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Fibromyalgia Syndrome AmongIraqi Patients with Systemic Lupus Erythematosus: A Case Control Study

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Abstract:
Objective:*To determine the prevalence of fibromyalgia syndrome (FMS) among Iraqi patients with systemic lupus erythematosus (SLE) and its association with disease activity.*
Patients and methods: *This case control study included 100 patients with SLE and 100 healthy controls comparable in age and sex. Baseline characteristics [age, sex, disease duration, and SLE clinical features] were documented. Lupus disease activity was measured using systemic lupus erythematosus disease activity index (SLEDAI). The American College of Rheumatology 1990 Criteria for fibromyalgia were applied for both groups. Comparative statistics were done using Chi square test for categorical variables and students' independent 2 samples (t) test for continuous variables.*
Results: *FMS was present in 13 (26%) patients with SLE compared to 1(2%) patient in the control group ($p<0.05$). Female patients with SLE had significantly more FMS than males ($p<0.05$). SLEDAI score was not significantly different between FMS group and non FMS group ($p>0.05$). Also the FMS associated features were significantly more prevalent in SLE compared to control group($p<0.05$).*
Conclusions: *FMS was more prevalent in SLE patients than controls. No significant differences between FMS and non FMS groups in SLEDAI score.*
Keywords:*Fibromyalgia syndrome, systemic lupus erythematosus, SLEDAI.*

I. Introduction

Fibromyalgia (FM) is a rheumatic condition distinguished by a diffuse chronic pain, hyperalgesia and allodynia. Fatigue, sleep disturbances, morning stiffness, headache and paresthesia are symptoms often present[1]. Comorbidities like depression, anxiety, irritable bowel syndrome, myofascial pain syndrome and nonspecific urethral syndrome are also associated [2] The most important mechanism is the amplification of the transmission of painful stimuli,with changes in the perception of pain[1]. An imbalance in neurotransmitters involved in the physiology of pain was also observed. Among other abnormalities, an increase of substance P and nerve growth factor in the cerebrospinal fluid (CSF) of individuals with fibromyalgia was found [3]

Systemic lupus erythematosus (SLE) is a severe systemic autoimmune disease characterized by a wide spectrum of clinical and immunological abnormalities with significant morbidity and mortality [4]. SLE is primarily a disease of young adult women [5] The association of FM and SLE has been investigated by several authors, with conflicting results regarding the impact of a condition on the other [6-9]. The prevalence of a concomitant association between the two diseases is around 20% [6]. Thus, the presence of FM in SLE patients is much greater than in the general population.

No study of thisassociation was held in Iraq. The aim of this study was to assess the prevalence of FM in a sample of Iraqi patients with SLE and to determine the impact of FM on SLE clinical activity.

II. Patients and methods

Study design

This case control study was conducted at the Rheumatology unit, Department of medicine in Baghdad Teaching Hospital from October 2002 till March 2003.

Sample selection

A sample of 50 Iraqi patients with SLE who fulfilled 4 or more of the American College of Rheumatology revised Criteria for Classification of SLE [10] were included in this study. Another 50 healthy individuals matched for age and sex were studied as a control group. Patients were excluded from the study if they were less than 18 years old, or had evidences ofoverlapping connective tissue disease,or comorbid diseases, or had pregnancy. A signed consent was taken from all individuals in both groups for admission in the study.Ethical approval was obtained from the Ethics Committee of Baghdad University, College of Medicine, and Medical Department.

Clinical and laboratory evaluation

The American College of Rheumatology 1990 Classification Criteria [11] for fibromyalgia were applied to all SLE patients and healthy individuals included in the study. Individuals in both groups were inquired about the presence of chronic wide spread pain in left and right sides of the body, above and below the waist and axial skeleton for at least three months duration. They were examined for the presence of local tender points necessary for diagnosis of FMS.To meet the diagnostic criteria, musculoskeletal pain or stiffness must have been present for at least 3 months, pain must have been present in 11 or more out of 18 specific tender points on digital palpation [11].

All patients with SLE and control group were questioned about FMS associated symptoms that are: fatigue, morning stiffness, sleep disturbances, headache, anxiety, and irritable bowel.Disease activity of SLE was measured by a standardized chart of SLEDAI [12]. SLEDAI consists of 24 variables, covers 9 organ systems with a total score of 105. Patients with total score of less or equal to 10 were considered to be mild to moderately active disease [13]. Total score or more than 10 and up to 19 were considered as active (flare) of disease activity.SLEDAI of more or equal to 20 at presentation is bad prognostic factor and associated with high mortality.

Blood sample was obtained for measurement of erythrocyte sedimentation rate (ESR), C-reactive protein, packed cell volume (PCV), white blood cells count (WBC), blood urea, serum creatinine, total serum bilirubin, serum alkaline phosphatase, serum aminotransferase, hepatitis C virus antigens , and thyroid function tests (T3 ,T4, TSH) when indicated..

Statistical analysis

Categorical variables were presented as numbers and percentages and Continuous variables as mean ± standard deviation (SD). To test the significance of difference between two continuous variables; t test of two independent variables used if variables were normally distributed and Mann-Whitney test used if the distribution was not normally distributed. Chi square test for independence used to test the association between categorical variables. P value less than 0.05 was considered statistically significant

III. Results

The baseline characteristics of both SLE patients and controls was shown in table 1. There were 50 (45 female and 5 male) patients with SLE and 50 (36 female and 14 male) individuals in the control group. The mean age for SLE patients and controls was 29±10.4 and 32.3±9.5 years respectively. The mean disease duration was 4.4 years.

The prevalence of FMS among Iraqi patients with SLE was 26% compared to 2% in the controls (p=0.0001) as in table 2.

There were significantly more females with SLE having FMS compared to male patients (P<0.05), so there was a female predominance of FMS in SLE patients and we found no significant difference in the distribution of FMS between patients below the age of 40 years and those 40 years and above (p>0.05). Also there was no significant difference between FMS in SLE patients who were mild to moderately active and those who were severely active (p>0.05) as in table 3.

The FMS associated features were significantly more prevalent among SLE patients compared to the control group as shown in table 4.

Table1: Baseline characteristics of SLEpatients and controls.

Variable	SLE patients=50	Controls= 50
Age (Mean± SD), year	29.7 ± 10.4	32.3 ± 9.5
Gender		
Female n(%)	45 (90)	34 (68)
Male n(%)	5 (10)	16 (32)
Disease duration (Mean± SD), year	4.4	
SLEDAI		
Mild to moderaten(%)	20 (40)	
Severen(%)	30 (60)	
Clinical features		
Musculoskeletaln(%)	45 (90)	
Mucocutaneousn(%)	46 (92)	
Neurologicaln(%)	25 (50)	
Renaln(%)	25 (50)	
Serositisn(%)	15 (30)	
Immunological abnormalitiesn(%)	28 (56)	
Constitutional symptomsn(%)	35 (70)	
Hematological abnormalities n(%)	13 (26)	

SLE, systemic lupus erythematosus; SLEDAI, SLE disease activity index; n, number; SD, Standard deviation.

Table2: Comparison of fibromyalgia in SLE patients and controls

FMS	SLE=50	Controls=50	P	OR(95%CI)
Present n (%)	13 (26%)	1 (2%)	0.0001	17.22(2.16 to 137.57)
Absent n(%)	37 (74%)	49 (98%)		

FMS, fibromyalgia syndrome; SLE, systemic lupus erythematosus; OR, odd ration; CI, confidence interval

Table3: Distribution of SLE patients in FMS positive and FMS negative by gender, and disease activity according to SLEDAI

Variable	FMS Positive	FMS negative	p
Gender			
Female n(%)	13(38.8)	32(71.2)	0.04
Male n(%)	0(0)	5(100)	
Age , years			
<40	10(25.6)	29(74.4)	0.0.28
≥40	3(27.3)	8(72.7)	
SLEDAI			
Mild to moderate	4(20%)	16 (80%)	
Severe	9(30%)	21 (70%)	0.43

FMS, fibromyalgia syndrome; SLE, systemic lupus erythematosus;SLEDAI, SLE disease activity index

Table 4: Comparison of FMS associated features in SLE patients and controls

FMS associated feature	SLE patients =50 n(%)	Controls=50 n(%)	p
Headache	36 (72)	26 (52)	0.032
Sleep disturbance	40 (80)	8 (16)	0.0001
Fatigue	30 (60)	4 (8)	0.0001
Anxiety	24 (48)	9 (18)	0.01
Irritable bowel	10 (20)	3 (6)	0.03
Morning stiffness	10 (20)	1 (2)	0.004

FMS, fibromyalgia syndrome; SLE, systemic lupus erythematosus;n, number

IV. Discussion

This study assessed the prevalence of FMS in Iraqi patients with SLE and reported that FMS was significantly more in patients than controls. Female patients with SLE had significantly more FMS than males. No significant differences between FMS and non FMS groups in SLEDAI score. Also FMS associated features were significantly more prevalent in SLE compared to control group.

In this study, the prevalence of FMS among Iraqi patients with SLE was 26%. This finding was in agreement with the literature however it was slightly higher than reported range which was between 17- 22% [14-17].

All FMS patients and lupus were female patients with 13/45 and non among lupus male patient was FMS and although well known that female individual may proveto develop FMS in general[18].Yet,the number of our lupus male patient was too small to draw a conclusion.

We found no obvious influence of age on the prevalence of FMS among SLE patients, while there was an almost linear increase in the prevalence of FMS up to the eighth decade in general population [19].

In this study, we found no significant difference between FMS and non FMS group in the objective measurement of disease activity, but the concurrence of SLE and FMS can cause considerable confusion both in the initial diagnosis of SLE and in the subsequent evaluation of disease activity. Patients with FMS tend to over report symptoms and cope less well [20].

According to a Canadian study, the presence of FM in SLE patients was not related to an increase of the parameters that make up SLEDAI. Despite the contribution of FM to the worsening of thehealth status of patients with SLE, it has been shown in the literature that FMS causes little or no impact on the activity of SLE[7, 21] which corroborates the findings of our study, where no change in SLEDAI of respective groups (SLE, FM and SLE/FM) was noted.

In the current study, Headache, fatigue, and sleep disturbances were the most common non musculoskeletal manifestation recorded in our FMS patients which is comparable to reports from other parts of the world [22].Patients with FMS sleep poorly and they awake tired and they describe themselvesas being light sleepers and awakened frequently. This feature was also obvious among our patients and by itself is an

important aggravating factor, in our study reported in 80% of FMS patients, which was in agreement with two Iraqi studies on FMS in general population in which poor sleep disturbances was reported in 82% and 92% [23-24]. Although a precise etiology remains unidentified. A disturbance in stage 4 or delta wave sleep has been observed in patients with knowledge that growth hormone secretion peaks during stage 4 sleep. In addition to abnormal somatomedin C level in these patients [25].

The limitation of this study was the small sample size. In addition, the sample of patients with both FM and SLE may differ from that observed in the community because they were seen at a tertiary level center; Therefore, our sample may not reflect the general population of patients with fibromyalgia. However these drawbacks might be solved by a larger study sample size and assessment of patients seen at primary and secondary sectors. Despite these limitation, our study has strong inclusion and exclusion criteria and it is the first study in Iraq up to our knowledge that assessed FMS in SLE patients.

In conclusion, FMS was more prevalent in patients with SLE than in the general population. No significant differences between FMS and non FMS group in measurement of disease activity of SLE patients. This is clinically important and may suggest that early diagnosis of FMS in SLE patients may help in early management and subsequently improving health quality of life of our patients.

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Authors'contributions

All the authors involved in study design and conception, acquisition of data, and data analysis and interpretation.

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