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Elucidation of the levels of vitamin D, calcium, and magnesium in the serum of Egyptian migraine patients: a case-control study

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Abstract

Background: Migraine, although, is a prevalent disease; its pathogenesis is complex and still not fully elucidated. The effect of vitamin D on various neurological disorders is thought to be exerted either directly via its specific receptors or through the related minerals. We investigated the possible relationship between vitamin D level and its related minerals (calcium and magnesium) and migraine characteristics in patients.

Subjects and methods: 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.

Results: 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.

Conclusion: Vitamin D and magnesium were significantly deficient in migraine patients and were related to the severity and disability of migraine attacks. Low vitamin D and magnesium levels were associated with more frequency and longer duration of migraine attacks.

Keywords: Migraine, Vitamin D, Magnesium, Pain, Disability

Introduction

Migraine is one of the most common disabling neurological disorders. It is characterized by recurrent episodes of headache, variable in duration, intensity, and frequency, and is accompanied by nausea, vomiting, photophobia, and/or phonophobia. In some cases, migraine attacks are preceded by focal neurological symptoms called aura [1].

Although the diagnosis of migraine remains mostly clinical, researchers have made great efforts in the investigation of the role of the neurotransmitter, hormones, and other biochemical elements in the pathophysiology of this disease. Such efforts have permitted a better understanding of the cerebral and extra-neurological mechanisms underlying this type of headache leading to the identification of a treatment target [2].

Vitamin D has been suggested to play an important role in various physiological activities such as immune system regulation and resolution of inflammation, which

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are both proposed to be involved in the pathogenesis of several neurological diseases including migraine [3].

Among all the serum electrolytes, magnesium plays a significant role in the conversion of vitamin D by hepatic 25-hydroxylation and renal 1 α -hydroxylation into the active, hormonal form 1,25-dihydroxy-vitamin D [4]. Magnesium deficiency results in reduced levels of vitamin D and impaired parathyroid hormone response [5]. Magnesium supplementation was shown to markedly reduce the resistance to vitamin D treatment, and it has been implicated in magnesium-dependent vitamin D-resistant rickets. It also plays a key role in bone mineralization by influencing synthesis of the active vitamin D metabolites [6]. Magnesium deficiency is found in patients with chronic medical illnesses, including cardiovascular disease, diabetes, pre-eclampsia, eclampsia, sickle cell disease, and chronic alcoholism [7]. Henceforth, we investigated the impact of vitamin D and its related minerals (calcium and magnesium) on migraine characteristics.

Methods

This case-control study was carried out over a period of 6 months from July 2018 to December 2018, on 78 migraine patients, diagnosed according to the international classification of headache disorders, third edition (ICHD-3) [8]. The exclusion criteria were age < 18 years, patients with known history of other neurological diseases (cerebrovascular stroke, epilepsy, brain tumors, multiple sclerosis), those who have received vitamin D supplements in the previous 4 months, those with concomitant medical diseases especially tumors, hypertension, diabetes, renal or hepatic insufficiency, autoimmune disease, and thyroid

diseases, and the patients on medications that clearly affect electrolytes' levels such as diuretics, cyclosporine, aminoglycosides, and acetazolamide. Eighteen patients were excluded, leaving a sample of 60 patients; they were 40 (66.6%) females and 20 (33.3%) males, with an age range of (19–49) years and a mean age of 31.13 \pm 7.4 years. Apparently, 30 healthy individuals, 12 (40%) males, and 18 (18%) females, matched for age, gender, and menstrual status of the female patients, were served as a control group. The characteristics of the patients and control are summarized in (Table 1).

The detailed history of all migraine patients including, level of education, residence, and consumption of vitamin and mineral supplements was collected. General and neurological examinations and the assessment of migraine characteristics using the visual analogue score for pain intensity [9] were conducted. Migraine severity was assessed by the Migraine Severity Scale (MIGSEV) [10] and the Migraine Disability Assessment (MIDAS) questionnaires to evaluate the migraine-related disability in different life domains of the patients over the previous 3 months.

The venous blood samples (5 mL) were collected under complete aseptic conditions from all the subjects included in the present study. A fresh serum aliquot for each subject was used for the assay of electrolytes including serum calcium and magnesium, liver, and kidney functions. Regarding vitamin D, blood samples were collected, centrifuged, and stored at – 80 °C. Serum levels of vitamin D were measured using the enzyme-linked immunosorbent assay (ELISA) method. Vitamin D insufficiency was noted at 20–29 ng/mL and vitamin D deficiency at < 20 ng/mL [11]. Repeated freezing and thawing cycles were avoided.

Table 1 Demographic characteristics of migraine patients and control subjects

	Migraine (60 patients) N (%)	Control (30 subjects) N (%)	p value	
Age (mean \pm SD)	(19–49) 31.13 \pm 7.4	(21–50) 31.56 \pm 7.6	0.1	
BMI (mean \pm SD)	28.8 \pm 5.9	30.2 \pm 4.6	0.1	
Residence	Urban	34 (56.7%)	22 (73.3%)	0.1
	Rural	26 (43.3%)	8 (26.6%)	
Gender	Female	40 (66.7%)	18 (60.0%)	0.7
	Male	20 (33.3%)	12 (40.0%)	
Education	Higher (> 12 years)	44 (73.3%)	18 (60.0%)	0.2
	Basic (\leq 12 years)	16 (26.7%)	12 (40.0%)	
Smoking	Yes	8 (13.3%)	7 (23.4%)	0.1
	No	52 (86.7%)	23 (76.6%)	
Marital status	Single	18 (30.0%)	13 (43.3%)	0.21
	Married	42 (70.0%)	17 (56.7%)	
Oral contraceptive pills (in married females)	Yes	5 (23.8%)	3 (33.3%)	0.1
	No	21 (76.2%)	9 (66.7%)	

Continuous data are represented as mean \pm SD; categorical data are represented as number and percentage
N number, % percentage, M \pm SD mean \pm standard deviation

Statistical analysis

The collected data were coded, entered, presented, and analyzed by a computer using a database software program, Statistical Package for Social Science (SPSS) version 22 [12]. Quantitative variables were expressed as the mean \pm SD and range, and the categorical variables were expressed as a number and percentage. Continuous data were checked for normality by using the Shapiro-Wilk test. Student's *t* test was used to compare two independent groups of normally distributed data, while the Mann-Whitney *U* test was used for non-normally distributed data. The percentages of categorical variables were compared using the chi-square test. Spearman's rank correlation analysis was done between the selected study parameters. *P* value $<$ 0.05 was considered statistically significant.

Our institutional review boards approved this study, and informed consent was obtained from each patient before starting the study.

Results

Among the study participants who suffered from migraine, 38 patients (63.3%) were diagnosed with episodic migraine (EM), whereas 22 (36.7%) with chronic migraine (CM). Only ten patients (16.7%) experienced symptoms consistent with the diagnosis of migraine with aura; on the contrary, 50 (83.3%) patients had migraine without aura (Fig. 1). The age of onset of the disease ranged from 10 to 35 years of age, with a mean of 25.9 ± 5.5 years, and the whole duration of illness ranged from 1 to 19 years with a mean of 5.2 ± 5.1 years. While the frequency of attacks for the last month ranged from 4 to 30 with a mean of 14.37 ± 7.75 , the average duration of a headache attack was about 12 h with a mean of 11.43 ± 7.04 h. The intensity of migraine headache pain on the

VAS ranged from 2 to 9 with a mean of 6.30 ± 1.90 (Table 2). The severity of migraine was assessed by the migraine severity questionnaire (MIGSEV) and results showed that 43.3% (26 patients) had grade 1 (low) severe headache, and 16.7% (10 patients) suffered grade 3 (high) severity, with the rest of the patients (40%) were in the intermediate severity grade 2. The level of impairment in daily activities, as assessed by the Migraine Disability Assessment (MIDAS) questionnaire, indicated that 26.7% of the patients were associated with little or no disability, 46.7% with mild disability, 23.3% with moderate disability, and only 3.3% with severe disability (Table 3). The statistical analysis evaluated the mean (\pm SD) level of vitamin D to be significantly higher in the control group (27.23 ± 7.65) as compared to the migraines' group (16.77 ± 7.47) with $P < 0.001$. Vitamin D deficiency among migraine patients was 60 % (36 patients), and insufficiency was 33.3% (20 patients), whereas only 6.7% (4 patients) had normal levels. While 43% of participants of the control group had normal vitamin D levels, and 13% of them had deficient levels, 43% of healthy individuals also had vitamin D insufficiency (Fig. 2).

Serum magnesium was significantly higher in the control group (2.21 ± 0.40 mEq/L) than the patient's group (1.88 ± 0.20 mEq/L) ($p = 0.04$). On the contrary, the calcium level reported no significant difference between the two groups ($p = 0.62$). Other basic laboratory investigations showed no statistically significant differences between both the groups (Table 4).

Vitamin D level and calcium were significantly lower ($p = 0.002$ and $p < 0.05$, respectively) in patients of migraine without aura compared to patients having migraine with aura. However, there was no statistical difference between the two groups regarding magnesium level ($p = 0.11$). According to the type of migraine, vitamin D and

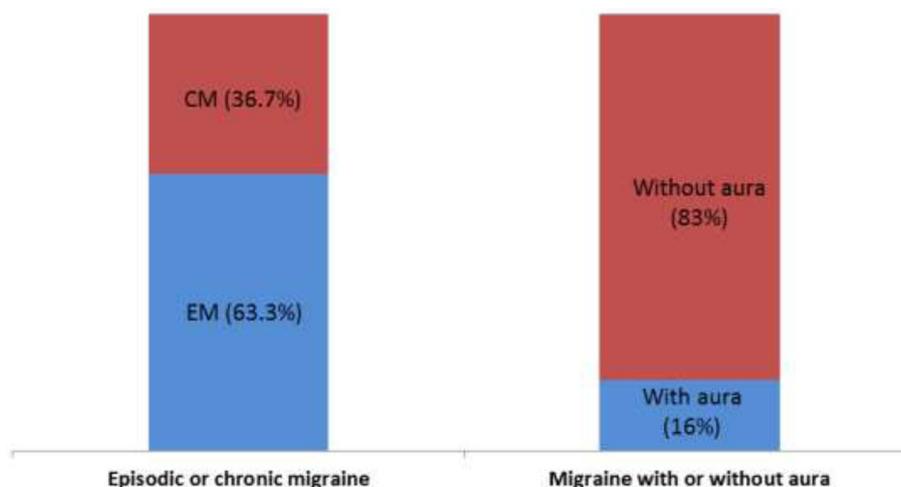


Fig. 1 Sub-groups of migraine patients

Table 2 Clinical characteristics of migraine attacks

Migraine group	Mean (\pm SD)	Median	Minimum	Maximum
Age of onset	25.9 (\pm 5.5)	26.5	10	35
Duration of illness (/years)	5.2 (\pm 5.1)	4	1	19
Attack duration (/hours)	11.43 (\pm 7.04)	12.00	3.00	24.00
Frequency of attacks (per month)	14.37 (\pm 7.75)	12.00	4.00	30.00
Pain intensity on VAS	6.30 (\pm 1.90)	6.00	2.00	9.00

SD standard deviation, VAS visual analog scale

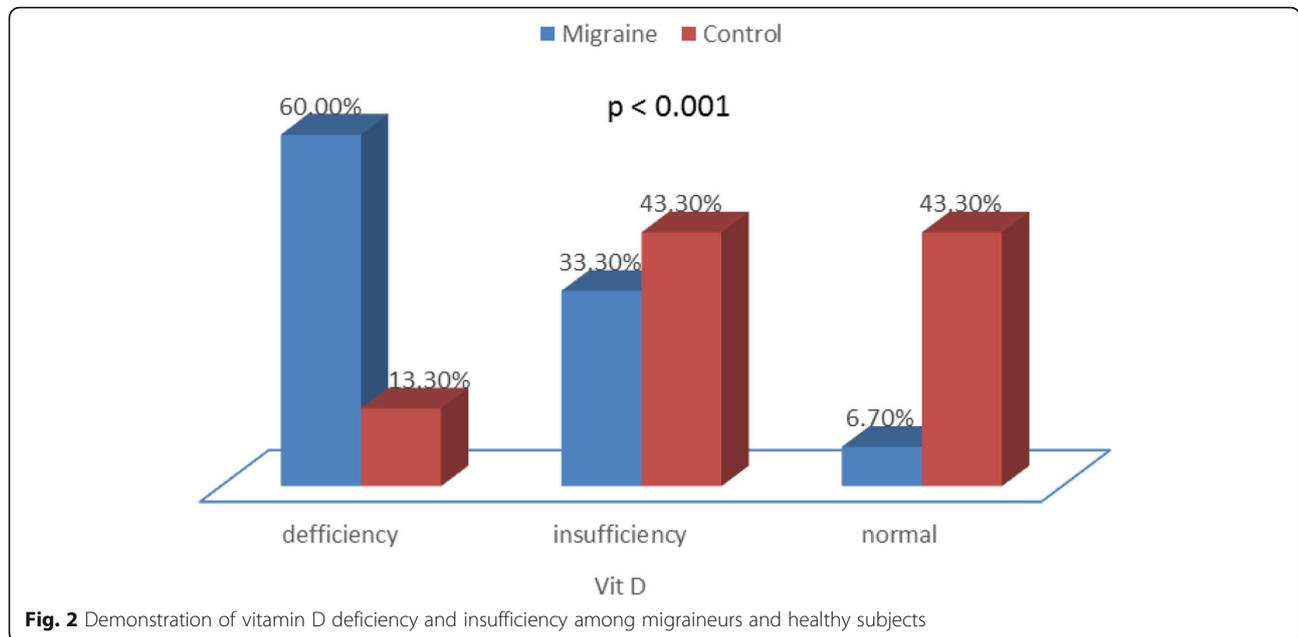
serum magnesium were higher in patients with episodic migraine (EP) than patients with chronic migraine (CM) with a statistically significant difference between two groups ($p < 0.001$ and $p = 0.04$ respectively). However, there was no statistical difference between the two types of migraine regarding serum calcium level ($p = 0.12$). When we compared serum level of vitamin D, calcium, and magnesium in patients taking prophylactic migraine medications and the other group of patients without any prophylaxis treatment, we found no significant difference between the two groups of patients (Table 5).

Both vitamin D and serum magnesium showed statistically significant negative correlation with body mass index (BMI) ($p < 0.001$ and $p = 0.017$), frequency of attacks of migraine ($p < 0.001$ and $P = 0.001$), duration of migraine attacks ($p = 0.004$ and $p < 0.001$), and level of disability measured by MIDAS ($p < 0.001$ and $P < 0.001$) respectively. However, they showed non-significant correlation with the age of patients or severity of pain according to VAS scores, based on statistical computations. On the other hand, serum calcium level showed only a statistically significant positive correlation with BMI ($p = 0.007$), with

Table 3 The severity of migraine and the level of impairment in daily activities were assessed by MIGSEV and MIDAS questionnaire

Questionnaire			Patients' numbers	
			Numbers	%
MIGSEV questionnaire	Intensity of pain	Mild	4	6.7%
		Moderate	28	46.7%
		Intense	28	46.7%
		very intense	0	0.0%
	Nausea	None	12	20.0%
		Mild	34	56.7%
		Intense	14	23.3%
	Disability in daily activities	Vomiting	0	0.0%
		No	16	26.7%
		Mild	28	46.7%
		Marked	16	26.7%
	Tolerability	Confined to bed	0	0.0%
		Tolerable	22	36.7%
barely tolerable		22	36.7%	
MIGSEV Score	Intolerable	16	26.7%	
	Grade 1 (low)	26	43.3%	
	Grade 2 (intermediate)	24	40.0%	
MIDAS questionnaire	Grade 3 (high)	10	16.7%	
	Little or no disability	(0–5)	16	26.7%
	Mild disability	(6–12)	28	46.7%
	Moderate disability	(11–12)	14	23.3%
	Severe disability	(+ 21)	2	3.3%

% percentage, MIGSEV migraine severity questionnaire, MIDAS Migraine Disability Assessment



no statistically significant correlation with age of patients, frequency, duration, the severity of migraine, or level of disability by MIDAS. Vitamin D and serum magnesium levels showed a significant negative correlation with the severity of migraine assessed by the MIGSEV score ($p < 0.001$ and $p < 0.001$ respectively). Calcium also showed a negative correlation; however, there was no statistical significance (Table 6).

Discussion

Migraine should be viewed as a complex brain network disorder with a strong genetic basis that involves multiple cortical, subcortical, and brain stem regions, to account for the pain and the wide constellation of symptoms characterizing the disease [13]. Multiple pathological changes contribute to the origin of migraine

pain. Considerable circumstantial evidence suggests neuro-inflammation in the intracranial meninges to be a key element responsible for the sensitization of trigeminal meningeal nociceptors in migraine [14].

The anti-inflammatory effect of vitamin D is well documented, and several studies have shown that vitamin D, at physiologic levels, can suppress the production of pro-inflammatory cytokines in human monocytes and macrophages [15].

The aim of this case-control study was to assess the serum level of vitamin D and its related minerals (calcium and magnesium) in patients with migraine and to evaluate its relation to the disease activity.

Our results confirmed the female predominance in migraine, where the female-to-male ratio was 2 to 1. This high female-to-male ratio was reported in several studies [16, 17].

Our study basically provides information on the association between serum vitamin D and migraine. We have demonstrated that migraine sufferers have significantly lower vitamin D levels compared to the healthy subjects ($p < 0.001$). In our patients, the prevalence of vitamin D was 60% deficiency, 33.3% insufficiency, and only 6.7% normal. This observation is in accordance with a cross-sectional prospective study conducted by Celikbilek and colleagues [18], where serum vitamin D levels were significantly lower in 52 newly diagnosed migraine patients than in controls ($p = 0.012$). In another prospective study conducted over 134 migraine patients in Italy, migraine sufferers had a severe vitamin D deficiency compared to the healthy subjects [19]. In Iran, Togha and colleagues [20] recruited seventy migraine patients and

Table 4 Basic laboratory investigations and serum electrolytes of migraine patients and control

	Migraine patients Mean ± SD	Control group Mean ± SD	p value
WBCs ($\times 10^3$ /cmm)	8.44 ± 2.7	6.35 ± 3.1	0.100
RBCs (/million)	4.8 ± 0.5	5.1 ± 0.3	0.080
Platelets ($\times 10^3$ /cmm)	263.7 ± 94	211.4 ± 57	0.090
HB (g/dL)	12.4 ± 3.3	11.9 ± 2.6	0.210
ESR (mm/h)	18.5 ± 13.5	8.5 ± 11.3	0.075
Total calcium (mg/dL)	9.58 ± 0.59	9.31 ± 0.45	0.62
Magnesium (mEq/L)	1.88 ± 0.20	2.21 ± 0.40	0.041*

WBCs white blood cells, RBCs red blood cells, HB hemoglobin, ESR erythrocyte sedimentation rate, SD standard deviation

*Significant

Table 5 Relation between vitamin D, calcium, and magnesium and migraine patient sub-groups

		Vitamin D level (ng/mL)		Calcium (mg/dL)		Magnesium (mEq/L)	
		Mean ± SD	p value	Mean ± SD	p value	Mean ± SD	p value
Aura	Without	15.44 ± 7.03 (4–31)	0.002*	9.51 ± 0.58 (8.70–10.50)	0.03*	1.86 ± 0.21 (1.50–2.20)	0.11
	With	23.40 ± 6.17 (15–33)		9.94 ± 0.53 (9–10.50)		1.98 ± 0.08 (1.90–2.10)	
Type of migraine	EM	20.58 ± 6.01 (9–33)	< 0.001*	9.55 ± 0.60 (8.7–10.5)	0.12	1.98 ± 0.12 (1.7–2.2)	0.04*
	CM	10.18 ± 4.62 (4–21)		9.61 ± 0.60 (8.8–10.5)		1.68 ± 0.14 (1.5–2)	
Prophylaxis treatment	yes	16.38 ± 8.20 (7–33)	0.650	9.63 ± 0.55 (8.80–10.30)	0.67	1.83 ± 0.20 (1.60–2.10)	0.17
	no	17.03 ± 7.05 (4–31)		9.54 ± 0.62 (8.70–10.50)		1.91 ± 0.19 (1.50–2.20)	

EM episodic migraine, CM chronic migraine, SD standard deviation
*Significant

found that they significantly had a lower mean of serum vitamin D (30 ± 16 ng/mL) than healthy subjects (43 ± 19 ng/mL) ($p < 0.001$). In addition, a higher level of serum Vitamin D (between 50 to less than 100 ng/mL) is associated with 80–83% lower odds of migraine headache than those with serum 25 (OH) D levels below 20 ng/mL. Vitamin D supplements can decrease inflammatory markers like C-reactive protein (CRP) which can suppress the neurogenic inflammation in migraine pathogenesis [21]. Vitamin D has a protective efficacy against endothelial dysfunction and this could explain the inverse relationship between nitric oxide (NO) and 25 (OH) D levels [22]. Elevated level of NO could lead to vasodilation [23] and elevate calcitonin gene-related peptide and substance P synthesis that ultimately may result in triggering nociceptive neurons and inflammation especially in trigeminovascular system [24].

Contrarily, Zandifar and colleagues [25] showed no significant differences in serum levels of vitamin D between cases and controls. However, they considered vitamin D sufficiency if it was > 20 ng/mL. Furthermore, Kjaergaard and colleagues [26] were only able to detect a significant relationship between serum vitamin D and the types of headaches other than migraines. These differences might be presumably due to differences in race or residence area and study design.

Vitamin D insufficiency is not an unusual finding in our country, Egypt [27]. Although being a sunny country, these findings might be explained by inadequate dietary intake and inadequate sun exposure, probably due to cultural factors like veiling [28]. Also, darker skin, like most Egyptians, needs much longer time for sun exposure than that needed by fair skin to produce adequate vitamin D due to the higher amount of cutaneous melanin in darker

Table 6 Correlation of data of patients and headache character with Vitamin D, calcium, and magnesium serum level

	Vitamin D level		Calcium		Magnesium	
	r value	p value	r value	p value	r value	p value
Age	-0.052	0.69	0.180	0.17	-0.082	0.53
BMI	-0.475	< 0.001*	0.348	0.007*	-0.307	0.017*
Frequency of attacks	-0.70	< 0.001*	-0.546	-0.55	-0.546	< 0.001*
Duration of attacks	-0.363	0.004*	-0.244	0.06	-0.533	< 0.001*
VAS	-0.174	0.18	0.152	0.25	-0.149	0.26
Level of disability on MIDAS	-0.51	0.001*	0.115	0.38	-0.552	< 0.001*
MIGSEV questionnaire						
Intensity of pain	-0.17	0.21	-0.25	0.05	0.16	0.23
Nausea	-0.14	0.29	-0.09	0.45	-0.34	0.007*
Disability in daily activities	-0.49	< 0.001*	0.12	0.35	-0.54	< 0.001*
Tolerability	-0.55	< 0.001*	-0.24	0.07	-0.52	< 0.001*
MIGSEV (total score)	-0.56	< 0.001*	-0.17	0.21	-0.51	< 0.001*

BMI body mass index, VAS visual analogue scale, MIGSEV migraine severity questionnaire, MIDAS Migraine Disability Assessment
*Significant

pigmented skin, which slows the conversion to cholecalciferol in the skin [29].

We also showed that serum magnesium level was lower in migraine patients than in healthy controls, and our results are consistent with those of various other studies [30, 31]. Magnesium, specifically, plays a crucial role in the synthesis and metabolism of vitamin D. Also, intestinal absorption of magnesium is dependent on vitamin D. Hence, lower levels of vitamin D are generally associated with lower serum magnesium levels [32]. Assarzagana and colleagues [33] in a case-control study showed that a sub-normal magnesium serum level increases the odds of a migraine attack up to 35-fold. It has been suggested that magnesium plays a role in the pathogenesis of migraine by counteracting vasospasm, inhibiting platelet aggregation, and cell membrane stabilization [34]. Magnesium deficiencies could contribute to a modified mitochondrial metabolism by altering oxidative phosphorylation and neuronal polarization resulting in cortical spreading depression [35]. Magnesium also might be involved in the control of vascular tone and reactivity to neurotransmitter and endogenous hormones through plugging the N-methyl-D-aspartate (NMDA) receptor and preventing calcium from entering the cell and exert its effects on neurons and cerebral vascular muscles. NMDA receptors may play pivotal role in nociceptive processes, resulting in neuro-plastic changes in the trigeminal nociceptive neurons. Thus, NMDA receptor antagonists may be useful as an analgesic in the treatment of persistent pain [36].

Dissimilar to Yin and colleagues [37], we did not find any significant correlation between serum calcium level and any headache-related variables in migraine patients.

In contrast to Celikbilek and colleagues [18] and Togha and colleagues [20], our research showed significantly low levels of vitamin D in migraine without aura patients, rather than migraine with aura. However, magnesium level was not significantly different in migraine patients with aura and without aura. Our results here go in the same line with those of Talebi and colleagues [38].

We also observed a significant decrease in the serum levels of vitamin D and magnesium among chronic than episodic migraineurs. We found a significant inverse correlation between the frequency of migraine headache attacks and serum levels of vitamin D and magnesium. This was in agreement with a previous study conducted by Song and colleagues [39] in South Korea, where they found that vitamin D deficiency was present in 77.1 % of patients, and that the duration of headache was related to the degree of vitamin D deficiency among migraineurs. Low vitamin D serum level is associated with a high incidence of chronic pain and headache [26]. Wheeler [40] reported that 14.8% of patients with chronic migraine had serum vitamin D level < 20 ng/mL, and 25.9% of them had serum vitamin D level between 20 and 30 ng/mL. Talebi and colleagues [38]

reported a significant linear relationship between the frequency of headaches and serum magnesium levels. These studies were in line with the findings of the present study.

In our study, there was a significant relationship between vitamin D and serum magnesium levels with migraine severity as assessed by the migraine severity questionnaire (MIGSEV). They both showed a significant inverse correlation with the MIGSEV questionnaire score especially “tolerability of pain” and “disability in daily activities” items. However, the “intensity of pain” item within the MIGSEV questionnaire or as assessed by the VAS scale showed no significant correlation with the levels of vitamin D and magnesium. Our results were in accordance with Song and colleagues [39] where they reported no significant difference in pain intensity on VAS and vitamin D level.

In a similar prospect, we showed that low vitamin D level is also linked to the degree of disability in daily activities in migraine patients as measured by the MIDAS scale, with a significant negative correlation between them. This is in agreement with the works of Rapisarda and colleagues [19]. Contrasting results were observed by Togha and colleagues [20], as they failed to find any correlation between vitamin D level and the MIDAS score.

Huang and colleagues [41] in a prospective case series of patients with chronic pain, who received 3 months of vitamin D supplementation, reported a significant decrease in the number of pain areas and in use of analgesics with improvement in sleep and quality of life, providing a more comprehensive evaluation of pain. Similarly, Thys-Jacobs [42] reported a dramatic reduction in frequency and duration of headaches after supplementation with vitamin D. Significant reduction in the intensity of photophobia and phonophobia was also observed in patients after receiving magnesium supplements [43].

Among all socio-demographic characteristics, we found a significant negative correlation of vitamin D level with body mass index (BMI), with a p value < 0.001. This result is in line with the works of Wortsman and colleagues [44] and Das and colleagues [45] who demonstrated that low serum levels of vitamin D have consistently been associated with higher adiposity represented in high BMI, as adipose tissue sequesters vitamin D.

In the present study, we found that BMI had a significant positive correlation with calcium and inversely a significant correlation with magnesium serum level. These findings are in context with Ekweogu and colleagues [46]. The proposed mechanism is that low serum magnesium can increase weight gain by enhancing intracellular Ca^{+2} [47]. Increased Ca^{+2} in adipocytes activates phosphodiesterase-3B which decreases lipolysis [48] and enhances lipogenesis [49]. In addition, inflammatory cytokines that are produced by adipose tissue, especially TNF, enhance renal Ca^{+2} reabsorption and magnesium urinary excretions [50].

In spite of these results, our study has some limitations. First, the severity and disability scales and questionnaires used in our study were self-reported by the patients, and although we offered easy translations and clarified vague questions; however, the validity and reliability of their answers are questionable. Second, we did not control some comorbidities of migraine that may influence levels of vitamin D, such as anxiety or depression.

Conclusion

The serum levels of vitamin D and magnesium are lower in migraine patients than in the control. The serum level of vitamin D and magnesium is linked to the frequency and tolerability of the headache attacks rather than the mere intensity of pain. Further, prospective large studies are essential to establish high-quality evidence for using vitamin D and/or magnesium supplements in the treatment of migraine.

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Authors' contributions

Elsayed DA, Amin KS, Elsayed IA, and Hashim NA carried out this work. Elsayed DA designed the study and had done the statistical analysis. Amin KS, Hashim NA, and Elsayed IA collected the patients, gathered clinical data, and wrote the manuscript. All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors read and approved the final version to be published.

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Availability of data and materials

Data and materials supporting the results of this article are included within the article (and its additional file(s)).

Ethics approval and consent to participate

The study was approved from the Institutional Ethics Committee of the Faculty of Medicine, Zagazig University (ZU-IRB #4511/4-2018). Written informed consent was obtained from all study participants after explaining the details and benefits as well as risks to them. Surrogate consent from the patient's legal guardian or designated health proxy was permitted in cases where the patient did not have decision-making capacity.

Consent for publication

Not applicable.

Competing interests

The authors declared that they have no conflicts of interest with respect to the authorship and/or publication of this article.

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