

## Calcium, Magnesium and Phosphorous Levels in Serum of Iraqi Women with Fibromyalgia

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### Abstract

Fibromyalgia (FM) is a common, debilitating, and chronic pain syndrome. The women are more likely to have more tender points on examination than are their male counterparts. Iraqi study showed that FM occur in 1.5% among adolescents of Iraqi population. In compare to normal healthy women, present study was revealed that Iraqi women with FM have significant elevation of calcium ( $p = 0.003$ ) with significant reduction of magnesium ( $p = 0.001$ ), whereas the inorganic phosphorous was not differs ( $p = 0.31$ ). In conclusion, magnesium and calcium would play a crucial role in etiopathogenesis of fibromyalgia.

**Key words:** calcium, magnesium, phosphorous, Fibromyalgia.

### الخلاصة

الفيبروميالاجيا او متلازمة ألم الليف العضلي هي متلازمة ألم مشترك منهك و مزمن. النساء أكثر عرضة للمزيد من نقاط الوهن اثناء الفحص السريري من نظرائهن من الرجال. وأظهرت دراسة عراقية ان الفيبروميالاجيا تحدث في 1,5 % من البالغين من العراقيين. بالمقارنة مع نساء غير مصابات, اظهرت الدراسة الحالية ان النساء العراقيات المصابات بالفيبروميالاجيا يظهرن ارتفاعا معنويا بمستوى الكالسيوم ( $p = 0.003$ ) وانخفاضا معنويا بمستوى المغنيسيوم ( $p = 0.001$ ) في المصل. بينما لم يظهرن اختلافا معنويا بمستوى الفسفور غير العضوي ( $p = 0.31$ ). يمكن الاستنتاج من نتائج الدراسة انه من الممكن أن يكون للكالسيوم والمغنيسيوم دورا هاما في امراضية الفيبروميالاجيا.

### Introduction

Fibromyalgia (FM) is a common, debilitating, and costly chronic pain syndrome characterized by widespread pain, fatigue, disrupted sleep, depression, and physical deconditioning. The lifetime prevalence of FM in women is approximately 7%<sup>(1)</sup>. FM symptoms negatively impact patients' quality of life and their ability to remain competitively employed. The current treatments impart minimal benefit on symptoms and long-term functioning<sup>(2-4)</sup>. The estimated annual direct cost of FM exceeds \$20 billion<sup>(5)</sup>. Diagnostic criteria of the American College of Rheumatology<sup>(6)</sup> include widespread pain and specific tender points. Patients often have other unspecific symptoms including fatigue, sleep disturbances, morning stiffness, anxiety and autonomic complaints such as irritable bowel and bladder syndromes<sup>(7)</sup>. The women are more likely to have more tender points on examination than are their male counterparts<sup>(8)</sup>. Prevalence of FM in the rheumatology clinic is 20%<sup>(9)</sup>, and an Iraqi study showed that FM occur in 1.5% among adolescents of Iraqi population<sup>(10)</sup>. Pathophysiological hypotheses of FM include impairment in the functioning of the hypothalamic-pituitary axis and

alterations in neuromodulators and neurotransmitters such as substance P (SP), nerve growth factor (NGF), N-methyl-D aspartate, norepinephrine (NE) and serotonin (5-HT)<sup>(11-13)</sup>. However, FM etiology and pathogenesis remain elusive<sup>(14,15)</sup>. Metals like calcium and magnesium compete with each other in modulating muscle contraction as well as in regulating many enzymatic reactions involved in energy metabolism, signal transduction and brain activity. Results concerning levels of calcium and magnesium in Fm are to some extent controversial; some authors observed reduced serum calcium and calcitonin levels in a small sample of FM patients<sup>(16)</sup>, while others report a normal range of plasma calcium and magnesium levels in patients affected by FM together with their reduced concentrations inside polymorphonuclear leukocytes<sup>(17)</sup>. Inorganic phosphorus is critical for numerous normal physiologic functions including skeletal development, mineral metabolism, cell membrane phospholipid content and function, cell signaling, platelet aggregation, and energy transfer through mitochondrial metabolism<sup>(18)</sup>.

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Higher concentrations of phosphodiesterase (PDE) products and inorganic phosphate (Pi) have been observed in FM patients in comparison to controls<sup>(19)</sup>, together with a decrease in phosphocreatine, ATP and phosphocreatine/inositol phosphate (IP) ratio in the quadriceps<sup>(20)</sup>. Within this study, it is fundamentally aimed to investigate serum calcium, magnesium and phosphorus level in Iraqi women with FM.

### Materials and Methods

Twenty five Iraqi women who were attending the Rheumatology Clinic of Baghdad Teaching Hospital, were diagnosed as having FM according to the ACR 1990 criteria<sup>(6)</sup>, and 25 normal healthy individuals (NHI) were included in this study. Both groups are age and sex matched. In the laboratory investigation, serum magnesium, calcium and phosphorus were measured by endpoint colorimetric spectrophotometry. All reagents used were of analytical grade. The serum calcium, magnesium and inorganic phosphorus level were measured with kits of Biomaghreb® (Biomaghreb, Tunis, Tunisia). The principle of the study is based on measuring the absorbance of a colored complex at a specific wave length. Absorbance is proportional to the analyte level<sup>(21)</sup>.

### Statistical Analysis

Microsoft office excel software 2007 for windows, was used for all statistical analysis. Differences between patients and NHI were evaluated by the Student's t test. The level of significance was set at P value less than 0.05.

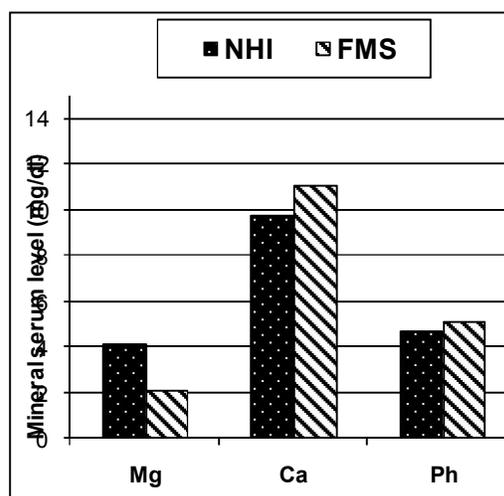
### Results

In present study, the age of patients in FM group and NHI were  $41.7 \pm 7.9$  (mean  $\pm$ SD) years and  $40.1 \pm 9.5$  (mean  $\pm$ SD) years, respectively. There was no significant difference between ages of the both groups ( $P = 0.465$ ). About the serum level of minerals, there was a significant decrease in serum magnesium level ( $P < 0.05$ ) in FM group in compare to NHI one. Also there is a significant increase in serum calcium level ( $P < 0.05$ ) in the FM group in respect to NHI group. In addition, the study was revealed no significant difference in serum level of inorganic phosphorus between the involved groups ( $P < 0.05$ ), (see table 1 and Figure 1).

**Table 1: Magnesium, Calcium and Phosphorus level [Mean  $\pm$ SD] in the FM and the NHI groups:**

Mineral serum level (mg/dl)	FM [Mean $\pm$ SD]	NHI [Mean $\pm$ SD]	P-value
Magnesium	2.1 $\pm$ 0.83*	4.17 $\pm$ 2.41	0.001117
Calcium	11.1 $\pm$ 1.19*	9.78 $\pm$ 1.57	0.003288
Phosphorus	5.1 $\pm$ 1.66	4.71 $\pm$ 2.52	0.311017

\* Significant changes in compare to normal healthy individuals.  $P < 0.05$ .



\* Significant changes in compare to normal healthy individuals.  $P < 0.05$ .

**Figure 1: Magnesium, Calcium and Phosphorus level in FM and NHI groups**

### Discussion

Although disturbances in the musculoskeletal system, the neuro-endocrine system and in the central nervous system have been implicated in the pathophysiology of FM, a primary mechanism underlying the etiopathogenesis of FM is unknown<sup>(17)</sup>. Serum trace element levels have been researched to reveal etiopathogenesis of patients with FM<sup>(18-20)</sup>. However, the results of these studies have appeared to be ambiguous. In this study, serum magnesium was found significantly lower and serum calcium was significantly

higher in patients with FM when compared to NHI, but the same difference was not observed between the two groups when calcium and inorganic phosphorus levels are considered. In contrast to our study; in past years, Prescott et al. reported that serum magnesium level of patients with FM did not change, but Eisinger et al. found decreased levels of red blood cell magnesium in patients with FM<sup>(20)</sup>. Similarly, Abraham and Flechas also found that magnesium deficiency plays a possible role in mechanism of pain in FM. They thought this was related to the role of magnesium in the production of ATP<sup>(18)</sup>. Some evidence exists supporting the possibility of deficiency of components required for ATP synthesis in etiopathogenesis of FM<sup>(11)</sup>. On the other hand, several fibromyalgia manifestations such as fatigue, muscle weakness, irritable bowel and paresthesia are similar to symptoms of magnesium deficiency<sup>(18)</sup>. Magnesium plays an important role in enzymatic reactions, especially in energy production. As the magnesium level decreases, the energy levels also decrease simultaneously. As a result of this situation, fatigue may occur<sup>(22)</sup>. Magnesium supplementation may benefit in the treatment of chronic fatigue<sup>(22, 23)</sup>. Magnesium is nature's physiologic calcium blocker. It can compete with calcium for binding sites on proteins and membranes<sup>(24)</sup>. We can suppose that subjects with a diagnosis of Fm have a scarce muscle fiber capacity to repair, presumably due to altered monoamine transmission and/or hormonal changes<sup>(25)</sup>, which, in turn, can provoke a reduced homeostasis of ATP, magnesium and calcium inside cells. The increase in muscle intracellular calcium level may produce myofiber damage through calcium activated proteolytic enzyme activity<sup>(26)</sup> and cause persistent muscle contraction without electromyographic activity. This uses adenosine triphosphate/phosphorylcreatine, depletes energy stores<sup>(27)</sup>, and may result in muscle weakness. Lund-Olesen and Lund-Olesen<sup>(28)</sup> put forward a similar hypothesis to explain the pathogenesis of chronic fatigue syndrome/fibromyalgia. They hypothesized that calcium channels of striated muscle cells in the conditions are injured and that an increased amount of calcium is permitted to enter the cells. This results in increased muscular tone. The association between these two elements and clinical parameters makes us to think that these elements may play role in etiopathogenesis of FM. Further investigations are required about trace elements and FM etiopathogenesis.

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