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# ARTICLE

# **Chronic Musculoskeletal Pain in Females as a Manifestation of Vitamin D Deficiency in Saudi Arabia**

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## Abstract

Objective: To determine the prevalence of vitamin D deficiency among females presenting with chronic musculoskeletal pain.

Methods: One hundred female patients with chronic pain were screened between January 2007 and November 2008 in the medical out-patient clinics in King Abdulaziz University Hospital, Jeddah. Serum (25- hydroxycholecalciferol) and bone chemistry levels were done. Vitamin D deficient patients were identified, treated with supplements, followed for improvement of symptoms. and Results: 84% were vitamin D deficient. Of that group, 67% were of childbearing age, and 50% were noted to have a severe deficiency. Only 14% were hypocalcaemic, 8% had hypophosphatemia, while 13% had high alkaline phosphatase levels. All responded after vitamin D and calcium supplement therapy was initiated, and symptoms improved.

<u>Conclusions:</u> Consideration of vitamin D deficiency during consultations for chronic musculoskeletal pain is

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warranted. Screening of such patients should be standard practice in clinical care. Diagnosis is missed or delayed if 25- hydroxycholecalciferol levels are not evaluated. Treatment is beneficial and improvement is rapid.

**Key Words:** Vitamin D deficiency, hypovitaminosis D, musculoskeletal pain, Saudi Arabia

#### Introduction

Patients with chronic, nonspecific musculoskeletal pain that is affecting their quality of life are seen frequently in the outpatient department, (OPD). Despite the prevalence of such pain, the precise diagnosis and effective treatment may remain complicated. Hypovitaminosis D can cause skeletal mineralization defect, leading to isolated or global bone discomfort along with aches and pain in joints and muscles (1, 2). As a result, these patients maybe misdiagnosed with fibromyalgia, degenerative joint disease, arthritis, chronic fatigue syndrome, or simply dismissed as depression (1, 3-6). Since hypovitaminosis D is markedly prevalent in Saudi Arabia, this prompted our investigation of chronic pain patients to determine the prevalence of vitamin D deficiency among those who seek medical advice in the medical clinics in King Abdulaziz University Hospital in Jeddah.

# **Materials and Methods**

This was a prospective observational study conducted on female patients presenting to the medical OPD at King Abdulaziz University Hospital from January 2007 to November 2008. One hundred patients were studied. All patients complained of persistent nonspecific musculoskeletal pains for more than six months, refractory to analgesic agents. They had no known chronic medical illnesses or other conditions to explain their symptoms, such as degenerative or rheumatologic diseases, thyroid disorders, anemia or chronic infections. None of the patients had fibromyalgia (as defined by American College of Rheumatology Criteria 1990). They had no history of renal or hepatic diseases, no malabsorption or family history of osteomalacia, and were not on anticonvulsant therapy. None had been evaluated for hypovitaminosis D and were not taking any vitamin supplements. All patients confirmed lack of sun exposure by direct questioning.

Laboratory investigations included serum bone chemistry (calcium, phosphate, and alkaline phosphatase) and serum concentration of 25-hydroxycholecalciferol (25-OHD), which was measured using enzyme linked immunosorbent assay (ELISA) technique (K2110, immuno diagnostic [Dutch Company], Holland).

Vitamin D deficiency was considered when serum 25-OHD concentration was <50nmol/L. Severe vitamin D deficiency was considered when serum 25-OHD concentration was <25nmol/L.

Patients diagnosed with vitamin D deficiency were treated with oral vitamin D and calcium. They were followed up in the OPD to assess clinical improvements of the symptoms. Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) version 10. Chi square testing was used to analyze group differences for categorical variables, t-test, and ANOVA were used for continuous variables. P value of  $\leq 0.05$  was considered significant.

# Results

Of 100 patients studied, 84 were vitamin D deficient, with levels ranging from 4-48 nmol/l ( $24.7 \pm 14,95\%$  CI 20.6 – 28.7 nmol/L). Also, 42 of 100 patients (which was 50% of deficient patients) had severe vitamin D deficiency ( $12.8 \pm 7,95\%$  CI 9.8 – 15.7 nmol/L).

Forty five of 84 (54%) deficient patients were Saudi. Age distribution and respective vitamin D levels are shown in Table 1. No positive correlation was noted between frequency of vitamin D deficiency and level to different age groups as shown by an insignificant P value. Those of child bearing age (14-50 years) totaled 67%.

Only 12 (14%) of vitamin D deficient patients had low serum calcium levels, seven (8%) had low serum phosphate levels, while 11 (13%) had high serum alkaline phosphatase levels. All patients with normal vitamin D levels had normal bone chemistry.

Table 2 shows the relationship between abnormal bone chemistry to vitamin D levels, which was statistically insignificant. All patients with deficient levels of vitamin D were given 1  $\alpha$  hydroxycholecalciferol 0.5-1 $\mu$ g with 800mg of calcium supplements orally daily according to the severity of the deficiency. All patients showed remarkable improvement of symptoms. The response was observed after three to four months of continuous treatment. The treatment was continued for six to eight months and thereafter changed to 400 I.U Vitamin D3. and 800 mg calcium carbonate daily together with recommended sun exposure of at least 15 minutes daily. Patients were followed for one year to confirm improvement and maintenance treatment continuation.

## Discussion

Π

Vitamin D deficiency presenting as persistent musculoskeletal pain has been reported in immigrants to Europe and the USA (5, 7-9). It has also been documented as a manifestation of hypovitaminosis D in Saudi Arabia (10-13). In all of these studies, women were particularly at risk.

In this study we found that 84% of females who presented with chronic pain had low levels of 25-OHD, and half had severe deficiency. The mean value was in the moderate severe range. The prevalence of vitamin D deficiency was similar to that observed by other authors in both developed and developing countries:

- 93.5% of patients presenting with chronic nonspecific pain to a community health center in Minnesota, USA (5)
- ☐ 78% of patients attending a rheumatology clinic in the United Kingdom (7)
- 90.9% of asylum seeking females attending a primary care center in Switzerland (9)
- 83% of patients attending spinal and internal medicine clinics in Riyadh, Saudi Arabia (12)
  - 74% of patients attending a musculoskeletal clinic

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14 – 19	7 (8)	$18.3 \pm 9.5$	3-33.4				
Age	NO. of patients (%)	Mean ± SD 25-OHD Level in nmol/L	95% CI for means				
95% CI = 95% (	Confidence Interval for mean	S					
SD = Standard I	Deviation of the mean						
Table 1. Age and vitamin d levels in 84 deficient patients							

14 - 19	7 (8)	$18.3 \pm 9.5$	3 - 33.4
20 – 29	9 (11)	29 ± 16.3	8.7 – 49.3
30 - 39	21 (25)	22 ± 12.4	14 – 29.8
40 – 49	19 (23)	$32.3 \pm 17.4$	20.7 – 43
50 – 59	16 (19)	17.4 ± 12.5	7.8 – 27
60 - 69	10 (12)	27.8 ± 8.7	18.7 – 37
70 – 100	2 (2)	25.6	_
	P = 0.5	P = 0.6	

Table 2. Relation of bone chemistry to severity of vitamin d deficiency								
Variable	Normal Vitamin D	Low Vitamin D	P.Value	Very low Vitamin D	P. value			
Mean Calcium ± SD (Normal = 2.1-2.6mmol/L)	2.30 ± 0.13	2.20 ± 0.09	0.06	2.19 ± 0.08	0.17			
Mean Phosphate ± SD (Normal= 0.81-1.58mmol/L)	1.16 ± 0.13	1.08 ± 0.17	0.19	1.06 ± 0.19	0.14			
Mean Alkaline Phosphatase ± SD (Normal = 0-125u/L)	76 ± 23.67	89 ± 38.36	0.21	91 ± 45.84	0.44			

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## in Dubai, United Arab Emirates (14)

However, the prevalence of vitamin D deficiency in our patients was significantly higher than what was reported at a pain rehabilitation clinic at a tertiary medical center in Minnesota, USA, which was 26% (15).

Our conclusions were similar to those from Saudi Arabia in 2003 (12). Patients there presented with back pain, and 83% were found to have vitamin D deficiency that improved after supplementations.

It could be argued that the increased prevalence of vitamin D deficiency in our patients may simply reflect the background tendency of hypovitaminosis D in our population since our study lacked a control group showing vitamin D prevalence in a normal population sample (the limitation of our study). According to a nationwide study done in1992, studying the prevalence of vitamin D deficiency in all regions of Saudi Arabia, in different age groups and both sexes, the prevalence of severe vitamin D deficiency was found to be 25.9% in females of the western province (16), whereas our patients reached 42%. In another recent study of systemic lupus erythematosus patients, prevalence of vitamin D deficiency in a control group of 214 Saudi citizens was 20% (17), while our patients totalled 84%. Hence, it appears that our patients appeared to have higher prevalence of vitamin D deficiency than the population in Saudi Arabia, which contributes to complaints of chronic musculoskeletal pain.

Sixty seven percent (67%) of our patients were of child bearing age (14-50 years). This carries an increased risk of adverse fetal effects and neonatal illnesses such as growth retardation and skeletal deformities. In adults, vitamin D deficiency can precipitate osteopenia, osteoporosis, and may increase the risk of hip fractures later in life (4).

It was noticed that very few patients had abnormal bone chemistry profiles in our study despite the degree of vitamin D deficiency. This finding was observed previously (13, 18, and 19). Therefore, we believe that routine measurement of calcium, phosphate, and alkaline phosphatase are unreliable predictors of hypovitaminosis D. When clinically suspected, serum 25-OHD levels should be checked, which is universally accepted as the most reliable test to measure vitamin D status (5).

Vitamin D deficiency is widely prevalent and nonspecific musculoskeletal pain is a common complaint,. It is necessary to have a high degree of suspicion by the physician and to test for vitamin D levels to avoid missing such a common preventable problem that has long term consequences. The treatment is beneficial with rapid resolution of symptoms.

Sadly, all the patients who presented to us were initially misdiagnosed and sub optimally treated. The remarkable improvement of their symptoms after the introduction of vitamin D supplements confirms hypovitaminosis D as the cause of the symptoms. The benefits of the treatment seem clear even though there were only assessed by direct questioning.

None of our patients had any underlying cause to explain their vitamin D deficiency except for lack of sun exposure. We believe that daily supplementations of vitamin D, minimum 800 – 1000 IU per day should be prescribed to the adult population (recommended by some authorities) (3, 4, and 20) to avoid hypovitaminosis D and its consequences. Diet is not adequate, as very few foods contain vitamin D. Fortified foods do not meet the expectations. Sun exposure habits will not change to any beneficial extent in our community.

# Conclusion

Vitamin D deficiency is common and may be a cause of chronic musculoskeletal pain. Therefore, all patients should be screened by measuring 25-OHD levels rather than by bone profile, which may be normal. Prompt diagnosis and treatment can result in resolution of symptoms and prevention of osteomalacia, osteoporosis, and possibly other long term complications such as cardiovascular disease.

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