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Original Article

Differentiating primary fibromyalgia cases and its subset that had deficient vitamin D3 using serum TNF-alpha and ultrasound of hands and knees

Rheumatology

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ABSTRACT

Background: Fibromyalgia syndrome (FMS) is characterized by ongoing musculoskeletal pain, muscle tightness, insomnia, malaise, mood disturbances, cognitive impairments, depression, general sensitivity, and challenges in carrying out daily activities. Lately, there have been numerous cases of bilateral hand and wrist arthritis that are combined with fibromyalgia and low serum vitamin D3, potentially linked to elevated serum parathormone hormone levels in certain cases.

Objective: To differentiate between primary FMS cases and its subset that had deficient vitamin D3 level and to determine ultrasound (US) changes in hands and knee joints.

Methodology: A cross-sectional comparative study was conducted on eighty patients with FMS. They were recruited from rheumatology and rehabilitation department, Al-Zahraa university hospital. Patients were divided into two groups; Group A: included 40 FMS patients with vitamin D3 deficiency, and Group B: included 40 patients with primary FMS. Both groups underwent tender point count, symptom severity scale assessment, measurement of serum tumor necrosis -α (TNF -α), widespread pain index assessment, and US for hands and knees.

Results: There was a statistically significant higher percentage of chondrocalcinosis of knee in group A than group B, and a statistically significant higher percentage of synovial hypertrophy was found in group B than group A. Also, a significant positive correlation was detected between TNF-α level and tender point count (from 11 up to 18), in both groups.

Conclusions: The degenerative changes are more in group A patient. This may be due to their association with secondary hyperparathyroidism (SHPT) and vitamin D3 deficiency which in turn accelerates the degenerative complications in joints.

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Keywords: Fibromyalgia; vitamin D3 deficiency; Secondary hyperparathyroidism; tumor necrosis factor alpha; ultrasound.

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INTRODUCTION

Fibromyalgia syndrome (FMS) is distinguished by ongoing musculoskeletal pain, muscle tightness, insomnia, malaise, mood disturbances, cognitive impairments, depression, general sensitivity, and challenges in carrying out daily activities [1]. Fibromyalgia syndrome is more common in women compared to men. In the United States the prevalence of FMS was 6.4% being more prevalent in women than in men (7.7% versus 4.9% respectively). Studies in Europe and South America showed a range from 3.3 to 8.3%. It increases with age. Between the ages of 20 to 55 years, the cause of generalized musculoskeletal pain in most women is FM [2].

The main abnormalities in FM involve dysfunctions in monoaminergic neurotransmission that leads to elevated levels of excitatory neurotransmitters like glutamate and substance P, while decreasing levels of serotonin and norepinephrine in the spinal cord's descending anti-nociceptive pathways. Additionally, dysregulation of dopamine and altered activity of endogenous cerebral opioids have been seen. These abnormalities help clarify the underlying pathophysiology of FM. Over time, researchers have recognized that pain sources outside the central nervous system may contribute to FM. People with FM often experience a range of symptoms beyond pain, including cognitive issues, persistent fatigue, disrupted

sleep, gut problems, bladder inflammation, and mood changes. These peripheral issues may increase pain signals to the spinal cord, potentially leading to heightened central nervous system sensitivity. The development of FM likely involves multiple factors, such as hormonal imbalances, genetic susceptibility, cellular stress from oxidation, and changes in a person's environment and mental state [3].

Lately, few studies involving both wrists and hands arthritis that are combined with fibromyalgia, and decreased serum vitamin D3 levels have been documented. Of these instances, elevated serum parathormone hormone (PTH) levels are observed, without any changes in parathyroid gland morphology [4].

Secondary hyperparathyroidism is caused by low calcium levels, insufficient vitamin D intake, or inability of the kidney to convert vitamin D2 into the active vitamin D3. Low calcium levels stimulate the secretion of PTH to boost calcium. Deficiency of vitamin D and increased PTH levels because of secondary hyperparathyroidism can impact kidney function. Persistent elevated levels of PTH have several hemodynamic effects [5].

In secondary hyperparathyroidism (SHPT), hypo-calcaemia is the key factor stimulating elevated PT secretion from the parathyroid glands. This increased PTH secretion can cause parathyroid hyperplasia. PTH further enhanced osteoclast activity, leading to the resorption of calcium and phosphorus from the bone. PTH causes activation of vitamin D in the kidneys to its active form. By elevating calcium and phosphorus absorption from the intestines and their reabsorption in the renal tubules, vitamin D plays a crucial role in regulating these minerals. Furthermore, it suppresses PTH secretion by the parathyroid glands and maintains balanced levels of calcium and phosphorus [6]. SHPT disrupts normal bone metabolism, affecting both remodelling and mineralization processes. Elevated PTH levels in the blood accelerate bone turnover, typically resulting in loss of bone tissue, particularly in the cortical regions. This altered bone remodelling leads to skeletal deformities and can cause bone deformation, pain, and in severe instances, fractures. The abnormal mineralization and remodelling can also manifest as chest wall deformities and abnormal curvature of the spine (kyphoscoliosis) [7]. Also, SHPT leads to ongoing calcium depletion from bones, resulting in bone pain and joint discomfort in individuals with reduced bone density (osteoporosis or osteopenia). This condition can also cause calcium deposits in cartilage (chondrocalcinosis) and a form of arthritis called pseudogout. The accumulation of calcium pyrophosphate crystals in joints can lead to pain, degenerative arthritis, loose joints, and muscle weakness [8].

Vitamin D production begins in the skin and other tissues, with further processing in the liver and kidneys to create its main circulating form, 1,25-dihydroxyvitamin D3. This process relies heavily on the enzyme cytochrome P450scc, particularly in the kidneys. Despite abundant sunshine in the Middle East, vitamin D3 deficiency persists due to several sociocultural factors. These include limited sun exposure resulting from cultural practices, lifestyles that involve minimal time outdoors, and extended breastfeeding without vitamin D supplementation. Collectively, these practices reduce skin exposure to sunlight, inhibiting the body's natural ability to produce adequate vitamin D3 levels [9].

Tumor necrosis factor alpha (TNF-α) is a multifunctional signaling protein that affects many different cell types. It regulates inflammatory processes and has been associated with various inflammatory and autoimmune disorders [10]. It is a pro-inflammatory cytokine secreted from mast cells and is significantly higher in fibromyalgia patients when compared to controls suggesting a possible neurogenic inflammatory component in the condition. These inflammatory molecules can trigger pain, increase pain sensitivity, and are linked to nerve pain in FM [11].

There is a necessity for early diagnosis of any degenerative or inflammatory changes in hands and knee joints by US and other measures to make proper control of this disease and its complication due to lack of typical clinical features as well as hyperparathyroidism is often undiagnosed or misdiagnosed. So, we aimed to differentiate between FMS cases and its subset that had deficient vitamin D3 and to determine US changes in hands and knee joints.

SUBJECTS AND METHODS

Study design and patients:

This study involved 80 patients with FMS aged 18-50 years recruited from the rheumatology and rehabilitation department outpatient clinic, Al-Zahraa university hospital from January 2023 to October 2023.

Each participant provided written informed consent after being informed about the study's procedure, purpose, and significance. The study was approved by the medical ethical committees of Al-Azhar University's Faculty of Medicine for Girls in Cairo, Egypt (IRB no 1340).

The sample size was calculated according to Epi Info program with confidence level 95%, and power of test 80%, accordingly, it was estimated to be 80 case. Fibromyalgia was diagnosed according to the American College of Rheumatology fibromyalgia criteria 1990 [12], College of Rheumatology fibromyalgia criteria 2010 [13], and 2016 modified American College of Rheumatology diagnostic criteria for fibromyalgia [14].

The American college of rheumatology (ACR) 1990 classification criteria for FMS are [12]:

- Chronic widespread pain for at least 3 months above and below the waist and on both sides of the body.
- Pain induced by palpation in at least 11 of 18 tender points.
- No other cause for symptoms based on physical examination, laboratory tests, and radiographs.

ACR 2010 new diagnostic criteria for FMS are [13]:

- Widespread pain index (WPI) ≥ 7 and symptom severity scale score (SSSS) ≥ 5 or
- WPI 3-6 and SSSS ≥ 9.
- Symptoms present for at least 3 months.
- No other disorder to explain symptoms.

The WPI is the number of areas in which the patient has had pain over the last week. There are 19 areas [bilateral TMJs (2), shoulders (2), upper arm (2), lower arm (2), hips (2), upper leg (2), lower leg (2), neck (1), chest (1), abdomen (1), upper back (1), lower back (1)]. The SSSS is the sum of severity of four items over the past week. The four items are (1) fatigue, (2) waking from sleep unrefreshed, (3) cognitive disturbances, and (4) somatic symptoms. Each is subjectively scored for severity using a Likert score (0 = none, 1 = mild, 2 = moderate, 3 = severe) so that the maximum score is 12.

The 2016 fibromyalgia diagnostic criteria are [14]:

- WPI ≥ 7 and SSSS ≥ 5 or WPI 4-6 and SSSS ≥ 9.
- Generalized pain: pain in 4/5 regions.
- Symptoms present ≥ 3 months.

The participants were divided into two groups:

- **Group A:** included 40 fibromyalgia patients (4 males and 36 females) with vitamin D3 deficiency and secondary hyperparathyroidism.
- **Group B:** included 40 patients (1 male and 39 females) with primary fibromyalgia.

Exclusion criteria for both groups included individuals younger than 18 years or older than 55 years, and those with a history of other rheumatic diseases (e.g., rheumatoid arthritis, psoriatic arthritis, erosive osteoarthritis, viral arthritis, reactive arthritis, inflammatory bowel diseases arthritis, Lyme's disease, and palindromic rheumatism) or systemic diseases (e.g., cardiovascular, neurologic, renal, metabolic conditions, or pregnancy/breastfeeding.

Study tools

Comprehensive history-taking and examinations including general and musculoskeletal assessments. The WPI, SSSS, and disease severity were evaluated using the Visual Analog Scale (VAS), which ranges from 0 to 10. Laboratory evaluation in the form of; erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), Anti citrullated peptid antibody (ACPA), liver function tests (LFT), renal function tests (RFT), serum 25-hydroxycholecalciferol the cut off point for 25-hydroxyvitamin D normal level is 30 ng/mL, PTH, total and ionized calcium, phosphorus, and serum uric acid (SUA).Measurement of serum TNF-α using serum human TNF-α ELISA Kit (BT LAB bioassay technology laboratory cat No E0082Hu) and analysed by sandwich ELISA detection technique.

Radiological investigation in the form of plain X-ray for hands were done for all patients.

Ultrasound (US) examination of hands and knees joints:

All subjects were examined with the commercially available equipment using a 7-11 MHz linear phased array transducer (Xario 200, Toshiba ultrasound machine, Tochigi, Japan),

The US examination was conducted with patients in a relaxed seated position. Their forearm was placed on the examination bed, first with the palm facing up and then facing down, while keeping their fingers in a neutral position. Following the 2017 EULAR (European League Against Rheumatism) standardized protocols for ultrasound imaging in rheumatology, the power Doppler settings were adjusted to a frequency of 9.1 MHz and a pulse repetition frequency of 750 Hz [15]. Longitudinal US image to detect: radiocarpal joint: from the dorsal aspect of the wrist, US of Metacarpophalangeal joint (MCP), proximal interphalangeal (PIP), distal interphalangeal joint (DIP) and distal phalanx scanning (figure 1).

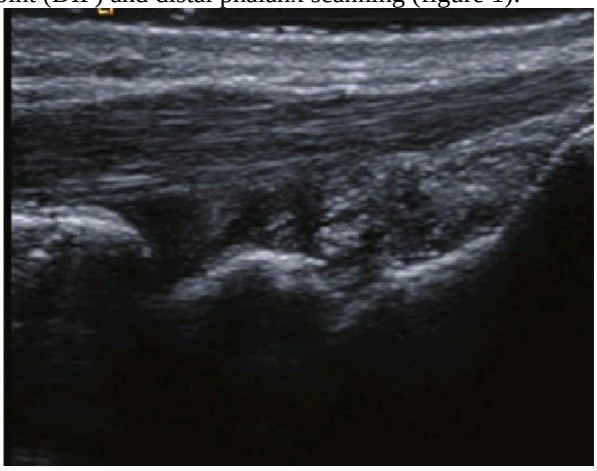


Figure (1): Ultrasound image of right wrist joint with synovial hypertrophy in patient with primary fibromyalgia

Knee ultrasound: Sonographic examination was performed with a standardized technique the knee joint is examined in long and short axis from the anterior, posterior, medial and lateral aspects, suprapatellar region, cartilage thickness and crystal deposition. All studies were performed in a dynamic fashion, scanning across the joint in a medial-lateral sweep for long axis views and proximal-distal sweep for short axis views (figure 2).

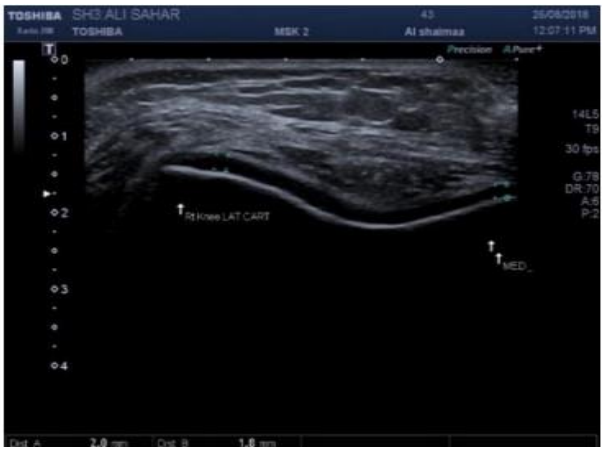


Figure (2): Ultrasound image of right knee joint cartilage showing an anechoic band with sharp hyperechoic margins due to crystal deposition (chondrocalcinosis)

Statistical analysis

The study's data analysis was performed using SPSS (Statistical Program for Social Science) version 24. Qualitative data were presented as frequencies and percentages. Since the quantitative data did not follow a normal distribution, it was expressed using median and interquartile range (IQR). The following tests were used; 1) Mann Whitney U test (MW): when comparing between two groups (for abnormally distributed data), 2) Chi-square test: was used when comparing between non-parametric data, and 3) Spearman's correlation coefficient (s): test was used for correlating data. Probability (p-value) < 0.05 was considered significant.

RESULTS

There was a female predominance in both groups (90% and 97.5%) with no significant difference between both groups. There was statistically significant increase of age in group A [(43.5 31.25-49.75)] years compared to B [38 (28- 42)] years (p 0.023). No statistically significant difference between studied groups as regard disease duration (p 0.389) (table 1).

Also there was statistically significant decrease of vitamin D level of group A [10, (8-11.8)] when compared with group B [20 (14.3- 28.8)] (p < 0.001). Statistically significant higher percentage of vitamin D deficiency below 30 ng/mL was found in group A compared to group B (100% vs. 75%) (p 0.001). No statistically significant difference between the studied groups regarding TNF-α (p 0.788). In group A, the TNF-α was [23.2 (17.4-29.5)], while in group B, the TNF-α level was 22.6 (16.6- 34)]. Statistically significant increase of PTH level in group A [100 (60 – 167.5)] versus group B [40 (30- 50) (p 0.001) (table 2).

The ultrasound findings revealed several statistically significant differences between both groups. In terms of wrist degenerative changes, the group A showed a statistical significant increase, with 47.5% of patients (19 out of 40) affected, compared to 25% in the group B (10 out of 40) (table 3). Conversely, the primary FMS patients (group B) exhibited a significantly higher percentage of synovial hypertrophy, with 40% of patients (16 out of 40) showing this feature, while no patient in group A showing this feature (< 0.001) (figures 1). Regarding chondro-calcinosis, the group A had a significantly higher prevalence, with 35% of patients (14 out of 40) affected, compared to none in the group B (0 out of 40), with a (p< 0.001) (figures 2).

Although there was no statistically significant difference in overall knee degenerative changes between the groups (p 0.160), the group A still had a higher percentage of knee degenerative changes. Specifically, 42.5% of the group A patients (17 out of 40) had knee degenerative changes compared to 27.5% in the group B (11 out of 40) (table 3), reflect the varying impacts on joint health.

Table (1): Comparison of demographic data between studied groups

Item		Group A n = 40	Group B n = 40	Stat. test	p-value
Age (yrs.)	**Median (IQR)**	43.5 (31.25- 49.75)	38 (28 -42)	MW = 564	0.023*
Sex	**Male**	4 (10%)	1 (2.5%)	X^2 = 1.92	0.166
	Female	36 (90%)	39 (97.5%)		
Disease duration (yrs.)	**Median (IQR)**	3 (2 - 4)	3(2 - 5)	MW = 712.5	0.389

MW: Mann Whitney U test, X^2: Chi-square test, *: Significant p-value (< 0.05).

Table (2): Comparison of laboratory data between both groups

Laboratory data		Group A n = 40	Group B n = 40	Stat. test	p-value
Vitamin D level	**Median (IQR)**	10) (8 - 11.8)	20 (14.3 - 28.8)	MW = 146	< 0.001*
Vitamin D status	**Deficient**	40 (100%)	30 (75%)	X^2 = 11.4	< 0.001*
	Normal	0 (0.0%)	10 (25%)		
TNF-α	**Median (IQR)**	23.2 (17.4 - 29.5)	22.6 (16.6 - 34)	MW = 772	0.788
PTH	**Median (IQR)**	100 (60 - 167.5)	40 (30 - 50)	MW = 120	< 0.001*

TNF-α: Tumor necrosis factor alpha, PTH: Parathormone hormone, MW: Mann Whitney U test, X^2: Chi-square test, *: Significant p-value (< 0.05).

Table (3): Comparison of wrist and hands, and knee ultrasound findings between studied groups

Ultrasound findings		Group A n = 40 no. (%)	Group B n = 40 no. (%)	Stat. test	p-value
Wrist and hands degenerative changes	No	21 (52.5%)	30 (75%)	$X^2 = 4.3$	0.036*
	Yes	19 (47.5%)	100(25%)		
Wrist and hands synovial hypertrophy	No	40 (100%)	24 (60%)	$X^2 = 20$	< 0.001*
	Yes	0 (0%)	16 (40%)		
Knee chondrocalcinosis	No	26 (65%)	40 (100%)	$X^2 = 16.9$	< 0.001*
	Yes	14 (35%)	0 (0%)		
Knee degenerative changes	No	23 (57.5%)	29 (72.5%)	$X^2 = 1.97$	0.160
	Yes	17 (42.5%)	11 (27.5%)		

X^2: Chi-square test, *: Significant p-value (< 0.05).

Table (4): Comparison of number of tender points, Widespread pain index, TNF-α: Tumor necrosis factor alpha between both groups

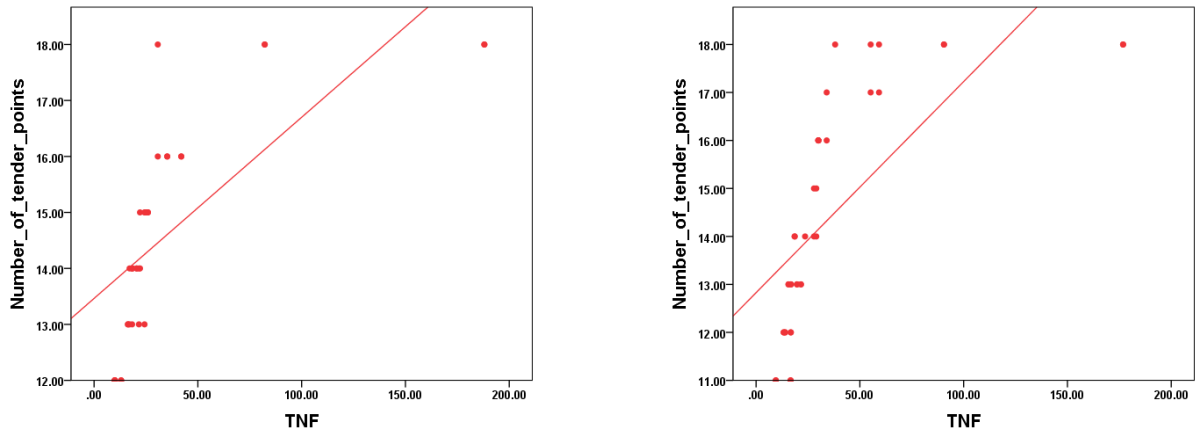
Item		Group A n = 40	Group B n = 40	Stat. test	p-value
Number of tender points	Median (IQR)	14.5 (13 - 15.8)	14 (12.3 - 16.8)	MW = 750	0.627
WPI	Median (IQR)	11 (10 - 13.8)	10 (8 – 13)	MW = 661	0.177
TNF-α	Median (IQR)	23.2 (17.4 - 29.5)	22.6 (16.6 – 34)	MW = 772	0.788

WPI: Widespread pain index, TNF-α: Tumor necrosis factor alpha, PTH: Parathormone hormone, MW: Mann Whitney U test, *: Significant p-value (< 0.05).

Table (5): Correlation of tumor necrosis factor alpha with number of tender points and widespread pain index in both groups

Item	TNF- α			
	Group A		group B	
	S	p-value	S	p-value
Number of tender points	0.95	< 0.001*	0.95	< 0.001*
WPI	0.93	< 0.001*	0.92	< 0.001*

WPI: Widespread pain index, TNF-α: Tumor necrosis factor alpha, S: Spearman correlation coefficient, *: Significant p-value (< 0.05).



a. Group A b. Group B

Figure (3): Scatter plot shows positive correlation between tumor necrosis factor - α and number of tender points in group A and B

No statistically significant difference between studied groups regards number of tender points; in group A, the median was 14.5 with IQR (13-15.8), while in group B, the median was 14 with IQR (12.3-16.8) (p 0.627). No statistically significant difference between studied groups as regard WPI; in group A, median was 11 with (10-13.8), while in group B, median WPI was 10 with IQR (8-13) (p 0.177). No statistically significant difference between studied groups regards TNF-α; in group A, median TNF-α was 23.2 with IQR (17.4 29.5), while, in group B,

median TNF-α was 22.6 with IQR (16.6-34) (p 0.788) (table 4). There was strong positive correlation between TNF-α and number of tender points in both groups (r = 0.95, p < 0.001). Also, there strong positive correlation between TNF-α and WPI in both groups (s = 0.93, p < 0.001) (table 5, figure 3).

DISCUSSION

This is study designed to differentiate between primary FMS cases and its subset that had deficient vitamin D3 as regards to TNF-α level and to determine ultrasound changes in hands and knee joints. Our results showed statistically significant decreased vitamin D level in group A as well as increased percentage of vitamin D deficiency among them versus group B. This agreed with Ellergezen et al. [16] who examined the connection between vitamin D levels and inflammatory cytokines in FMS patients and revealed that FMS patients had lower levels of vitamin D, vitamin D receptor, and vitamin D binding protein compared to the healthy controls, suggesting a potential link between vitamin D-related factors and FMS.

Oure results reported statistically significant increased PTH level and increased percentage of HPT in group A than group B. These results agreed with the study done by Costa et al. [4] who found high frequency of asymptomatic HPT in patients with FMS.

Regarding TNF-**α** level, the current study revealed no statistically significant difference between the studied groups. In agreement with us is a case-control study conducted by Kutu et al [17] aimed to investigate the potential role of inflammatory markers in fibromyalgia and to evaluate differences in serum levels of several key inflammatory markers and oxidative stress indicators between these two groups, they revealed no statistically significant differences in the serum levels of the pro-inflammatory cytokines (TNF-α, IL-1β, IL-8) or Oxidized-low density lipoprotein between fibromyalgia patients and the healthy control group. In contrast to our results, Tsilioni et al. [18] found elevated plasma levels of TNF-α in fibromyalgia patients when compared with controls. However, our results showed statistically significant positive correlation between TNF-α level and number of tender points, WPI, SSSS and VAS in both groups. These results are consistent with the study by Kutu et al. [17], which found a statistically significant correlation between VAS scores and serum TNF-α levels in patients with FM. These findings support the hypothesis that TNF-α levels may influence pain severity by increasing the number of tender points, WPI, SSSS, and VAS, thereby contributing to hyperalgesia in FM patients.

Regarding US findings of wrists and hands joints between studied groups our results revealed statistically significant increased percentage of degenerative changes in wrists and hands of group A when compared to group B. These results are consistent with the study by Patel et al. [19] who evaluated imaging findings of metabolic bone disease.

Our results revealed statistically significant increased percentage of synovial hypertrophy in group B patients when compared to group A. This finding highlights a notable difference in the types of joint inflammation present between the two groups**.**

Regarding US findings of knee joints between studied groups our results revealed statistically significant increased percentage of chondrocalcinosis of group A than group B. This suggests a strong association between SHPT and chondrocalcinosis. No statistical significant difference was found between groups regards degenerative changes in knee joints, but results showed increased percentage of degenerative changes in group A when compared with group B. Dzekan and Stanislavchuk [20] agreed with our results and reported increased frequency of knee osteoarthritic degenerative changes among patients with FMS. Bergman et al [21]. disagree with our results as he reported decreased frequency of knee osteoarthritic degenerative changes among patients with FMS.

CONCLUSION

Our study showed that the decreased vitamin D level and increased PTH in fibromyalgia result in degenerative changes of wrist and hands and knee joints as SHPT accelerate the degenerative changes. The study also revealed increased synovial hypertrophy with FMS as it is inflammatory disorder. Also there is strong association between TNF-α level and number of tender points, WPI, SSSS and VAS in both groups suggesting that this inflammatory cytokine may be concerned with increasing pain perception in these diseases.There is a necessity for early diagnosis of any degenerative or inflammatory changes in hands and knee joints by US and other measures to make proper control of this disease and its complication due to lack of typical clinical features as well as hyperparathyroidism is often undiagnosed or misdiagnosed.

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الملخص العربي

التمييز بين مرض متلازمة الألم العضلي التليفي الاولي و بعض حالاتها التي لديها نقص في فيتامين د عن طريق قياس تركيز عامل نخر الورم ألفا في الدم وما يصحبه من تغيرات باليدين والركبتين باستخدام الموجات فوق الصوتية

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ملخص البحث:

الخلفية: متلازمة الألم العضلي التليفي الاولي من الأمراض الروماتيزمية الشائعة التي تسبب ألما واسع المدي في البنية العضلية الهيكلية (العضلات- الأوتار- الأربطة وغيرها) ويصحبه الشعور بالإرهاق واضرابات النوم والذاكرة والحالة المزاجية . وقد تبين حديثا ان هناك نسبه من المرضي المصابين بهذا المرض لديهم نقص واضح في فيتامين د ينتج عنه زياده في افراز الغده الجار درقيه ومن ثم ظهور بعض الاعراض لدي هولاء المرضي مثل التهاب المفاصل والترسيبات لاملاح الكالسيوم علي مفاصل الركبتين وزياده التغيرات التهتكيه بالمفاصل عن غيرهم ممن ليس لديهم نقص في فيتامين د عامل نخر الورم ألفا هو بروتين ينتج من الخلايا الوحيدات والبراعم وهي نوع من خلايا الدم البيضاء ويكون قادرا علي مهاجمه وتحطيم خلايا الورم كما يثير أمراض الالتهاب المزمنه. ويعد معامل نخر الورم الفا مسؤولا عن زياده الشعور بالألم والتهاب العضلات والاكتئاب واضطرابات النوم في متلازمه الالم العضلي التليفي.

الهدف: التمييز بين مرض متلازمة الألم العضلي التليفي الاولي و بعض حالاتها التي لديها نقص في فيتامين د عن طريق قياس تركيز عامل نخر الورم ألفا في الدم وما يوجد من تغيرات باليدين والركبتين في كلا منهما باستخدام الموجات فوق الصوتية.

الطرق: تم اجراء دراسه مقارنه مقطعيه علي 80 مريضا بمتلازمه الالم العضلي التليفي الاولي بقسم الروماتيزم والتاهيل بمستشفي الزهراء الجامعي, 40 منهم لديهم نقص فيتامين د. وقد استوفي جميع المرضي معايير الاصابه بمتلازمه الالم العضلي التليفي طبقا لمعايير الرابطة الأمريكية الروماتيزميه 1990 و 2010.تم تقسيم المرضى الى مجموعتين أ شملت مرضى الفايبرومايلجيا الذين يعانون من نقص فيتامين د, المجموعه ب شملت مرضى الفايبرومايلجا الاولى . وقد خضع كل من المشاركين فى المجموعتين الي تاريخ مرضي مفصل- فحص شامل للجسم والجهاز الهيكلي العضلي - تقييم الألم باستخدام المقياس التناظري المرئي - صورة كاملة للدم ومعامل سرعة الترسيب والمعامل التفاعلي سي والمعامل الروماتيدي - فيتامين د وهرمون الغده الجار درقيه ونسبه الكالسيوم - معامل نخر الورم الفا باستخدام الأليزا، عمل أشعه عاديه علي اليدين ، عمل موجات فوق صوتيه علي اليدين والركبتين .

النتائج: اظهرت النتائج ان هناك علاقه قويه بين معامل نخر الورم الفا ومقياس شده الالم في كلا المجموعتين كما اظهرفحص الموجات الفوق صوتيه للمفاصل ان نسبه التغيرات التهتكيه بمفاصل اليدين والركبتين اعلي في المرضي الذين لديهم نقص في فيتامين د وتزداد هذه التغيرات بزياده العمر.

الأستنتاجات: تم العثور على زيادة نسبه حدوث التغيرات التهتكيه بمفاصل اليدين والركبتين في المرضي الذين لديهم نقص في فيتامين د عنها في مرضي متلازمه الالم العضلي التليفي وتعد الموجات الفوق صوتيه اداه هامه في التشخيص المبكر لتلك التغيرات.

الكلمات المفتاحيه: متلازمه الالم العضلي التليفي، نقص فيتامين د زياده افراز الغده الجار درقيه الثانوي، الموجات الفوق صوتية، دراسه تقارنيه.

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