred patients with Fibromyalgia (97 females: 3 male) diagnosed according to 2012 Canadian Guidelines

for diagnosis of Fibromyalgia [24] were included in the study and compared with 50 healthy controls (47 female: 3 male).

Ethical approval was obtained from the Ethics Committee of Baghdad University, College of Medicine, Medical Department. Prior to the participation in the study, a verbal consent was obtained from each participant (patient and control). Data and information of the participants were kept confidentially and each personal or private information that identify the participant were kept secret.

### Exclusion Criteria

Subacute or acute infections, Chronic inflammatory disorders, diabetes mellitus, hypertension, hypercholesterolemia, psychiatric or neurological disorders, malignancy, propensity to thrombotic or bleeding disorders or to be using anti-coagulant therapy.

### Data Collection

Data were collected using a paper clinical research form through interview and questionnaires. It consisted of two parts:

The first part for the demographic data and full history including the age, gender, height, weight, Body Mass Index (BMI) calculated according to the equation  $BMI = \text{weight}/\text{height}^2$ . Each participant was asked about generalized body pain for more than 3 months, fatigue, sleep disturbance, cognitive changes (poor memory) and mood changes (anxiety or depression) in addition to other associated somatic symptoms like headache, dizziness, muscle cramp, chest pain, irritable bowel syndrome, abdominal pain ...etc.

The second part laboratory data white blood cells count (WBC count), neutrophils count, lymphocytes count, platelets count, Platelet Distribution Width (PDW), Mean Platelet Volume (MPV) and ESR were recorded. Blood neutrophil-lymphocyte ratio for each participant was calculated manually by dividing the neutrophils count by lymphocytes count.

### Collection of Blood Samples

Blood samples were collected from each participant under aseptic venipuncture and 5 ml of blood were collected from each patient and control.

We collect the blood in Ethylene Diamine Tetra Acetic acid (EDTA) tubes before sending them to laboratory to read the final results of Complete Blood Count (CBC) and ESR by automated analyzers in photometric pathway. NIHON KOHDEN® (Celltac α) and The VITAL MICROSED-SYSTEM® ESR analyzer are the automated analyzer for getting the final results of CBC and ESR respectively.

### Statistical Analysis

The data underwent a process of translation into a computerised database structure. The database undergone a thorough examination to identify errors via the use of range and logical data cleaning techniques. The

statistical analyses were conducted using IBM SPSS version 21 software, often known as the Statistical Package for Social Sciences, in conjunction with Microsoft Excel 2016.

The analysis of the conformity of quantitative random variables to a Gaussian curve (normal distribution) was conducted via the use of the Kolmogorov-Smirnov test. The quantitative continuous outcome variables, including blood White Blood Cell (WBC) count, blood neutrophil count, blood lymphocyte count, Neutrophil to Lymphocyte Ratio (NLR) and Body Mass Index (BMI), were seen to follow a normal distribution. These variables are characterised by their mean, Standard Deviation (SD) and Standard Error (SE). The statistical significance of the difference in means between two groups was evaluated by the use of the independent samples t-test. On the other hand, for comparisons involving more than two groups, the Analysis of Variance (ANOVA) test was employed.

Blood platelets count, PDW and MPV were shown to be non-normally distributed quantitative variables. Such variables can be described by median and interquartile range. The difference in median between 2 groups was assessed by non-parametric test (Mann-Whitney), while between 3 groups Kruskal-Wallis test was used. A statistical estimate was deemed to be statistically significant if its P value was below a predetermined level of significance ( $\alpha$ ) of 0.05. The 95% Confidence Interval (CI) is a statistical method used to estimate the range of possible values for a calculated sample statistic in the reference population, with a confidence level of 95%. This procedure allows for the anticipation or prediction of the expected range of values with a high degree of confidence.

Spearman's rank linear correlation coefficient was used to assess the statistical significance, direction and strength of the linear correlation between two quantitative variables, with the consideration that one or both of these variables may not follow a normal distribution.

## RESULTS

The results presented in this chapter were based on the analysis of a case-control study with a random sample of 100 cases (mean age of 35.7 +/- 10.2 years SD) with an established diagnosis of Fibromyalgia syndrome (FMS)

and 50 healthy control subjects (mean age of 34.8 +/- 10 years SD). The age ranged between 17 and 60 years. The majority of cases were females (97%) and no significant case-control differences were observed in gender distribution. In addition, no case-control differences in age was observed.

The mean BMI should no obvious or statistically significant differences between cases with FMS (28.11 kg/m<sup>2</sup>) and healthy controls (28.01 kg/m<sup>2</sup>). In conclusion the two comparison groups were well matched for age, gender and BMI. These factors will not qualify as confounding variables when exploring for possible case-control differences in blood counts and platelets measurements (Table 1).

### Description of FMS Cases

As shown in Table 2, a list of five basic clinical features were looked for among cases group. Four of these features were almost universal available (prevalence rate ranging between 96% to 100%), namely: diffuse pain for more than three months, fatigue, mood changes and sleep disturbance. The last feature, which is cognitive changes was less commonly reported (87%).

A list of 20 other clinical features were assessed among FMS cases. The prevalence of these clinical features in the current study sample was reported. The most commonly reported features include: headache, gases, abdominal pain and numbness/tingling reported in more than four fifths of cases. Ranked second in the list were frequent urination, easy bruising and shortness of breath with a prevalence rate between 60% and 70%. More than two fifths of FMS cases group reported shortness of breath, itching, palpitation, oral ulcers and tinnitus. Between a fifth and one third of cases had the following five features, namely: altered bowel motion, chest pain, bladder spasms, muscle cramps and Raynaud's. The remaining three features, namely: painful urination, dizziness and dry eyes were reported in  $\leq 15\%$  of cases.

### Case-Control Difference in Blood Counts

As shown in table 3, the mean blood WBC count was marginally and not significantly higher in cases with FMS (8.07) compared to healthy controls (7.63). The lymphocytes component of blood count did not show any obvious or statistically significant difference between cases and controls.

Table 1: Demographic Features of Cases and Controls

Parameters	Study group				P-Value
	Healthy controls		Cases (FMS)		
	N	Percentage	N	Percentage	
<b>Age group (years)</b>					0.66[NS]
<30	16	32.0	26	26.0	
30-44	25	50.0	51	51.0	
45+	9	18.0	23	23.0	
<b>Gender</b>					0.40[NS]
Female	47	94.0	97	97.0	
Male	3	6.0	3	3.0	
<b>BMI</b>					0.91[NS]
Range	(19.9-39.9)	-	(18.7-41.5)	-	
Mean	28.01	-	28.11	-	
SD	4.45	-	5.22	-	
SE	0.63	-	0.52	-	

BMI: BODY MASS INDEX, N: Number, NS: Non-Significant, P: Probability Value

In contrast, the mean of both neutrophil count and neutrophil to lymphocyte ratio were significantly higher among cases with FMS (5.35 and 2.18 respectively) compared to healthy controls (4.77 and 1.92 respectively).

Table 2: The Relative Frequency (Prevalence Rate) of Selected Basic and Other Clinical Features of FMS in Cases Group.

Basic clinical features (n = 100)	N	Percentage
Diffuse pain >3 months	100	100.0
Fatigue	100	100.0
Mood Changes	97	97.0
Sleep Disturbance	96	96.0
Cognitive Changes	87	87.0
Other clinical features (n = 100)		
Headache	88	88.0
Gases	85	85.0
Abdominal Pain	83	83.0
Numbness/tingling	81	81.0
Hair Loss	70	70.0
Frequent Urination	65	65.0
Easy bruising	60	60.0
Shortness of Breath	46	46.0
Itching	44	44.0
Palpitation	43	43.0
Oral ulcers	43	43.0
Tinnitus	42	42.0
Altered bowel motion	33	33.0
Chest Pain	31	31.0
Bladder Spasms	27	27.0
Muscle Cramps	20	20.0
Raynaud's	19	19.0
Painful Urination	15	15.0
Dizziness	13	13.0
Dry eyes	5	5.0

N: Number

Table 3: The Case-Control Difference in Mean Blood Counts

Parameters	Study group		P
	Healthy controls	Cases (FMS)	
Blood WBC count			0.17 [NS]
Range	(4.6 to 11)	(4.1 to 15)	
Mean	7.63	8.07	
SD	1.45	2.00	
SE	0.20	0.20	
N	50	100	
Blood Neutrophil count			0.021
Range	(2.4 to 7)	(2 to 11.6)	
Mean	4.77	5.35	
SD	1.03	1.61	
SE	0.14	0.16	
N	50	100	
Blood Lymphocytes count			0.96 [NS]
Range	(1.7 to 4.6)	(0.9 to 4.5)	
Mean	2.60	2.59	
SD	0.69	0.75	
SE	0.10	0.07	
N	50	100	
Neutrophil to Lymphocytes ratio			0.033
Range	(0.89 to 3.29)	(1.04 to 5)	
Mean	1.92	2.18	
SD	0.54	0.75	
SE	0.08	0.08	
N	50	100	

FMS: Fibromyalgia Syndrome, N: Number, NS: Non-significant, P: Probability Value, SD: Standard Deviation, SE: Standard Error, WBC: White Blood Cell

### Case-Control Difference in Platelets Parameters

As shown in Table 4, all the three platelets parameters showed an obvious case-control difference in median, which only failed short of statistical significance in case of platelets count (316 for cases Vs 294 for controls). The median MPV was significantly higher in cases with FMS (8.3) compared to healthy controls [8]. In contrast, the median PDW was significantly lower among cases with FMS (16.7) compared to healthy controls [17] (Figure 1).

### FMS Effect Size on Blood Counts and Platelets Parameters

The ROC analysis gives an idea about ranking the tested parameters according to the effect size for FMS compared to healthy controls. At the top of the list is the PDW was the parameter most affected by FMS, followed by blood neutrophil count and MPV. The blood platelets count and neutrophil to lymphocytes ratio occupied the 4th and 5th places in the list of tested parameters. The blood WBC and lymphocytes counts failed to show a statistically significant or noticeable effect for FMS (Figure 2).

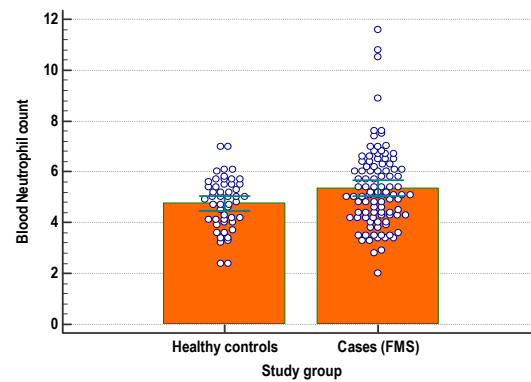


Figure 1: Dot Diagram with Error Bars Showing the Case-Control Difference in Mean Blood Neutrophil Count (with its 95% Confidence Interval)

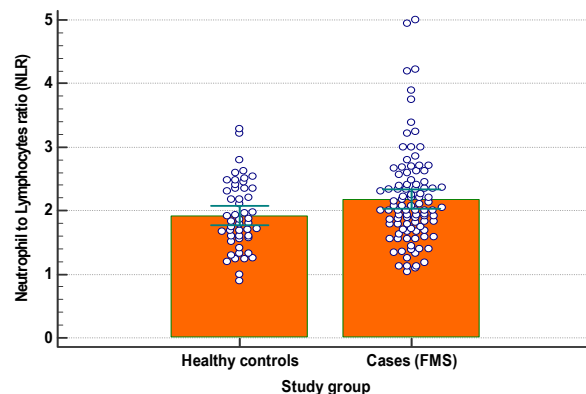


Figure 2: Dot Diagram with Error Bars Showing the Case-Control Difference in Mean Blood Neutrophil to Lymphocytes Ratio (With Its 95% Confidence Interval)

Table 4: ROC Area for Selected Quantitative Tests When Used to Predict a Diagnosis of FMS Differentiating it from Healthy Control

Parameters	Area under ROC curve	P
PDW	0.628	0.011
Blood Neutrophil count	0.602	0.041
MPV	0.600	0.046
Blood platelets count	0.597	0.05 [NS]
Neutrophil to Lymphocytes ratio	0.595	0.06 [NS]
Blood WBC count	0.566	0.19 [NS]
Blood Lymphocytes count	0.508	0.88 [NS]

FMS: Fibromyalgia Syndrome, MPV: Mean Platelet Volume, NS: Non-Significant, P: Probability Value, PDW: Platelet Distribution Width, ROC: Receiver Operating Characteristic, WBC: White Blood Cell

Table 5: Validity Parameters for Selected Quantitative Tests when Used to Predict a Diagnosis of FMS Differentiating it from Healthy Control (Higher Values are in Favor of Positive Diagnosis)

Positive if ≥ cut-off value	Sensitivity	Specificity	Accuracy	PPV at pretest probability =		NPV at pretest probability = 10%
				50%	90%	
<b>Blood WBC count</b>						
4.70 (Highest sensitivity)	98.0	2.0	66.0	50.0	90.0	90.0
7.85 (Optimum cut-off)	55.0	64.0	58.0	60.4	93.2	92.8
11.45 (Highest specificity)	3.0	100.0	35.3	100.0	100.0	90.3
<b>Blood Neutrophil count</b>						
2.60 (Highest sensitivity)	99.0	4.0	67.3	50.8	90.3	97.3
5.05 (Optimum cut-off)	55.0	60.0	56.7	57.9	92.5	92.3
7.01 (Highest specificity)	9.0	100.0	39.3	100.0	100.0	90.8
<b>Blood Lymphocytes count</b>						
1.75 (Highest sensitivity)	89.0	2.0	60.0	47.6	89.1	62.1
2.55 (Optimum cut-off)	48.0	66.0	54.0	58.5	92.7	92.0
4.05 (Highest specificity)	4.0	98.0	35.3	66.7	94.7	90.2
<b>Neutrophil to Lymphocytes ratio (NLR)</b>						
1.02 (Highest sensitivity)	100.0	4.0	68.0	51.0	90.4	100.0
1.99 (Optimum cut-off)	57.0	62.0	58.7	60.0	93.1	92.8
3.34 (Highest specificity)	7.0	100.0	38.0	100.0	100.0	90.6
<b>Blood platelets count</b>						
200 (Highest sensitivity)	100.0	10.0	70.0	52.6	90.9	100.0
306 (Optimum cut-off)	56.0	68.0	60.0	63.6	94.0	93.3
536 (Highest specificity)	1.0	100.0	34.0	100.0	100.0	90.1
<b>MPV</b>						
6.80 (Highest sensitivity)	99.0	2.0	66.7	50.3	90.1	94.7
8.10 (Optimum cut-off)	56.0	66.0	59.3	62.2	93.7	93.1
16.50 (Highest specificity)	1.0	98.0	33.3	33.3	81.8	89.9

FMS: Fibromyalgia Syndrome, MPV: Mean Platelet Volume, NP: Negative Predictive Value, PPV: Positive Predictive Value, WBC: White Blood Cell

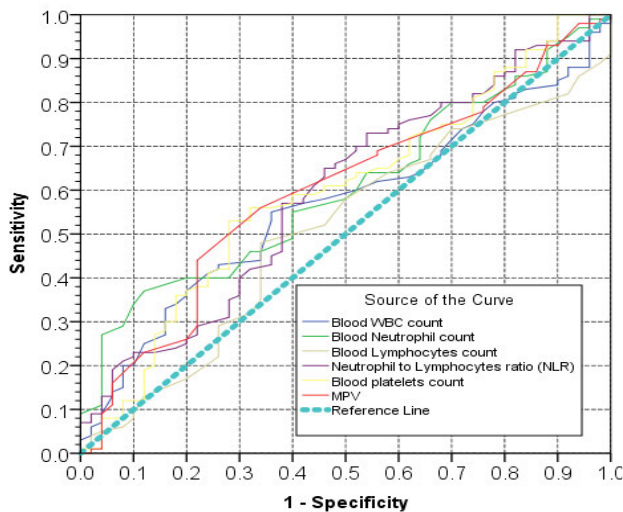


Figure 3: ROC Curve Showing the Trade-Off Between Sensitivity (Rate of True Positive Test Results) and 1-Specificity (False Positive Rate) for Selected Quantitative Measurements when Used as Test to Predict FMS Differentiating it from Healthy Controls

### Screening for FMS

As shown in Table 5, none of the 6 tested parameters qualified as an acceptable test for predicting a diagnosis of FMS, since the ROC area associated with any of them did not reach the minimum ROC area value of 0.65.

The optimum cut-off value for each parameter is stated in table 6. One can see that at the optimum cut-off value for any of the tests the highest accuracy will not exceed 64% at best. The contribution of a positive test at the optimal cut-off value for any of the 5 parameters in which the test follows a positive direction (higher values are in favor of positive diagnosis of FMS) would not be much compared to a pretest probability of 50% or 90%. The same applies to PDW, which operates in the negative direction (smaller values are in favor of positive diagnosis of FMS) which is considered positive when <16.85 at the optimum cut-off value (Figure 3).

### DISCUSSION

Up to the best of our knowledge this is the first study that investigate the NLR, PDW and MPV values in FMS patients in comparison with healthy control in a sample of Iraqi patients.

From the data collected in the study, the mean age of patients included in the study was 35.7 +/- 10.2 SD years, which was comparable to that of the control group 34.8 +/- 10 years SD, (p-value = 0.66), females were the dominant gender (97%). This had also been concluded by Aktürk S *et al.* [36], in their study on Fibromyalgia patients in Turkey. Moreover, the difference in the height, weight and body mass index between the two groups were statistically insignificant (p-value = 0.91).

Regarding the basic clinical features prevalence in FMS, all of the patients in this study have fatigue and diffuse pain >3 months which were similar to Bennett R *et al.* [37], results. On the other hand, the prevalence of mood changes, sleep disturbance and cognitive changes were 97%, 96% and 87% respectively, which were comparable to the study done by Fitzcharles M *et al.* [38].

Other clinical features including headache, gases, abdominal pain, numbness/tingling, hair loss, frequent urination and easy bruising were ranging from (60%-88%), while less than half of those patients had shortness of breath, itching, palpitation, oral ulcers, tinnitus, altered bowel motion, chest pain, bladder spasms, muscle cramps, raynaud's, painful urination, dizziness and dry eyes.

Neither the mean blood WBC count nor the lymphocytes component showed statistically significant difference between cases and controls. In contrast, the mean of both neutrophil count and neutrophil to lymphocyte ratio were significantly higher among cases with FMS compared to healthy controls, which were consistent with that reported in a study done by Aktürk S *et al.* [36] in 2017.

It was reported that NLR can be utilized as a predicting marker to estimate the response of systemic inflammatory. Neutrophil-to-Lymphocyte Ratio (NLR) has been extensively investigated in systemic illnesses characterised by elevated neutrophil counts and reduced lymphocyte counts. This observed correlation between NLR and lymphocyte reduction may be attributed to factors such as acute inflammatory, lymphocyte reduction and physiological stress [27,39-41].

In their study, Taşoğlu *et al.* [39], conducted an assessment of the association between severe knee osteoarthritis and Neutrophil-to-Lymphocyte Ratio (NLR). The findings of their investigation revealed that individuals diagnosed with severe knee osteoarthritis had elevated NLR values in their blood samples when compared to those with moderate knee osteoarthritis. In contrast, FMS is chronic but not degenerative and in the current study, the NLR levels were significantly higher in FMS patients compared to healthy controls, this agreed with Aktürk S *et al.* [36] results.

It was reported that MPV increase in thrombotic diseases or inflammatory [42,43]. In this study, the median MPV was significantly higher in patients with FMS compared to healthy controls, which was consistent with the result reported by Haliloğlu *et al.* [44] that showed the MPV was increased in FMS patients.

On the other hand, the median PDW in the present study was significantly lower among FMS patients compared to healthy controls which was similar to the results done by Aktürk S *et al.* [36].

The validity of (NLR, MPV and PDW) was assessed as a predictor for the diagnosis of FMS, using two methods of analysis; the first method used the ROC curve and the second method cut-off value.

Regarding the ROC curve, the PDW was the most affected one followed by blood neutrophil count and MPV, whereas the blood platelets count and NLR occupied the 4th and 5th places respectively. The NLR had 57% sensitivity, 62% specificity and 58.7% accuracy, MPV had 56% sensitivity, 66% specificity and 59.3% accuracy, PDW had 62% sensitivity, 68% specificity and 64% accuracy.

The most important limitations of our study are: first, the parameters values were measured only once in each patient. Second, Restriction in the studies that assessed the role of these parameters in the diagnosis of FMS. Third, small sample size and short period of time for the study.

However, they are cheap and easy tests to be performed as it is a common component of the Complete Blood Count (CBC) test that is nowadays widely distributed in nearly every health care facility and by an automated machine.

## CONCLUSIONS

The NLR is significantly higher in FMS patients compared to healthy controls. The MPV is significantly higher in patients with FMS compared to controls. The PDW was significantly lower among FMS patients compared to healthy controls. None of these tested parameters qualified as an acceptable test for predicting a diagnosis of FMS.

## Recommendations

The three tested parameters alone may not be dependent as a marker or predictor for diagnosing FMS. Larger sample size and longer duration study to further validate the findings of this study.

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