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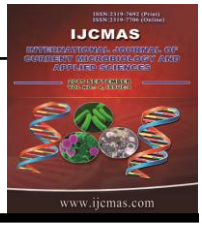

Original Research Article

Hypo Vitaminosis D in Chronic Muscular Skeletal Pain

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Keywords

25 hydroxy vitamin D, CRP, Musculo-skeletal pain

A B S T R A C T

The purpose of performing this cross-sectional study was to evaluate the hypothesis that serum vitamin D levels are abnormally low in patients complaining of chronic musculoskeletal pain and to assess the association of hypovitaminosis with inflammatory marker. A total of 355 patients referred by a rheumatologist for an examination of 25 hydroxyvitamin D, who reported musculoskeletal pain and fatigue from three seasons in rheumatology unite from Shahid Baxtyar outpatient clinic in period of June - December 2014. Hypovitaminosis D (25-hydroxyvitamin D < 30 nmol/L) was found in 85.35%, that affect all age group with female to male ratio (5/1), with different occupation. Our study shows a high prevalence of hypovitaminosis D in patients with non-specific musculoskeletal pain.

Introduction

There is a well-established link between the low serum vitamin D and musculoskeletal pain, and it's one of the consequence of hypovitaminosis D (Sanjay Prakash et al., 2013). Vitamin D is a fat-soluble steroid hormone ingested in the diet and produced in the skin following exposure to ultraviolet rays in sunlight, and conversion to active forms of vitamin D occurs in the liver and kidneys (McCarty et al., 2013). It modulates a wide range of molecular and cellular functions, most readily recognized are its beneficial effects on musculoskeletal parameters (Darina Bassil et al., 2013).

The metabolic processes regulated by vitamin D include serum calcium and phosphate homeostasis, bone remodeling, neuromuscular function, inflammation, and transcription of proteins involved in cell growth and apoptosis (Holick et al., 2006) and affects calcium absorption and bone metabolism; so the decreased vitamin D levels are associated with several diseases such as type I diabetes mellitus, hypertension, cancer, and altered immune function (Jung Won Yoon et al., 2012).

Inadequate levels of serum 25-hydroxyvitamin D are not only detrimental to musculoskeletal health and calcium homeostasis but may also have a role in immunopathology (Mouyis et al., 2008) and increased levels of inflammation and oxidative load (Wang et al., 2008), also it has been implicated as a possible

underappreciated risk factor for the development of cardiovascular disease (Nathan Carlson et al., 2013) and recent research reveals the existence of vitamin D receptors in a variety of cells including antigene-presenting cells. that indicates the influence of vitamin D in various physiologic processes such as immune system (Zohreh Sabbagh et al., 2013) that active metabolite of vitamin D (1,25 OH 2D) inhibits the synthesis of IL-1, IL-6, IL-12 and TNF-α by macrophages (Alicij Grazanka et al., 2014), it also decreases MHC-II expression on cell surface and molecules such as CD86, CD80 and CD 40 and apoptosis induced by T lymphocytes (Cutolo and Straub, 2009). Hypovitaminosis D is a prevalent disorder in developing countries. Clinical manifestations of hypovitaminosis D include musculoskeletal disorders, such as nonspecific muscle pain, poor muscle (Arabi et al., 2010). Low serum 25-hydroxi-vitamin D (25OHD) concentrations reduce the absorption of calcium, leading to decreased bone mass and onset of bone pain (Silva et al., 2013).

Materials and Methods

Study design: The type of study is cross sectional study, conducted at Shahid Baxtyar primary health care center clinic from June 2014 -December 2014. Patient of all age group with muscular skeletal pain included in the study.

Exclusion criteria: patients with secondary causes of musculoskeletal pain such as disk prolapsed, proven neurological problems affecting the spine, diseases that could affect bone metabolism, and use of drugs that interfere with vitamin D metabolism were excluded from study.

Study population and sampling: Patients with persistent nonspecific musculoskeletal pain were admitted to the study with completed a questionnaire screening for age, sex, occupation, dietary intake, sun exposure and the presence of various symptoms were subsequently reviewed and verified in a face-to-face interview by a rheumatology physician.

The participants in this study were divided into three groups according to vitamin D level. In clinical practice; vitamin D status was assessed by measuring the circulating levels of 25 -hydroxy vitamin D, which is the best indicator of vitamin D deficiency (Arabi et al., 2010).

Serum Vitamin D was measured using Elisa kit (DRG Diagnostic Germany) for quantization of the total 25(OH) Vitamin D; three levels were differentiated according kit recommendation; normal value 30-100 ng/ml, Insufficiency 10-29 ng/ml and deficiency < 10 ng/ml.

Serum C. Reactive Protein were measured by the latex agglutination test (Plasmatic UK) by semi-quantitative measurement. Levels of CRP were analyzed in all the patients and grouped categorically as normal CRP < 6mg/L; 12,24,48,96 mg/L.

All the data were analyzed by using SPSS program version 18 Inc., Evanston (Chi-square test ($\chi 2$) and relation correlation) with a p value of <0.05 regarded as a level of significant.

Results and Discussion

The study group consist of three hundred fifty five (355) patients from three different seasons; summer, autumn and winter (Table 1), the median of low vitamin D level was higher in autumn months in comparison to winter and summer months ($p < 0.05$) as clear from figure 1.

In the all subject; the prevalence of hypovitaminosis was 85.35 % with low

serum vitamin D levels < 30 ng/mL. female predominate over male by a ratio 5.32/1 as shown in figure 2, in which 176 cases were had insufficient level with deficient level lower than that.

Several factors were tested in order to find any relation with hypovitaminoses from this study such as age group. The age group of all the participant that attending the clinic for analysis of vitamin D level were grouped (Table 2), and it was clear that 146 (41.12%) adult with age group 16-30 years old were the most complaining victims followed by 132 (37.18%) patients from age group 31-45 years old. statistically this distribution is not significant ($p > 0.05$).

Other parameter such as occupations was analyzed among attendance as observed in table 3. It was found that house holders female were the most attending group to the hospital followed by officer and other occupations ($p < 0.05$).

No informative data were obtained regarding the dietary intake and only 6 (2.13 %) males among those attendance were subjected to regular sun light exposure weekly.

In spite of vitamin D level; one of the inflammatory marker such as CRP were tested among all the attendance as illustrated in table 4, and found to be positive in 100 (35.58%) patients from which 57 (41.6 %) patients had vitamin D deficiency and 31 (31.95%) patients with insufficiency, while 12 (25.53%) patients had normal vitamin D concentration. Titration of CRP were assessed among all positive samples as in table 5, and statistically no significant relation was observed in relation to hypovitaminosis ($p >0.05$). Skin exposure to solar ultra violet radiation is a significant source of vitamin D, and in most cases vitamin D deficiency occurs when individuals do not get enough exposure to and do not eat foods that are rich in vitamin (Silva et al., 2013).

The causes of vitamin D deficiency among the Middle Eastern population remain uncertain, as well as the factors that may increase their risk for low vitamin D. Studies indicate that lack of sun exposure in Middle Eastern population results from cultural practices such as conservative clothing in addition to their lifestyle habit of spending most time indoors (Ann, 2008).

In the general population; vitamin D deficiency, assessed by low levels of 25-hydroxy vitamin D (25(OH)D), has been associated with diverse conditions, of which many have become of concern in the virally infected population, cardiovascular disease, insulin resistance diabetes, dyslipidemia, cancer and neurocognitive impairment (Camille Legeai et al., 2013).

There was an interest in studding Vitamin D deficiency over last 10 years. Several studies revealed high prevalence rate of Vitamin D deficiency in spite of adequate sun exposure in developed countries (Ole Grønli et al., 2014). Recent studies have shown that the rate of vitamin D deficiency is also higher in the sunniest areas of the world, including the

Middle East countries, such as Saudi Arabia, Qatar, and United Arab Emirates, Turkey, India, and Iran because of low exposure to sun due to cultural factors (Silva Hovsepian et al., 2011; Nathan Carlson et al., 2013; Narchi et al., 2015).

In this study patients whom suffering from muscle cramps and muscle weakness were recorded to had low serum vitamin D level (85.35 %), the same result recorded by Alshahrani (2014). In this study high level

of hypovitaminosis were recorded in autumn months but high level also recorded in summer months due to life style of population in this regions and closed clothes which were recorded in 85% of female patients. But there is a study in which sever hypovitaminosis related to winter months also (Silva Hovsepian et al., 2011). Dietary factor also has effect on hypovitaminosis although inadequate information was recorded by the entire participant.

Table.1 Study group

Seasons	Normal	Insufficiency	Deficiency	Total
Summer	36	34	48	118
Autumn	11	103	48	162
Winter	5	39	31	75
Total	52	176	127	355

The chi-square statistic is 50.2634
The *P*-Value < 0.00001

Table.2 Age group of all the participant

Age	Normal		Insufficiency		Deficiency		Total
	M	F	M	F	M	F	
< 15	1	3	6	8	1	11	30
16…..30	4	17	16	61	8	40	146
31…..45	1	15	6	60	7	43	132
46…..60	2	6	0	16	0	13	37
61……75	2	1	1	2	1	3	10
Total	10	42	29	147	17	110	355

The chi-square statistic is 5.5881.
The *P*-Value 0.69326.

Table.3 Occupations of participants

Occupation	Hypovitaminosis		Normal		Total
	Male	Female	Male	Female	
House hold	2	134	0	32	168
Workers	20	30	0	2	52
Officer	14	79	4	3	100
Students	10	14	6	5	35
Total	46	257	10	42	355

The chi-square statistic is 108.3743.
The *P*-Value < 0.00001.

Table.4 CRP level

CRP	Hypovitaminosis	Normal	Total
Positive	97	12	109
Negative	206	40	246
Total	303	52	355

The Chi-square statistic is 1.6658.
The *P* value 0.19682.

Table.5 Titration of CRP

CRP Concentration	Hypovitaminosis	Normal
96 mg/l	10	0
48 mg/l	65	10
24 mg/l	18	1
12 mg/l	4	1
Total	97	12

The chi-square statistic is 2.7035
The *P*-Value 0.439636

Figure.1 Study group in all three seasons

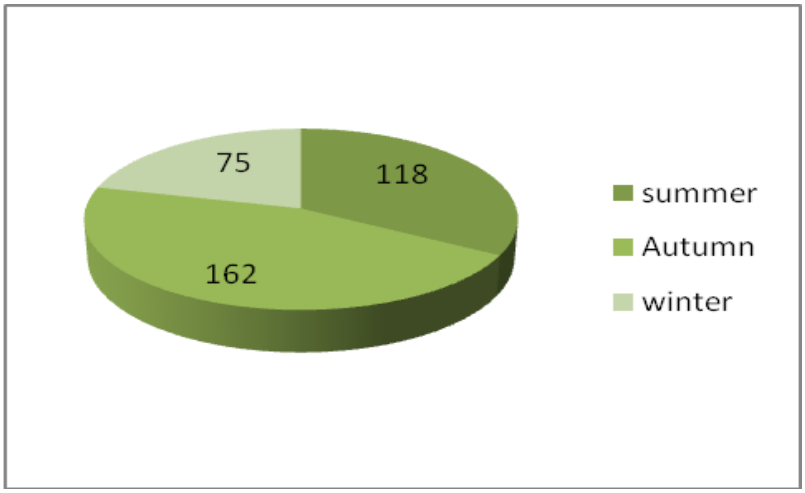
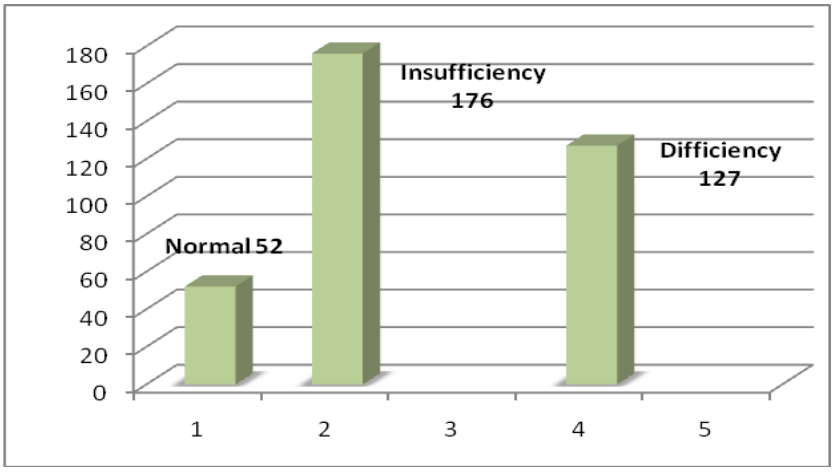


Figure.2 Hypovitaminosis among study group



In region of Middle Eastern countries whom are poor in food fortification in general and in vitamin D specifically, only wheat flour fortification is mandatory in terms of legislation, some countries such as Lebanon and Syria have no fortification of any type of wheat, while Qatar and the United Arab Emirate have voluntary fortification (Alshahrani, 2014; Anna, 2012).

There was a study done on Saudi Arabia's population, in which high prevalence of vitamin D deficiency at (28nmo/L- 33 nmol/L) in both summer and winter seasons recorded and even higher levels recorded in the winter season (Raed et al., 2012).

Skin pigmentation and dark skin may be one of the factors in this study; as most of the population in this region is brown to dark colored skin which contain more melanin, possibly decrease skin vitamin D production and reduce the production of cholecalciferol (Jessica, 2011).

Occupation also has its effect on hypovitaminosis from this study, and it was clear that most of the muscular pain were recorded from house hold female and less participant from male that complain of muscular skeletal pain.

All age group had been affected although by this condition specifically adult with age group 16-30 although this age was more active and they are outdoor, this result is compatible to study done by Narchi et al. (2015) which conclude that age has no any relation to hypovitaminosis D. Recent studies suggest that genetic factor contribute up to 50% of inter individual variability in serum vitamin D concentration (Darina Bassil et al., 2013).

CRP level were assessed in this study as one of the inflammatory markers and found to be non significant in association of hypovitaminosis, although positive results were recorded among hypovitaminosis but there were cases in which negative result were observed, the causes of this variation may be due to other inflammatory condition as a causes and found to be less dependable in relation to low vitamin D level, the same as observed in researches (Mouyis et al., 2008; Muhamed Amir and Riham Qayym, 2012; MiaMoberg et al., 2014).

In conclusion, High prevalence rate of hypovitaminosis were observed among chronic muscular skeletal pain in this country in spite of good sun light due to same cultural habit and life style.

Recommendation

Educational programs seem essential; not only for general population, but also for the more educated people regarding regular sun exposure and dietary intake of vitamin D.

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