Original Paper

Shinbone Pain and Fatigue Are the Commonest Musculoskeletal Presentation in Vitamin D Deficiency

Mahdi Abdul Sahib[1*], Ali Al Mousawi[2], Husam M. Abdulsahib[2]

[1]Al Imam Al Hussain Medical City, Kerbala Health Directorate, Holy Kerbala, Iraq
[2] Kerbala Medical College, University of Kerbala, Holy Kerbala, Iraq

Abstract

Background: In the past few decades, great attention has been paid to vitamin D deficiency and has been reported to be associated with a growing list of conditions. Nonspecific musculoskeletal manifestations are a common problem in vitamin D deficiency.
The aim of this case series study was to explore the different nonspecific musculoskeletal presentations of this deficiency among adult people.
Patients and methods: A descriptive study was designed to determine the prevalence of nonspecific musculoskeletal symptoms with vitamin D deficiency among adult patients visiting a private clinic in holy Kerbala/ Iraq during two years period.
Result and discussion: Shinbone pain and fatigue were the most prevalent symptoms and showed positive association with vitamin D level. Other symptoms included low backache, proximal muscle ache and knee osteoarthritis. The association of these symptoms with demographic and anthropometric measures were explained. Vitamin D deficiency is a prevalent condition and need to be investigated even in countries with apparently high sun light exposure.
Keywords: Shinbone pain, Fatigue, Musculoskeletal Presentation, Vitamin D Deficiency.

Introduction

Vitamin D deficiency (VDD) is a common global health problem. There is a large bulk of literatures covering the association between Vitamin Deficiency (VD) and nonspecific musculoskeletal (MSK) disorders , in addition to its potential role in the prevention of several non-MSK conditions [1-17]. However, the prevalence of VDD is greatly variable and depends on age, gender, obesity, physical activity, skin color, exposure to sun light, geography in addition to the pattern of diet intake [15-17] .It is common among all age groups, but more prevalent among elderly people [16, 17].
Vitamin D is produced mainly (80-90%) in the skin under the effect of sunlight exposure and to a lesser degree, from dietary sources [11, 12]. Therefore, exposure to sun light play a profound role in preventing VDD. However, many studies showed that VDD is also common in sunny Middle East and Gulf countries, especially in women and mainly during menopausal ages [11, 16-22]. Limited sun exposure - in the Middle East women - is attributed to wearing traditional an "abayah" (a full black veil that covers the whole body except the face) and limited outdoor activity for social reasons [6, 16-20, 22].

Vitamin D deficiency presentation varies in accordance with its roles and impact played in human being body. Many studies concluded that, VDD increases sensitivity to pain and even a slight decline in this vitamin intensifies pain, whereas modification of this vitamin through supplementation relieves pain [8, 18, 20].
The type of pain in patients with VDD ranged between diffused nonspecific to a localized bone pain. Common manifestations of VDD are proximal muscle weakness and aches, low back pain and throbbing bone pain elicited with pressure over the sternum or tibia (shinbone) [8, 13, 14, 18, 23-30]. Leg pain in adults, is usually attributed to osteoarthritis of the knee and hip joints,

*for correspondence email: mahdiabdalsahib@yahoo.com

or because of the radiating pain of lumbar spine conditions and other causes.

In holy Kerbala/Iraq, population-based studies in healthy female subjects by Darwish (2016) and Al.Araji. and his colleagues [(2017)], showed that VDD is prevalent (71.25%) and (86%) respectively [(19)] [(31)]. Similar conclusion was drawn by a study in a nearby city (Hilla) (2019), VDD prevalence (76%) among healthy women in the reproductive age [(32)].

The objective of this descriptive study was to determine the prevalence of nonspecific symptoms, especially shinbone pain among patients with deficient VD in holy Kerbala/ Iraq. Holy Kerbala is a sunny city located in the central part of Iraq 100 Km to the south of the capital Baghdad.

Patients and Methods

This study represents a case series descriptive study performed in a private clinic in holy Kerbala/ Iraq between 1st January 2017 to 31st December 2018. It included all patients visiting the private clinic with VD level below 30 ng/ml. Two hundred forty-seven patients were included, and all presenting symptoms and signs were registered through interviews and physical examination. Demographic information including age, gender and residency were obtained in addition to anthropometric measures (weight and height), were collected.

The chief complaint of nonspecific MSK pain among the patients were one or more of the fallowing complaints: low backache, proximal muscle ache, fatigue, shinbone pain and knee osteoarthritis for ≥ 6 weeks were studied.

Patients with secondary causes of MSK pain; such as trauma, hepatic or renal disease, malignancy as indicated through appropriate clinical, radiological and laboratory examinations, were excluded from the study.

Low back pain due to strain or intervertebral disc displacement were excluded. Osteoarthritis in knee or spine was confirmed through medical history clinical examination, in addition to radiography, if necessary. Physiologic fatigue characterized by diminished capacity to perform daily functions, and usually accompanied by a feeling of tiredness. The shinbone pain and tenderness was elicited with moderate force exerted by pressing the thumb on the anterior surface of tibia [(9)].

Proximal muscle ache presents as symmetrical weakness of muscles closest to the body's midline in upper and/or lower limbs. Vitamin D level was assessed by measuring 25-hydroxyvitamin D [25(OH) D] concentrations, using Cobase 411 analyzer (Roche) Hitachi high-Technologies corporation (Tokyo-Japan) 14/11/2016. Serial No Sn 6396-07 REF. 04775279001 GTIN. 0401563093703. According to Current International Osteoporosis Foundation Guidelines and the Institute of Medicine (IOM), 25(OH)D ranged between 30-60 ng/ml is considered as normal level, whereas 20-30 ng/ml is insufficient, 10-20 ng/ ml is deficient and lower than 10 ng/ml is regarded as severe deficient [(33, 34)]. Serum Calcium level was estimated by using Bs-240 Pro (Minidray / China).

Anthropometric measurements: Weight was measured by accurate calibrated balance weighting scale that recommended by the World Health Organization (WHO), without shoes. Height was measured without shoes using tape measure from upper most point on the head. The reliable indicator of obesity is using Body Mass Index (BMI) (Quetelet's index) that is defined as the individual's body weight divided by the square of height [(35)].

According to BMI, people might be underweight when BMI is <18.5; normal healthy when 18.5 - < 24.9, over weight when ≤25d and obese when it exceeds 30. Additionally, obesity might be mild or class I (BMI=30 - < 35), moderate or class II (BMI=35 - 40) and sever or class III (BMI> 40**).**

All the patients received a weekly dose of 50000 IU of cholecalciferol orally for 6-8 weeks and reexamined afterward to deter-

mine clinical and biochemical response assessment. A data matrix was produced from the answered questionnaires using the Statistical Package for Social Sciences version 21 (SPSS-21). The statistical analysis includes using descriptive statistics, chi-squared test for comparing categories, t-test and ANOVA test for comparing means and correlation analysis for continuous quantitative variables. The p-value < 0.05 was considered as statistically significant.

Results

Two hundred forty-seven patients were included in the study, and the main demographic and other characteristics are shown in table 1. Females formed the majority of patients (84.9%), and male to female ratio was 1: 5.64 and two thirds of them were above 40 year in age. Three quarters of the participants (73.7%) reported partial or no sunlight exposure, while a great majority (82.2%) reported no or occasional milk consumption (table 1). The mean age of the participants was 45.67±15.91 year (range 12-80 years), however, the age distribution was almost normal (table 1, figure 1).

The mean blood 25(OH) D3 level was 15.09 ±.19 ng/ml. (range 4.20 -29.30 ng/ml, figure 2), while the mean serum Calcium level was 8.92±1.133mg. (Range 0.93-13.60mg.). The mean weight was 75.51±16.22 Kg., while the mean height was 147.42±11.02 cm. making the mean Body Mass Index (BMI) 34.82±8.05, which indicate right shifted BMI index of the sample. The mean VD level in male patients was highly significantly more than females 16.54±5.06ng/ml vs. 12.72±5.73ng/ml, <.001). Similarly, a highly significant gender difference was found in the distribution of VDD categories (p=.002). The proportion of sever VDD was 8.1% among male patients compared to 36.7% among females. More than one half of the sample had deficient VD, level while one third had sever VDD (figure 3).

The majority of the participants were from urban residency (table 1, figure 4); however, there was no significant difference in VD mean level between these two categories (p=0.962). For residency, the proportion of sever VDD was 34.5% among urban resident patients compared to 24.5% among rural resident patients, but here again the difference was not significant (p=.356). The serum level of VD showed a rising trend as the frequency of milk consumption was reported to be higher (17.3 ng/ml for those who take milk daily vs. 13.5 ng/ml for those who consume milk occasionally), however the difference was not significant.

Only a small minority of the patients had normal BMI (9.3%), while the remaining majority (91.7%) were overweight or obese. One fifth were in class I, while one quarter was in each of class II and III (figure 4).

The clinical presentation of this group of patients with VDD showed that the most common symptom was shinbone pain (59.5%), followed by fatigue (43.3%) and then backache (40.5%, table 2).

Patients with shinbone pain were found to have a significantly lower mean VD level than those with no shinbone pain (p=.032). Similarly, when the mean VD level was compared among those who have fatigue and those who do not, the difference was significant (p=.023). For the other symptoms, the difference was also significant for muscle ache and knee osteoarthritis (p=.031 and .012, respectively). However, for backache the difference was not significant (p=.901).

When ANOVA test was used to compare mean VD level among the different groups according to their exposure to sun light, the difference was highly significant (p=.006) towards higher sunlight exposure, while for age groups and BMI groups, the differences were not significant (p=.240 and .143, respectively).

Table 1. The distribution of demographic and other characteristics among patients with vitamin deficiency in a private clinic in holy Kerbala / Iraq in 2018 (n=247)

Variable	Group	Frequency	Percentage
Gender	Male	37	15.0
	Female	210	85.0
Age group	Children (less than 15 year)	5	2.0
	Teenager (15 -19 year)	8	3.2
	Young adult (20 - 25 year)	11	4.5
	adult (25 - 40 year)	68	27.5
	Middle age (40 - 60 year)	109	44.1
	Old age (more than 60 year)	46	18.6
Residence	Urban	194	78.5
	Rural	53	21.5
Milk consumption	Daily	35	14.2
	Weekly	29	11.7
	Occasionally	65	26.3
	Null	138	55.9
Sun light exposure	Daily	65	26.3
	partially	138	55.9
	Null	44	17.8
BMI Classification	Normal healthy weight	23	9.3
	Over weight	48	19.4
	Obese	176	71.3
Total	247		100

Figure 1. The age distribution of patients with vitamin deficiency in a private clinic in holy Kerbala / Iraq in 2018 (n=247)

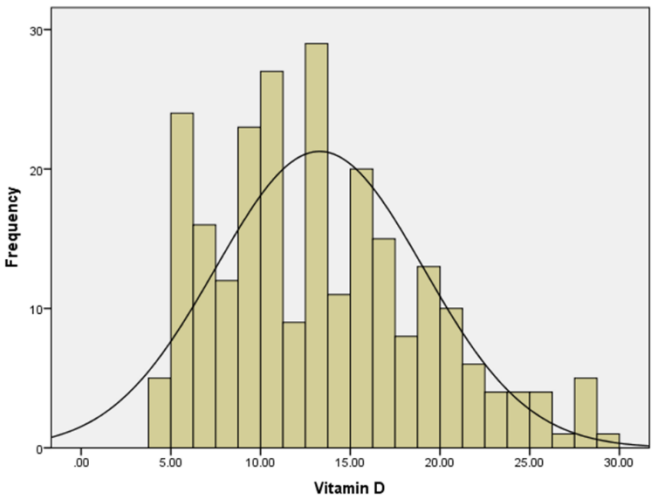

Figure 2. The distribution of serum vitamin level among patients in a private clinic in holy Kerbala / Iraq in 2018 (n=247)

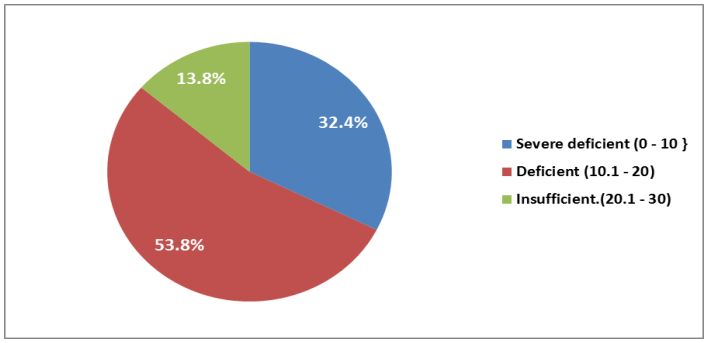

Figure 3. The distribution of serum VD level categories among patients in a private clinic in holy Kerbala/Iraq in 2018 (n=247)

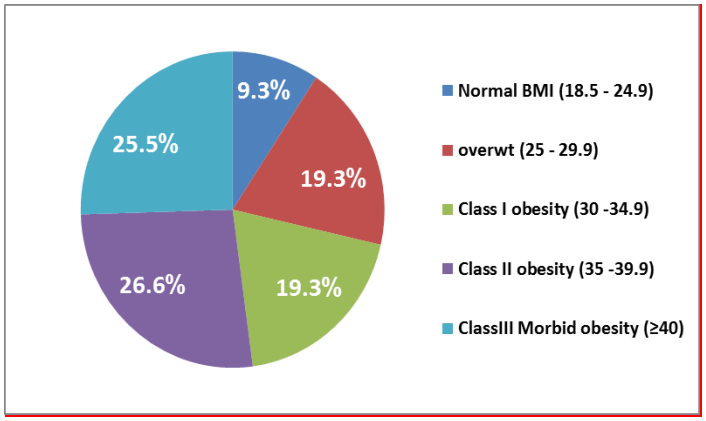

Figure 4. The Body Mass Index (BMI) distribution of patients with vitamin deficiency in a private clinic in holy Kerbala / Iraq in 2018 (n=247)

Table 2. The distribution of symptoms among patients with VD deficiency in a private clinic in holy Kerbala / Iraq in 2018 (n=247)

Variable	Group	Frequency	Percentage
Backache	Positive	100	40.5
	Negative	147	59.5
Muscle ache	Positive	77	31.2
	Negative	170	68.8
Fatigue	Positive	107	43.3
	Negative	140	56.7
Shin bone pain	Positive	147	59.5
	Negative	100	40.5
Osteoarthritis	Positive	96	38.9
	Negative	151	61.1
Total		247	100

Correlation analysis between the symptoms with VD level showed very low or low correlation coefficients (r = 0.05-0.16), and this might be related to the small size sample.

Of 151 patients with shinbone pain, only 42 patients could be followed up until VD level was brought within normal range after 3-6 months, where only thirteen patients were still complaining of local tibial (shinbone) pain in varying degrees. This means that cure rate was 69%. For those [13] patients who did not responded to VD supple-

mentation, further biochemical investigations have been done to exclude the possibility of osteomalacia. Two of them showed clinical and biochemical abnormalities compatible with osteomalacia, while the majority (11 patients) continue to complain in spite VD supplementation.

Discussion

Traditional risk factors for low VD include advancing age, female gender, obesity and low sun light exposure [15-17]. Two hundred forty-seven patients with a wide range of age (12 - 82 years), a mean of 45.67 years were encountered in this group of patients with VDD (figure 1). This finding is consistent with a previous study in holy Kerbala by Al-Faissaly (2016) [36] and with most other published studies in other places [16-18, 20, 22]. The skin of older age, is usually associated with a decreased ability to produce active VD [26].

Females were found to have a significantly lower mean VD and higher proportion of VDD, and this is similar to the results of earlier studies in holy Kerbala [19, 31, 36, 37], Sulaimani/Iraq [24] and other studies in Middle East and Gulf region [16, 20, 22, 38, 39]. In these countries, VDD was attributed to the lack of sunlight exposure; due to the fact that women tend to spend more time indoors and to their style of clothing [38, 39], and the findings in the present study indicated that sunlight exposure was a highly significant predictor.

In the present study, occasionally or no milk consumption formed 82.2%, and there was a positive rising mean VD level as the frequency of milk consumption was increased. Al.Araji and his colleague study in holy Kerbala (2017) found a significant association between VD level and amount of milk taking [31] The Canadian Health Measures Survey (2013) reported that people who consumed milk once or more per day had a higher average VD level than those who consumed milk less than once per day [40, 41]. Additionally, lack of food items fortified with VD in the market of Middle Eastern countries may add to the problem [39].

In Iraq, more than two thirds of population are overweight [42, 43]. In this study, overweight patients formed 90.7 % of the sample. Obesity is considered as a risk factor in VDD, due to excess fat-soluble VD deposition in body fat tissue [7, 22, 44, 45], or other unexplained mechanism [34]. In addition, obesity may decrease movement and then outdoor activities and sun exposure is restricted [17]. On the contrary, low VD level may increase adiposity through increased lipogenesis as a result of elevated parathyroid hormone concentrations [46].

The majority of the participants in the present study were from urban residency, but on comparing mean VD level and VDD prevalence, there was no significant difference between urban and rural categories (p=0.962). It is true that most of rural women in holy Kerbala work in agricultural fields, but their bodies are fully dressed by "abayah" during their outdoor activities.

Sun exposure is considered as a major contributor to VD status as was indicated by the present study. Al.Araji. and his colleagues, found a significant association between VD level and the duration of sun exposure [31].

A large number of studies have suggested that there is an association between VDD and variety of non-specific MSK manifestations. The common conditions are muscle weakness, fatigue, osteoporosis, low back pain, arthralgia, rib and leg pain [8, 13, 18, 20, 22, 23, 25, 27, 47]. Pain due to VDD is well defined and felt in the bones, not in the joints due metabolic changes [23].

In this study, the MSK presentation of VDD showed that the most common symptom was shinbone pain, followed by unexplained fatigue and then backache (table 1). When the mean VD level was compared among those who have shinbone pain and those who do not, the difference was significant (p=.032). However, the mean VD level was only lower in those who complained from shinbone pain, while for all other symptoms it was higher among those who did not have the symptom (Table 1). This result indicate an association between

VDD with non-specific shinbone pain and tenderness. This result consistent with findings of other previously published studies in Iran (2011, 2018) [10, 13]. Similarly, when the mean VD level was compared among those who have unexplained fatigue and those who do not; the difference was significant (p=.023). This finding consistent with conclusion of Al-Faissaly's study (2016), but, it is inconsistent with the study of Shaheed Beheshti Hospital, Babol, Iran, (2011) in which arthralgia was the second common complaint [10].

However, for backache the difference was not significant (p=.901). For the other symptoms, significant association was found with muscle ache and knee osteoarthritis (p=.031 and .012, respectively).

Many studies confirmed that VD supplementation could relieve the pain in the patient with VDD [22, 25, 29, 30, 47-49]. However, some other studies have found no association of VDD with MSK pain and no effect of VD supplementation on pain [28,50-53]. Contradictory results of different studies may be related to patient selection and definition of pain and its regions. However, the possibility of VDD can aggravate or accelerate MSK pain in genetically predisposed people cannot be ruled out [18].

Unfortunately, of (151) patients with shinbone pain only [42] one followed up until VD level raised within normal range through 3-6 months. Of those patients, only [13] they still complained of local shinbone pain in varying degrees, i.e. 69% the pain is resolved or much better. This result consistent with other studies which reported that many patients with VDD and leg pain responded to VD supplementation (2010, 2014) [53, 54].

There are few limitations in this study, such as 42 patients with shinbone pain which returned back for follow up and these formed only (27.8%) of all patients with shinbone pain. The second limitation is lack of control group. Another limitation is lack serum alkaline phosphatase estimation, which is consider as the best test for suspected cases of subclinical osteomalacia in spite of a high false positive rate. However, a definitive diagnosis of osteomalacia requires bone biopsy [55].

Conclusion

In conclusion, the results of this case series descriptive study showed that there is a positive association between VDD and nonspecific MSK complaints, including bone pain, muscle weakness, backache, fatigue, and osteoarthritis and this result consistent with large bulk of studies indicative of these findings. Shinbone pain and fatigue were the most prevalent symptoms particularly in women. These results need to be confirmed by further studies. This outcome emphasizes the need of education among the general population that, nonspecific shinbone pain alone and or other nonspecific MSK symptoms might indicate to check of vitamin D status.

Acknowledgements

We would like to express our appreciation and gratitude's to Humam M. Abdulsahib (College of Engineering /University of Kerbala/ holy Kerbala/ Iraq) for his efforts in using data entry in SPSS to achieve this study. As well as we would like to thank all people who participate in this study.

References

1. Isaacs J. Oxford textbook of rheumatology: Oxford University Press; 2013.(Google Schoolar).
2. Bikle DD. Vitamin D insufficiency/deficiency in gastrointestinal disorders. Journal of Bone and Mineral Research. 2007;22(V50-V54). (Google Schoolar).
3. Mishal AA. Effects of different dress styles on vitamin D levels in healthy young Jordanian women. Osteoporosis International. 2001;12:931-5. (Google Schoolar).
4. Meddeb N, Sahli H, Chahed M, Abdelmoula J, Feki M, Salah H, et al. Vitamin D deficiency in Tunisia. Osteoporosis International. 2005;16:180-3. (Google Schoolar).

5. Woo J, Lam CW, Leung J, Lau WY, Lau E, Ling X, et al. Very high rates of vitamin D insufficiency in women of child-bearing age living in Beijing and Hong Kong. British Journal of Nutrition. 2008;99:1330-4. (Google Schoolar) (PubMed)
6. Mallah EM, Hamad MF, ElManaseer MA, Qinna NA, Idkaidek NM, Arafat TA, et al. Plasma concentrations of 25-hydroxyvitamin D among Jordanians: Effect of biological and habitual factors on vitamin D status. BMC clinical pathology. 2011;11:8. (Google Schoolar)
7. Van Dam RM, Snijder MB, Dekker JM, Stehouwer CD, Bouter LM, Heine RJ, et al. Potentially modifiable determinants of vitamin D status in an older population in the Netherlands: the Hoorn Study–. The American journal of clinical nutrition. 2007;85:755-61. (Google Schoolar)
8. Heidari B, Javadian Y, Heidari P, Hakimi N, Tilaki KH, Firouzjahi AR. Vitamin D Deficiency is Associated with Nonspecific Low Back Pain in Young Women, a Case-Control Study. 2014. (Google Schoolar)
9. Heidari B, Shirvani JS, Firouzjahi A, Heidari P, Hajian-Tilaki KO. Association between nonspecific skeletal pain and vitamin D deficiency. Int J Rheum Dis. 2010;13:340-6. (Google Schoolar)
10. Heidari B, Heidari P, Hajian-Tilaki K. Association between serum vitamin D deficiency and knee osteoarthritis. International orthopaedics. 2011;35:1627-31. (Google Schoolar)
11. Alshishtawy MM. <Vitamin D Dificiency This clandestine endemic disease is veiled no more.pdf>. Sultan Qaboos Univ Med J 2012 May; 12: 2012;12:140–52. (Google Schoolar) (PubMed)
12. Sahota O. Understanding vitamin D deficiency. Age and ageing. 2014;43:589-91. (Google Schoolar) (PubMed)
13. Babaei M, Esmaeili Jadidi M, Heidari B, Gholinia H. Vitamin D deficiency is associated with tibial bone pain and tenderness. A possible contributive role. International journal of rheumatic diseases. 2018. (Google Schoolar) (PubMed)
14. Heidari B, Heidari P, Samari E, Ramzannia Jalali M. Frequency of vitamin D deficiency in common musculo skeletal conditions. Journal of Babol University of Medical Sciences. 2014;16:7-15. (Google Schoolar)
15. Heidari B, Mirghassemi MBH. Seasonal variations in serum vitamin D according to age and sex. Caspian journal of internal medicine. 2012;3:535. (Google Schoolar)
16. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, et al. Global vitamin D status and determinants of hypovitaminosis D. Osteoporos Int. 2009;20:1807-20. (Google Schoolar) (PubMed)
17. Alshahrani AA. <Vitamin D Deficiency and Possible Risk Factors Among Middle Easte.pdf>. 2014. (Google Schoolar)
18. Al-Jarallah K, Shehab D, Abraham M, Mojiminiyi OA, Abdella NA. Musculoskeletal pain: Should physicians test for vitamin D level? International journal of rheumatic diseases. 2013;16:193-7. (Google Schoolar)
19. Darwish LAAI. Vitamin D status in healthy female individuals Al-Kufa University Journal for Biology 2018;10:11-9.
20. Michael F. Holick MD, Ph.D. <Vitamin-D-deficiency.pdf>. 2009. (Google Schoolar)
21. Elamin I.E.; Rashid F. BAMKFA, Al Suwidi H.; . Vitamin D Deficiency, the Volum of the Problem in the Unted Arab Emirates. A Cohort from the Middle East. J Endocrinol Diab;. 2016;3:1-5. (Google Schoolar)
22. Arabi A, El Rassi R, El-Hajj Fuleihan G. Hypovitaminosis D in developing countries-prevalence, risk factors and outcomes. Nat Rev Endocrinol. 2010;6:550-61. (Google Schoolar)
23. de La Jara GdT, Pecoud A, Favrat B. Female asylum seekers with musculoskeletal pain: the importance of diagnosis and treatment of hypovitaminosis D. BMC family practice. 2006;7:4. (Google Schoolar)
24. Anoar KA, Amin BAM. Hypo Vitaminosis D in Chronic Muscular Skeletal Pain. Int J Curr Microbiol App Sci. 2015;4:696-703.
25. Abbasi M, Hashemipour S, Hajmanuchehri F, Kazemifar AM. Is vitamin D deficiency associated with non specific musculoskeletal pain? Global journal of health science. 2013;5:107. (Google Schoolar)
26. McCarty DE, Reddy A, Keigley Q, Kim PY, Cohen S, Marino AA. Nonspecific pain is a marker for hypovitaminosis D in patients undergoing evaluation for sleep disorders: a pilot study. Nature and science of sleep. 2013;5:37. (Google Schoolar)
27. Heidari B, Heidari P, HajianTilaki K. Relationship between unexplained arthralgia and vitamin D deficiency: a case control study. Acta Medica Iranica. 2014;52:400. (Google Schoolar)
28. Straube S, Derry S, Straube C, Moore RA. Vitamin D for the treatment of chronic painful conditions in adults. The Cochrane Library. 2015. (Google Schoolar)
29. Le Goaziou MF, Kellou N, Flori M, Perdrix C, Dupraz C, Bodier E, et al. Vitamin D supplementation for diffuse musculoskeletal pain: Results of a before-and-after study. The European journal of general practice. 2014;20:3-9. (Google Schoolar)

30. Schreuder F, Bernsen RM, van der Wouden JC. Vitamin D supplementation for nonspecific musculoskeletal pain in non-Western immigrants: a randomized controlled trial. The Annals of Family Medicine. 2012;10:547-55. (Google Schoolar)
31. Al.Araji. Khalid H. AhAAE, ALjanaby. Saba A.R , ALtemmemi. Gazwa S. , ALkhrasni. Rana K. , ALtemmemi. Baidaa I. , ALhadidy Nidal R. , ALkhafaf. Dhamiaa J. , ALhussiny. Shimaa H. , ALganimy. Hawra K. . Prevalence of vitamin D deficiency of females in Karbala, Iraq (Un published study). 2017.
32. Hayder A. Hantoosh MHMBWIAAY. Prevalence of Vitamin D Deficiency in Iraqi Female at Reproductive Age. Medical Journal of Babylon 22-16:119;2019 .مجلة بابل الطبية.
33. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism. 2011;96:1911-30. (Google Schoolar)
34. Beata M-M, Monika L-L, Ewa W. Clinical implications of vitamin D deficiency. Przegląd Menopauzalny. 2015;14:75-81 (Google Schoolar).
35. Deurenberg P, Yap M, Van Staveren WA. Body mass index and percent body fat: a meta analysis among different ethnic groups. International journal of obesity. 1998;22:1164 -71. (Google Schoolar)
36. Al-Faissaly ADM. Vitamin D Deficiency among Iraqi Females Fifth anuual conference of Imam Hussein Medical City Kerbala/ Iraq2017.
37. Karem KK, Al Mousawi AM, Salih SI. Physiological analysis of vitamin D deficiency in food and its impact on osteoporosis and heredity. EurAsian Journal of BioSciences. 2018;12:425-30. (Google Schoolar)
38. Golbahar J, Al-Saffar N, Diab DA, Al-Othman S, Darwish A, Al-Kafaji G. Predictors of vitamin D deficiency and insufficiency in adult Bahrainis: a cross-sectional study. Public health nutrition. 2014;17:732-8. (Google Schoolar)
39. Fields J, Trivedi NJ, Horton E, Mechanick JI. Vitamin D in the Persian Gulf: integrative physiology and socioeconomic factors. Current osteoporosis reports. 2011;9:243. (Google Schoolar)
40. Survey TCHM. Vitamin D status of Canadians -Results from the Canadian Health Measures Survey. 2013.
41. Janz T, Pearson C. Vitamin D blood levels of Canadians: Statistics Canada Ottawa (Canada); 2013. (Google Schoolar)
42. Jasim HM, Hussein HMA, Al-Kaseer EA. Obesity among females in Al-Sader city Baghdad, Iraq, 2017. Journal of the Faculty of Medicine Baghdad. 2018;60:105-7. (Google Schoolar)
43. Mohammed S. Association between Vitamin D and Body Weight in Iraqi Population: Case-Control Study. J Obes Weight Loss Ther. 2018;8:2. (Google Schoolar)
44. Turer CB, Lin H, Flores G. Prevalence of vitamin D deficiency among overweight and obese US children. Pediatrics. 2013;131:e152-61. (Google Schoolar) (PubMed)
45. Sadaf Alipour AS, Akram Seifollahi, Nooshin Shirzad, Ladan Hosseini,. Risk Factors and Prevalence of Vitamin D Deficiency Among Iranian Women Attending Two University Hospitals, . Iran Red Crescent Med J 2014;16(10):15461. (Google Schoolar)
46. Snijder MB, van Dam RM, Visser M, Deeg DJ, Dekker JM, Bouter LM, et al. Adiposity in relation to vitamin D status and parathyroid hormone levels: a population-based study in older men and women. The Journal of Clinical Endocrinology & Metabolism. 2005;90:4119-23. (Google Schoolar)
47. Elspeth E. Shipton EAS. <Vitamin D Deficiency and Pain.pdf>. Pain and Therapy. 2015;4:67-87. (Google Schoolar) (PubMed)
48. Bischoff-Ferrari HA, Willett WC, Wong JB, Giovannucci E, Dietrich T, Dawson-Hughes B. Fracture prevention with vitamin D supplementation: a meta-analysis of randomized controlled trials. Jama. 2005;293:2257-64. (Google Schoolar) (PubMed)
49. Al Faraj S, Al Mutairi K. Vitamin D deficiency and chronic low back pain in Saudi Arabia. Spine. 2003;28:177-9. (Google Schoolar) (PubMed)
50. Warner AE, Arnspiger SA. Diffuse musculoskeletal pain is not associated with low vitamin D levels or improved by treatment with vitamin D. J Clin Rheumatol. 2008;14:12-6. (Google Schoolar) (PubMed)
51. Thorneby A, Nordeman LM, Johanson EH. No association between level of vitamin D and chronic low back pain in Swedish primary care: a cross-sectional case-control study. Scand J Prim Health Care. 2016;34:196-204. (Google Schoolar)
52. M. Gaikwad SV, M. Mittinity, G. L. Moseley, N. Stocks. <Does vitamin D supplementation alleviate chronic nonspecific musculoskeletal pain.pdf>. Clinical Rheumatology. 2017;36:1201-8. (Google Schoolar)
53. Whitehurst JL, Reid CM. Vitamin D deficiency as a cause of chronic pain in the palliative medicine clinic: two case reports. Palliat Med. 2014;28:87-9. (Google Schoolar)
54. Kessenich C. <Vitamin D deficiency and leg pain in the elderly.pdf>. The Nurse Practitioner. 2010 35:12-3. (Google Schoolar) (PubMed)

55. Peach H, Compston JE, Vedi S, Horton LW. Value of plasma calcium, phosphate, and alkaline phosphatase measurements in the diagnosis of histological osteomalacia. Journal of clinical pathology. 1982;35:625-30. (Google Schoolar)