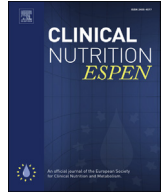




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## Correlation of symptoms to serum vitamin D levels?

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## SUMMARY

**Background and Objective:** Recent studies have shown that vitamin D plays an important role in many disease processes. However, data is lacking which correlates the common symptoms attributed with vitamin D levels. This study was undertaken to find the correlation of symptoms and Vitamin D levels among ethnic Saudi Arabian population.

**Methods:** A structured questionnaire was made and translated in the Arabic language, which included, age, weight and height, ethnicity and marital status. Patients who were visiting orthopaedic clinics for the first time were included after a detailed history, which ruled out any associated metabolic conditions. Patient's biometric data and the answering of the questionnaire were conducted by one of the senior members of the research group. The symptoms which were included in the questionnaire were fatigue, muscle cramps, joint and back pain, blood sugar levels, recurrent infections, hair loss, mood swings, weight gain, irritable bowel, fractures and history of malignancy. All the scores were graded between 1 and 9 (mildest 1 and severe 9) and only for fracture and malignancy it was yes/no answer. A score of  $\leq 4$  was accepted as no impact of the vitamin D levels on symptoms and answer of  $\geq 5$  was accepted as impact on the symptoms. Residents whose mother tongue was Arabic conducted all interviews. Blood was collected for 25 OHD levels, calcium and parathyroid hormone levels. Deficiency of vitamin D was defined as  $\leq 20$  ng/ml, insufficiency 21–29 ng/ml and normal level  $\geq 30$  ng/ml. The data was entered in the data base and analyzed using SPSS Inc Version 20.

**Results:** Two hundred one patients completed the questionnaire but for final analysis the data of 187 was available for analysis as in 14 patients some of the data was missing. All were females and the average age was  $55.9 \pm 12.4$  years, weight  $78.9 \pm 14.2$  kg and height was  $1.56 \pm 7.01$  m. The mean calcium level was  $9.12 \pm 0.33$  mg/dl and, parathyroid hormone was  $8.1 \pm 6.06$  pc/ml. The average 25 hydroxy vitamin D3 (25OHD) level was  $21.8 \pm 10.22$  ng/ml. Forty-four (23.5%) of women had a normal vitamin D level, 51 (27.27%) had insufficiency and 92 (49.19%) had deficiency. Patients who complained of muscle cramps had 25OHD level of  $18.86 \pm 8.73$  compared to patients who had no complains of cramps,  $23.45 \pm 9.2$  ng/ml ( $p < 0.001$ ) and symptom severity score (SSC) p value of  $p < 0.000$ . The results were similar for fatigue, Back pain, hair loss, mood swings and weight gain of  $P < 0.04$ ,  $p < 0.07$ ,  $p < 0.05$ ,  $< 0.03$  and  $p < 0.09$  for vitamin D levels and  $p < 0.001$  for SSS. Forty-eight (25.6%) had a previous fracture in their history.

**Conclusions:** This study shows that many symptoms, which have been attributed to low vitamin D levels, are not true. Muscle Cramps, fatigue, mood swings, hair loss, back pain and weight gains appears to be more common in patients with low 25OHD levels.

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## Introduction

Vitamin D, a fat-soluble vitamin is important in the absorption of calcium from the gut and renal tubules. It also helps with parathyroid hormone to mobilize calcium from bone in states where

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there is low serum calcium [1], it was estimated a decade ago that over 1 billion people worldwide have low vitamin D levels [2] making one of the most studied vitamin and its effects on the human body. Initially it was believed that Vitamin D was only involved in the calcium metabolism but lately the identification of role of the vitamin D receptor and its presence in the target tissues like kidney, intestine, and bone, heart and in a variety of tissues [3] raised the speculation of its role in other systems of the body. Epidemiological studies have shown a significant association between low Vitamin D levels and risk of cardiovascular disease, diabetes and metabolic syndromes [4,5]. Reports indicate if vitamin D levels are maintained at normal levels, this could reduce the incidence of cancer [2,6] reduction of risk of fractures [7,8], prevention of depression and mood disorders [9], hair loss [10] and weight gain [11]. All the proof of association between the disease and low vitamin D levels is indirect and we could not identify studies which directly investigated all the symptoms of Vitamin D deficiency and insufficiency. This study was done with the objective to correlate the symptoms with vitamin D levels.

## Methods

This is a cross sectional study involving 201 Saudi Arabian females. Approval was taken from the Institutional review board of Imam AbdulRahman Bin Faisal University, Dammam. The study was carried out between 1st March and July 2017. A structured questionnaire was made and translated in the Arabic language, which included, age, weight, height, ethnicity and marital status. Patients who were visiting orthopaedic clinics for the first time were included after a detailed history, which ruled out any associated metabolic conditions. Patient's biometric data and the answering of the questionnaire were conducted by one of the senior members of the research group. The symptoms which were included in the questionnaire were fatigue, muscle cramps, joint and back pain, blood sugar levels, recurrent infections, hair loss, mood swings, weight gain, irritable bowel, fractures and history of malignancy. All interviews were conducted by residents whose mother tongue was Arabic. The scores were graded between 1 and 9 (mildest 1 and severe 9) and only for fracture and malignancy it was yes/no answer. A score of  $\leq 4$  was accepted as no impact of vitamin D levels on the symptoms and answer of  $\geq 5$  were accepted as impact of vitamin D levels. Patients who had any doubt of a metabolic disease were excluded from the study. Blood was collected for 25 OHD levels, calcium and parathyroid hormone levels. Deficiency of vitamin D was defined as  $\leq 20$  ng/ml, insufficiency 21–29 ng/ml and normal level  $\geq 30$  ng/ml. The data was entered in the data base and analyzed using SPSS Inc Version 20. The data was analyzed using SPSS (Statistical Package for the Social Sciences), version 14.0, Chicago, Illinois. Data is expressed as mean  $\pm$  standard deviation (SD). Statistical significance differences between groups were determined with Student's *t*-test and *p* values of  $< 0.05$  using 95% Confidence Interval (CI) were considered as significant.

## Results

Two hundred one patients completed the questionnaire but for final analysis the data of 187 was available for analysis as in 14 patients some of the data was missing. The average age was  $55.9 \pm 12.4$  years, weight  $78.9 \pm 14.2$  kg and height was  $1.56 \pm 7.01$  m. The mean calcium level was  $9.12 \pm 0.33$  mg/dl and, Parathyroid hormone was  $8.1 \pm 6.06$  pc/ml. The average 25OHD level was  $21.8 \pm 10.22$  ng/ml (Table 1). Forty-four (23.5%) of women had a normal vitamin D level, 51 (27.27%) had insufficiency and 92 (49.19%) had deficiency. Table 2 gives the comparison of demographic characteristics of the patients with the vitamin D

**Table 1**  
Demographic data of all patients N=187.

Characteristics	Mean (SD)
Age (years)	55.90 (12.2)
Weight (Kilograms)	78.96 (14.2)
Height (Centimeters)	156.3 (7.06)
Calcium (mgm/dl)	9.13 (0.3)
Vitamin D3 (ng/ml)	21.85 (10.2)
Parathyroid Hormone (pc/ml)	8.18 (5.5)

categories. Vitamin D levels between patients who reported cramps and no cramps was  $18.86 \pm 8.73$  versus  $23.45 \pm 9.2$  ng/ml ( $p < 0.001$ ) and symptom severity score *p* value of  $p < 0.001$  The results were similar for fatigue, mood swings, hair loss, back pain and weight gain of  $P < 0.001$ ,  $p < 0.001$ ,  $p < 0.004$ ,  $p < 0.002$  and  $p < 0.002$  for vitamin D levels and  $p < 0.001$  for symptom severity score (SSS) (Table 3). Forty-eight (25.6%) had a previous fracture in their history and there were significant low vitamin D levels inpatients with fractures  $16.57 \pm 7.39$  to  $21.87 \pm 9.72$  ng/ml ( $P < 0.001$ ). In 15 (8.02%) patients had a malignancy for which they were treated.

## Discussion

Our study shows that patients with low vitamin D levels have severe symptoms of cramps, fatigue, mood swings, hair loss, back pain and weight gain. Other symptoms, which are commonly, associated to low vitamin D levels such as irritable bowel syndrome, fluctuating blood sugar levels and low immunity is not borne by this study. Recently low vitamin D was found to be associated with fatigue in both healthy and clinical populations [12–14]. The hypothesis put forward for fatigue in low vitamin D levels causes skeletal demineralization and muscle weakness and fatigue being the end [15]. Recently Roy et al. (2014) [16] reported that low vitamin D levels was found in 77.2% of patients who presented with fatigue and surprisingly once the vitamin D levels became normal the symptom of fatigue significantly improved. In our study 72.19% of patients presented with fatigue as a symptom with SSS of  $6.7 \pm 1.6$  out of 9, suggesting that fatigue could be one of the important early symptoms of low vitamin D levels.

Depression, mood swings and irritability is common around mid 20's with women being affected more than men. In the ratio of 10–25% in women to 5–12% in men, with a recurrence of 50–60% [17]. Jorde and colleagues (2008) [18] showed a relationship between vitamin D status and depression with remarkable improvement of symptoms who were treated with vitamin D supplementation and recently after an extensive review came to the conclusion that vitamin D deficiency may be a risk factor for late-life depression [19].

Vitamin D level–mood associations were observed in most, but not all, observational studies. In our study all the patients had never being to a psychiatric clinic nor were on any treatment but 102 (54.5%) of the patients voluntarily indicated that they suffered with mood swings and often irritability without any cause with an average of high SSS of  $7.03 \pm 1.59$  out of 9 and low vitamin D levels  $18.7 \pm 7.34$  ng/ml compared to those who did not complain vitamin D level was  $23.2 \pm 11.1$  ng/ml. This does indicate that vitamin D has influence on the mood changes.

Some degree of hair loss is a normal but exaggerated hair loss is usually seen in chronic diseases, poor nutrition and stress related conditions. In the recent past vitamin D deficiency has been linked to excessive hair loss. In 2016 two studies with matched healthy controls correlated significantly low vitamin D levels to female pattern hair loss in young women [20,21]. Majority (67.3%) of

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