



**Republic of Iraq**

**Ministry of higher education and scientific research**

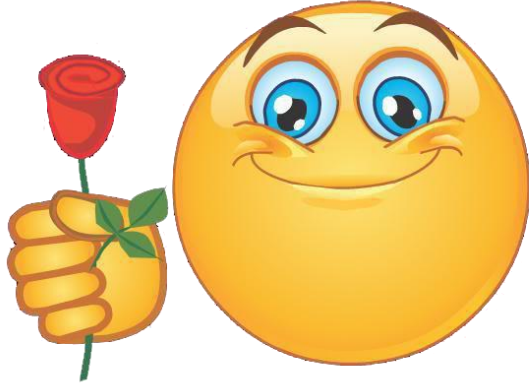
**University of Diyala**

**College of medicine**

# **Vitamin deficiency and migraine**

**Done by :**

**Supervised by : Dr. Wisam Falih**



شكر وتقدير...

اقدم شكري وامتناني بعد الله الى  
عمادة جامعة ديالى ...  
والى السيد العميد المحترم .....  
والى الدكتور وسام فالح المحترم

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا ۗ إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ )

اية ٣٢ سورة البقرة

## الاهداء

لن تكفي جُمل الشُّكر، وحتى لو بلغت ملء الأرض والسماء، أن تُعبِّر عن فضل  
أمي.

رُفقاء الدَّرب، والأهل، والخلَّان.

أهديكم جميعًا بحثي المتواضع

## Abstract

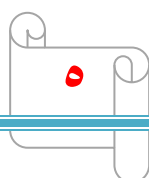
**Background:** Serum vit. D levels have been correlated with migraine. Seasonal variation of serum vit. D levels depicting higher levels in summer and lower levels in autumn-winter were matched with that of migraine attacks. A lower level of serum vit. D was correlated with migraine. Despite a probable correlation between migraine and serum vit. D, clinical associated with vitamin D deficiency were not clearly identified in migraine patients. Thus, in this study, we evaluate relationship between serum vit. D levels with migraine.

**Materials and Methods:** The study was a cross-sectional. Seventy-six patients aged 10-61 years were included. The several linear regression was used to see correlation between serum 25-OH-D3 and migraine. Adjustments were performed for age, sex, waist circumference (wc), body mass index (BMI), number of chronic diseases, and education level.

**Results:** The positive weak relationship was seen serum vit. D and headache diary result ( $P = 0.042$ ,  $r = 0.19$ ). But, no significant correlation was observed between serum vitamin D and migraine severity ( $P = 0.741$ ).

**Conclusion:** High levels of serum 25-OH-D3 was related to higher headache diary result (HDR). After adjustment for confounding variables, this significant correlation remained. No significant relationship was shown between serum vitamin D and migraine severity.

Key words: Migraine, relationship, vitamin D

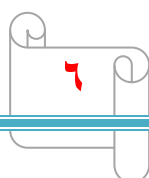


## Introduction

Headache is common during childhood and adolescence.[1] Migraine and tension-type of headache are most typesommon primary headache disorders, that influence about 80% of people worldwide.[2] Migraine is a neurological disease[3] that is debilitating, progressive and chronic.[4] Mechanism of migraine pain in the brain is due to release of pain enhancing inflammatory materials around the nerves and blood vessels in the head.[5]

Main characteristic of the migraine attacks is headache[6] that may take many hours to 2-3 days[5] and is often severe,[6] pulsating, and unilateral. [5]Other related symptoms include nausea, sometimes vomiting, photophobia and sonophobia ,[5] neck pain, and muscle tension.[7] Migraine is related to almost 2-fold more risk of ischemic attacks.[8] In addition, migraine in adults are associated with seasonal allergies, asthma, epilepsy, nightmares, atopic disease, stroke, cardiovascular disorders, sleep disorder, motion sickness, nose bleeding and among women of reproductive age are related to preeclampsia and uterine bleeding. [1]

The most common causes of migraine is hunger or not eating enough, which is important particularly in young people.[6] Migraine is the nineteenth cause of disability in the world[9] and involves in 10-20% of the population during their life.[10] Recent data indicate that one in every 4 American adults, suffer from frequent or severe headache including migraine.[1]



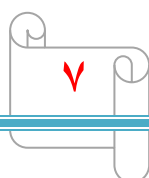
Pharmacologic agents used for the treatment of migraine can be classified as abortive (ie, for alleviating the acute phase) or prophylactic (ie, preventive).

Acute/abortive medications aims to reverse, or at least stop the progression of, a headache. It is most effective when given within 15 minutes of pain onset and when pain is mild. [14] Abortive medications include the following: triptans , Serotonin 5-HT<sub>1F</sub> agonists (ditans) (eg, lasmiditan), Calcitonin gene-related peptide (CGRP) receptor antagonists (ie, rimegepant, ubrogepant) , Ergot alkaloids (eg, ergotamine, dihydroergotamine [DHE]) , NSAIDs , and antiemetics

The following may be considered indications for prophylactic migraine therapy:

- Frequency of migraine attacks is greater than two per month
- Duration of individual attacks is longer than twenty four hours
- The headaches cause major disruptions in the patient's lifestyle, with significant disability that lasts three or more days
- Abortive therapy fails or is overused
- Symptomatic medications are contraindicated or ineffective
- Use of abortive medications more than twice a week

Prophylactic medications include the following: Antiepileptic drugs , Beta blockers , Tricyclic antidepressants , Calcium channel blockers , SSRIs , NSAIDs , Serotonin antagonists , Botulinum toxin , CGRP inhibitors

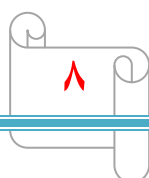


Other measures :

- Lowering of migraine triggers (eg, lack of sleep, fatigue, stress, certain foods)
- Nonpharmacologic therapy (eg, biofeedback, cognitive-behavioral therapy)
- Integrative medicine (eg, butterbur, riboflavin, magnesium, feverfew, coenzyme Q10)

Women are 3 times more likely to get migraine disease in comparison with men.[6] In last years, vitamin D deficiency has been known as a worldwide public health problem.[11] A total of 30-80% children and adults have vitamin D deficiency globally .[20] The prevalence of vitamin D deficiency is greater in winter and autumn than in summer and spring.[12]

Vitamin D deficiency is associated with various types of disorders such as musculoskeletal problems (rickets, osteomalacia, osteoporosis, myopathy), cancer (at least seventeen cancers such as cancers of the breast, prostate, colon, ovary, pancreas, etc.), autoimmune disease ( DM, MS , osteoarthritis, rheumatoid arthritis, Crohn's disease, etc.), cardiovascular disorders (hypertension, congestive heart failure, MI ), kidney disorders, mental disorders (depression, schizophrenia), skin disorders (psoriasis), etc.[13]





## LITERATURE REVIEW

### **1-Vitamin D Deficiency and Its Correlates in Migraine Patients(14)**

Jong-Geun Seo and Sung-Pa Park

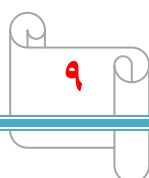
We conducted a prospective, cross-sectional study. We invited new patients with migraine who visited our headache clinic. The Institutional Review Board of Kyungpook National University Hospital approved the study (approval number KNUH 2016-03-009). All participants gave written informed consent. We collected their clinical characteristics and conducted the Migraine Disability Assessment Scale, the Patient Health Questionnaire-9, the Generalized Anxiety Disorder-7, the Insomnia Severity Index, and the Fatigue Severity Scale. All eligible patients measured serum vitamin D levels by radioimmunoassay. Vitamin D deficiency is defined as a serum 25 (OH) D of less than 20 ng/ml.

Although we cannot conclude vitamin D deficiency is specific for migraine patients due to the lack of data for healthy controls, we presume migraine chronicity may accentuate vitamin D deficiency. As vitamin D supplementation is effective for decreasing frequency of migraine attacks in EM, further studies should be warranted to prove the therapeutic efficacy of vitamin D supplementation on CM. In addition, the relationship between serum vitamin D levels and therapeutic response should be also identified .

### **2- Vitamin D Status in Migraine Patients: A Case-Control Study (15)**

Alireza Zandifar, Samaneh sadat Masjedi, Mahboobeh Banihashemi, Fatemeh Asgari, Navid Manouchehri, Homa Ebrahimi, Faraidoon Haghdoost,<sup>2</sup> and Mohammad Saadatnia

**Background.** There have been few studies on the relation between vitamin D and migraine. We investigated the prevalence of vitamin D deficiency in migraine patients and compared it with a control group. We also evaluated the relationship of vitamin D deficiency with severity of migraine. **Methods.** 105 newly diagnosed migraine patients and 110 controls, matched for age, sex, socioeconomic status, education, and sun exposure, were enrolled during the spring of 2011. 25-Hydroxy vitamin D [25(OH)D] plasma levels were measured by chemiluminescence immunoassay. **Results.** The mean  $\pm$  SE concentration of 25(OH)D was



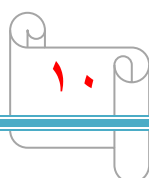
$13.55 \pm 0.91$  ng/mL in cases and  $13.19 \pm 1.19$  ng/mL in controls. There was no significant difference in 25(OH)D concentration between cases and controls. We found no relationship between severity of headache and 25(OH)D status. *Conclusions.* We did not find any association between migraine and vitamin D status; also, severity of headaches was not related to 25(OH)D level. Further studies with larger sample sizes are required to confirm our results.

### **3- Elucidation of the levels of vitamin D, calcium, and magnesium in the serum of Egyptian migraine patients: a case-control study (16)**

Dorreyya A. Elsayed, Karam S. Amin, Ibrahim A. Elsayed & Noha A. Hashim

Thirty healthy individuals and 60 age- and sex-matched migraineurs (22 chronic and 38 episodic migraineurs), diagnosed according to the International Headache Society criteria (ICHD-III), were recruited. After obtaining basic data, a visual analogue scale (VAS) for the severity of migraine pain was assessed. Migraine severity questionnaire (MIGSEV) and the Migraine Disability Assessment (MIDAS) questionnaire were given and illustrated to the participants. Blood samples were obtained, and serum concentrations of vitamin D, calcium, and magnesium were determined.

migraine patients had significantly lower level of serum vitamin D and magnesium than healthy subjects with ( $P < 0.001$  and  $P = 0.04$ ), respectively. However, the difference between the serum calcium levels of the patient and the control group was not statistically significant. Moreover, vitamin D and magnesium had a significant negative correlation with frequency, duration, severity, and disability in migraine.



## **MATERIALS AND METHODS**

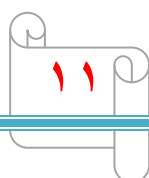
**Study population** : This cross-sectional study was conducted between migraine patients in AL-Basra city, Iraq , in autumn 2012. Totally, 89 migraine patients (72.4% women and 27.6% men) aged 10-61 years were selected.

**Baseline data and anthropometric assessment** : First, for every participant, data regarding age, sex, weight, height, waist circumference (WC) , body mass index (BMI), education, medical history, consumption of vitamin and other mineral supplements were collected. Body mass index was determined using body weight (in kilogram) divided by height (in meter square). Waist circumference was measured by inelastic tape at narrowest part of body, below the ribs.

**Biochemical assessment** : To assess serum levels of vitamin D, 25(OH) D3 was measured by ELISA . Results of serum vitamin D were classified. According to the ELISA way in laboratory:

- Deficiency (serum vitamin D less than 12 ng/ml)
- Insufficiency (serum vitamin D between 12 and 30 ng/ml)
- Sufficiency (serum vitamin D more than 30 ng/ml).

Calcium, phosphor, and albumin also measured for the diagnosis of primary hyperparathyroidism.

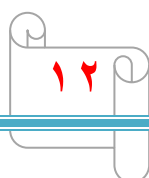


**Migraine assessment** : Migraine disease was established by neurologist. Severity, duration of migraine attacks, and frequency of attacks each month was completed by neurologist. Migraine severity was measured by Visual Analogue Scale The headache diary result (HDR) was determined as: Duration of headache multiplied by frequency of headache.

**Statistical methods** : Statistical analysis was conducted by applying the SPSS 18.0 software (SPSS, Inc. Chicago, IL, USA). Several linear regression analysis was performed to determine relationship among serum vitamin D levels and migraine headaches. P values less than 0.05 were considered as significance levels.

**RESULTS** : In this study, from 89 migraine patients at baseline, thirteen patients refused to participate. Finally, 76 patients with mean age of  $33.1 \pm 11.1$  years were included for the analysis. There were 55 women with mean age of (  $33.4 \pm 10.5$  ) years and 21 men with mean age of (  $32.4 \pm 12.8$  ) years. Demographical characteristics of patients are shown in Table 1. Mean migraine severity was  $6.6 \pm 1.1$ , which was more between males. But, mean HDR was more between females. Deficiency, insufficiency, and sufficiency of vitamin D were observed 13.2%, 68.4%, and 18.4% between patients, respectively. Table 2 appear unadjusted Pearson's correlation coefficients of serum 25-OH-D3 with another variable.

No important correlation was observed between serum vitamin D levels with migraine severity. However, a significant positive association was found among serum vitamin D levels and HDR.



Several linear regression was used to determine the relationship among serum 25-OH-D3 with migraine severity and HDR.

Results of several linear regression for relationship among patients characteristics with migraine severity and HDR are shown in Tables 3 and 4, respectively. In addition, after adjustment for confounding variables such as age, sex, BMI, waist circumference ( WC) , education and number of chronic diseases, significant association was not present between serum levels of vitamin D and migraine severity (P = 0.741). But, a significant positive connection was shown between serum vitamin D levels with HDR (P = 0.042). So that, one unit increase in serum levels of vitamin D is related to increased 0.014 log HDR .

According to values seen in Tables 3 and 4, effect of gender on migraine severity and HDR is more than other variables. However, when we compared the relationship among vitamin D groups (deficiency, insufficiency, and sufficiency) with migraine severity and HDR, no association was seen . These results are shown in Table 5.

**Table 1: Demographical characteristics of patients with migraine**

Variables	Male	Female	Total
Age (years)	32.4±1.4	33.4±1.2	33.1±1.2
BMI (kg/m <sup>2</sup> ) <sup>†</sup>	24.5±0.5	26.8±0.5	26.2±0.5
Waist circumference (cm)	92.1±1.1	91.7±1.2	91.8±1.1
Numbers of chronic diseases <sup>**</sup>	0.2±0.04	0.4±0.1	0.4±0.09
Education (years)	11.0±0.4	10.5±0.4	10.7±0.4
Migraine severity	7.2±0.1	6.4±0.1	6.6±0.1
Frequency <sup>***</sup>	8.5±0.5	8.4±0.9	8.4±0.8
Duration (hour)	11.7±0.9	27.9±2.3	23.4±2.1
HDR <sup>∴</sup>	105.5±12.7	192.9±22.6	168.8±20.8
Serum 25(OH) D3 (ng/ml)	24.4±1.6	22.9±1.9	23.3±1.8

**Table 2: Correlation of serum 25-OH-D3 with demographical variables and variables related to migraine**

Variables	25-OH-D3	
	r	P value
Age (years)	0.184	0.056
BMI (kg/m <sup>2</sup> )†	0.058	0.309
Waist circumference (cm)	0.101	0.193
Numbers of chronic diseases	0.008	0.471
Education (years)	0.039	0.368
Migraine severity	0.069	0.277
HDR††	0.199	0.043

**Table 3: Results of multiple linear regression for relationship between patients characteristics and migraine severity**

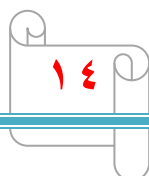
Variables	Unstandardized $\beta$ -coefficients	Standardized $\beta$ -coefficients	P value	R <sup>2</sup> for multiple model
Sex	0.97	0.384	0.002	0.21
Age (years)	-0.002	-0.020	0.877	
BMI (kg/m <sup>2</sup> )	0.083	0.359	0.110	
Waist circumference (cm)	-0.009	-0.083	0.708	
Numbers of chronic diseases	0.101	0.076	0.509	
Education (years)	0.053	0.183	0.100	
25-OH-D3 (ng/ml)	0.003	0.036	0.741	

**Table 4: Results of multiple linear regression for relationship between patients characteristics with HDR†**

Variables	Unstandardized $\beta$ -coefficients	Standardized $\beta$ -coefficients	P value	R <sup>2</sup> for multiple model
Sex	-0.702	-0.312	0.013	0.184
Age (years)	-0.004	-0.041	0.759	
BMI (kg/m <sup>2</sup> )	-0.064	-0.310	0.177	
Waist circumference (cm)	0.005	0.056	0.806	
Numbers of chronic diseases	0.095	0.080	0.497	
Education (years)	-0.006	-0.024	0.834	
25-OH-D3 (ng/ml)	0.014	0.232	0.042	

**Table 5: Results of multiple linear regression for relationship between vitamin D groups with migraine severity and HDR†**

Variable	25-OH-D3		
	Unstandardized $\beta$ -coefficients	Standardized $\beta$ -coefficients	P value
Migraine severity	0.035	0.017	0.877
HDR†	0.130	0.072	0.541



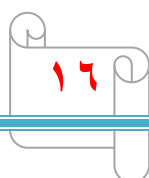
## DISCUSSION

In this study, we have seen a significant positive correlation among serum levels of vitamin D and HDR, and this relationship remained significant upon adjustment for confounding variables such as age, sex, BMI, waist circumference (WC), education, and number of chronic diseases. However, there was no significant connection among serum vitamin D and migraine severity. In this study, also, we investigated this relationship according to various vitamin D groups, but, relationship was not seen among vitamin D groups and migraine.

A few case reports have indicated the role of Vit. D in headache, including migraine.[18,19,20] Thys-Jacobs conducted two case reports in this field in 1994.[18,19] A case report study was conducted in 2 female patients with migraine associated with menstruation and premenstrual syndrome (PMS). These patients had low levels of vit. D and with consumption of vit. D and calcium supplement (1600-1200 IU per day) significant lowering in migraine attacks and premenstrual symptoms (PMS) were seen during two months treatment.[18] Another study performed among postmenopausal patients with migraine and low levels of vit. D showed that with supplementation of vit. D and calcium, the frequency and duration of migraine attacks lowered.[19] Prakash and Shah found that daily intake of vit. D calcium supplementation (1500 IU vitamin D3 and 1000 mg calcium) between 8 patients with vit. D deficiency, osteomalacia, and chronic tension-type headache confirmed an improvement in headache during 4-6 weeks.

In this study, serum levels of calcium became normal upon a week of treatment, but improvement in headache was after many weeks of treatment, hence, vitamin D is probably more important than calcium in improving headache.[18] A few studies have shown an correlation between low levels of vitamin D with greater incidence of chronic pain and headache.[21,22 ] In 2008, Turner et al. reported the prevalence of vit. D deficiency at 26% between 267 patients with chronic pain (including 25 patients with headache).[20] In another study, chronic pain was significantly correlated with vit. D status between English women, but, this correlation was not seen between men.[22]

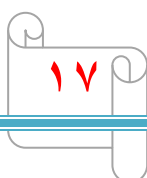
In Norway, a multi-ethnic study with cross-sectional descriptive designs, decrease level of vit.D (levels less than 50 nmol/l) were reported between 58% of patients with musculoskeletal pain, headache, and fatigue. There was an inverse relation among headache with vitamin D, and lowering in frequency of headache attacks was seen with increased levels of vitamin D; also this connection remained after adjustment for age, sex, season, and geographical region (OR = 2.6, P = 0.008). Serum levels of vit. D were lower in patients with headache than in other patients. Vit. D levels was lower in winter and spring than in summer and autumn. Wheeler and O'Brien showed that patients with migraine have low vit. D levels.[24,25] Wheeler, reported that 14.8% of patients with chronic migraine had serum levels of vitamin D less than or equal to 20 ng/ml and 25.9% of patients had serum vit. D levels among 20 and 30 ng/ml.[21] In Greece, prevalence and frequency of headaches was greater in northern areas and regions with average low temperature than in southern regions.[27]





Serum vit. D levels is higher between individuals who live at lower latitudes and is an essential factors for low prevalence of headache.[11] Data have shown an increasing frequency of attacks during the fall and winter and less attacks in summer,[11] which is probably due to low levels of vit. D in the fall and winter and indicates role of vitamin D in causing headache.[11] In a cross-sectional study including 11,614 participants in the 6<sup>th</sup> survey of Tromsø study, significant correlation was not seen among serum levels of vitamin D and migraine, but association between non-migraine headache and vit. D levels was only important in nonsmokers group and adjustments were performed for age, BMI, sex, season, chronic diseases, education level, physical activity, and alcohol consumption.[27]

Accurate role of vit. D deficiency in headache is unknown.[23] The main mechanisms in causing headache include sensitization of 2<sup>nd</sup> and 3<sup>rd</sup> neurons due to continuous stimulation of sensory receptors of periosteal coverage (because of bone swelling) and , central sensitization (because of bone swelling). Other mechanisms of headache in patients with vit. D deficiency are low serum levels of magnesium (Mg) .[19] Abnormal metabolism of magnesium(Mg) is involved in the pathogenesis of tension-type headache.[19] Magnesium deficiency in the brain, blood, erythrocyte, monocyte, and platelet have been present between patients with tension-type headaches and other types of headache. About 40-50% of patients with tension-type headache have decrease level of serum levels of magnesium. In different studies, patients with tension-type headache have responded to treatment with magnesium (Mg).[19]



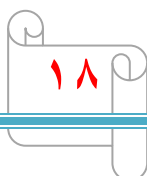
Vit. D deficiency may lead to tension-type headache using decreased absorption of magnesium, since , intestinal absorption of magnesium through food is dependent on vit. D.[19] Another mechanisms include the presence of vitamin D receptors, 1-hydroxylase and vitamin D binding protein in the brain, especially hypothalamus.[11]

### **This study has many limitations**

**First**, the study is cross-sectional, hence, we cannot see a causal link, thus, more clinical trial studies are required to be performed.

**Second**, the sample size of study is small and more studies are needed to do with larger sample size.

**Third**, further adjustments for confounding variables such as physical activity and alcohol consumption will be required since these variables may influence the serum levels of vitamin D.

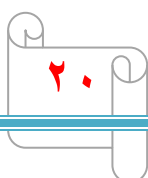


## **CONCLUSION**

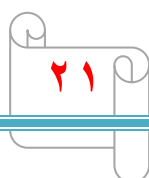
High levels of serum 25-OH-D3 were related to higher headache diary result( HDR) . After adjustment for confounding variables, this significant correlation remained. No significant relationship was shown among serum vitamin D and migraine severity. Additional studies are required to be performed with a larger sample size.

## REFERENCES

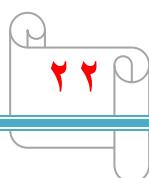
1. Lateef TM, Cui L, Nelson KB, Nakamura EF, Merikangas KR. Physical Comorbidity of Migraine and Other Headaches in US Adolescents. *J Pediatr* 2012;161:308-13.
2. Yoon MS, Katsarava Z, Obermann M, Fritsche G, Oezuyurt M, Kaesewinkel K, et al. Prevalence of primary headaches in Germany: Results of the German Headache Consortium Study. *J Headache Pain* 2012;13:215-23.
3. Battista J, Badcock DR, McKendrick AM. Migraine increases centre-surround suppression for drifting visual stimuli. *PLoS One* 2011;6:e18211.
4. Inaloo S, Dehghani SM, Farzadi F, Haghghat M, Imanieh MH. A comparative study of celiac disease in children with migraine headache and a normal control group. *Turk J Gastroenterol* 2011;22:32-5.
5. Headache disorders. Available from: <http://www.who.int/mediacentre/factsheets/fs277/en/>. [Last accessed on Mar 2004].
6. Steiner TJ. Lifting The Burden: The Global Campaign to Reduce the Burden of Headache Worldwide. Aids for management of common headache disorders in primary care. *J Headache Pain* 2007;8:S26-9.
7. Unalp A, Dirik E, Kurul S. Prevalence and clinical findings of migraine and tension-type headache in adolescents. *Pediatr Int* 2007;49:943-9.
8. Schürks M. Genetics of migraine in the age of genome-wide association studies. *J Headache Pain* 2012;13:1-9.



9. Mahdavi R, Tarighat EA, Ebrahimi M, Talebi M, Ghaemmaghami J. Effects of Oral Magnesium for Migraine Prophylaxis. *J Pharm Sci* 2009;15:103-8.
10. Schürks M, Rist PM, Bigal ME, Buring JE, Lipton RB, Kurth T. Migraine and cardiovascular disease: Systematic review and meta-analysis. *BMJ* 2009;339:b3914.
11. Prakash S, Mehta NC, Dabhi AS, Lakhani O, Khilari M, Shah ND. The prevalence of headache may be related with the latitude: A possible role of Vitamin D insufficiency? *J Headache Pain* 2010;11:301-7.
12. Andıran N, Çelik N, Akça H, Doğan G. Vitamin D deficiency in children and adolescents. *J Clin Res Pediatr Endocrinol* 2012;4:25-9.
13. Moradzadeh K, Larijani B, Keshtkar AA, Hossein-Nezhad A, Rajabian R, Nabipour I, et al. Normative Values of Vitamin D among Iranian Population: A Population Based Study. *Int J Osteoporos Metabolic Dis* 2008;1:8-15.
14. Jong-Geun Seo and Sung-Pa Park, Vitamin D Deficiency and Its Correlates in Migraine Patients , 2020 Mar-Apr; 23(2): 233–235. Published online 2020 Feb 25. doi: 10.4103/aian.AIAN\_229\_19
15. Alireza Zandifar, Samaneh sadat Masjedi, Mahboobeh Banihashemi, Fatemeh Asgari, Navid Manouchehri, Homa Ebrahimi, Faraidoon Haghdoost, Mohammad Saadatnia, "Vitamin D Status in Migraine Patients: A Case-Control Study", *BioMed Research International*, vol. 2014, Article ID 514782, 7 pages, 2014.  
<https://doi.org/10.1155/2014/514782>
- 16 . Elsayed, D.A., Amin, K.S., Elsayed, I.A. *et al.* Elucidation of the levels of vitamin D, calcium, and magnesium in the serum of Egyptian migraine patients: a case-control study. *Egypt J Neurol Psychiatry Neurosurg* **56**, 43 (2020). <https://doi.org/10.1186/s41983-020-00174-3>



17. Matchar DB, Young WB, Rosenberg JA, et al. Evidence-based guidelines for migraine headache in the primary care setting: Pharmacological management of acute attacks. American Academy of Neurology. Accessed February 10, 2011
18. Hovsepian S, Amini M, AminorroayaA, Amini P, Iraj B. Prevalence of vitamin D deficiency among adult population of Isfahan City, Iran. J Health Popul Nutr 2011;29:149-55.
19. Prakash S, Shah ND. Chronic tension-type headache with vitamin D deficiency: Casual or causal association?. Headache 2009;49:1214-22.
20. Thys-Jacobs S. Vitamin D and calcium in menstrual migraine. Headache 1994;34:544-6.
21. Thys-Jacobs S. Alleviation of migraines with therapeutic vitamin D and calcium. Headache 1994;34:590-2.
22. Knutsen KV, Brekke M, Gjelstad S, Lagerløv P. Vitamin D status in patients with musculoskeletal pain, fatigue and headache: A cross-sectional descriptive study in a multi-ethnic general practice in Norway. Scand J Prim Health Care 2010;28:166-71.
23. Atherton K, Berry DJ, Parsons T, Macfarlane GJ, Power C, Hypponen E. Vitamin D and chronic widespread pain in a white middle-aged British population: Evidence from a cross-sectional population survey. Ann Rheum Dis 2009;68:817-22.
24. Turner MK, Hooten WM, Schmidt JE, Kerkvliet JL, Townsend CO, Bruce BK. Prevalence and clinical correlates of vitamin D inadequacy among patients with chronic pain. Pain Med 2008;9:979-84. 2250 1.7



25. Wheeler SD. Vitamin D deficiency in chronic migraine. *Headache* 2008;48:S52-3.

26. O'Brien H, Hershey AD, Kabbouche MA, Austin SB, Frazier AL, Wright RJ. Prevalence of vitamin D deficiency among pediatric patients with recurrent headaches. *Headache* 2010;50:23.

27. Mitsikostas DD, Tsaklakidou D, Athanasiadis N, Thomas A. The prevalence of headache in Greece: Correlations to latitude and climatological factors. *Headache* 1996;36:168-73

