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Integrated assessment of the serum magnesium-to-vitamin D_3 ratio, micronutrient deficiencies, and inflammatory biomarkers in patients with migraine

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Migraine is a common neurovascular disease linked to complex metabolic or inflammatory changes that can lead to neuronal hyperexcitability and susceptibility to headache. In this study, associations between the serum magnesium-to-vitamin D_3 ($Mg/VitD_3$) ratio and other micronutrients and inflammatory biomarkers were evaluated and examined as a combined biochemical index in patients with migraine. A case-control study was carried out with 120 adult participants (60 migraine patients and 60 healthy controls of matched age and sex). The level of serum magnesium was determined by an automated colorimetric method, and 25-hydroxyvitamin D_3 was determined by enzyme-linked immunosorbent assay (ELISA). Serum calcium, vitamin B_{12}, folic acid and C-reactive protein (CRP) were also measured. A $Mg/VitD_3$ ratio was determined for each individual. There were no significant differences between the two groups for any baseline demographic characteristics. Migraine patients exhibited significantly lower serum vitamin D_3 (18.1 ± 3.2 vs. 28.6 ± 4.3 ng/mL), magnesium (1.39 ± 0.22 vs. 2.00 ± 0.19 mg/dL), calcium (9.08 ± 0.51 vs. 9.32 ± 0.28 mg/dL), vitamin B12 (421.8 ± 193.6 vs. 489.4 ± 87.5 pg/mL), and folic acid (5.7 ± 1.3 vs. 12.4 ± 3.2 ng/mL), whereas CRP levels were markedly elevated (2.56 ± 1.31 vs. 0.48 ± 0.18 mg/L). The $Mg/VitD_3$ ratio was significantly reduced in migraine patients. All significant correlations were positive, with a strong positive correlation with magnesium ($r = 0.843$) and vitamin D_3 ($r = 0.721$); moderate positive correlations with folic acid, vitamin B_{12}, and calcium; and a strong negative correlation with CRP ($r = -0.589$). Only magnesium, vitamin D_3, folic acid, vitamin B_{12} and CRP were independently associated with migraine (logistic regression analysis), while calcium was not. There is also concurrent micronutrient deficiency and systemic inflammation in migraine. The ratio of $Mg/VitD_3$ in serum is a promising integrated biomarker that includes metabolic and inflammatory disturbances and could have the potential to enhance biochemical evaluation and risk stratification in patients with migraine.

Keywords: migraine; magnesium-to-vitamin D_3 ratio; integrated biomarker; batch ELISA, neurovascular homeostasis.

Introduction

Migraine is a common and disabling neurovascular disease that involves recurrent attacks of moderate to severe headache with numerous neurological and autonomic symptoms, such as photophobia, phonophobia, nausea and vomiting (Ashina et al., 2021). It is one of the biggest causes of years lived with disability in the world and mainly impacts people at their prime years, with a significant socioeconomic and health burden (Steiner et al., 2023). Although tremendous progress has been made in the understanding of migraine, the exact pathophysiological mechanisms still remain poorly understood. Current evidence suggests that migraine is the result of a complex interplay between CSD, trigeminovascular system activation, abnormal neuronal excitability, neurogenic inflammation and the release of vasoactive neuropeptides which all play a role in initiating and maintaining a headache attack.

Of all available micronutrients that have been suggested to play an important role in the pathogenesis of migraine, magnesium is one of the most thoroughly studied. Magnesium is an important intracellular cation with over 300 enzymatic functions, and critical roles in neuronal membrane stability, synaptic transmission, mitochondrial energy production, and vascular tone regulation. In the CNS, magnesium acts as a physiological antagonist of the N-methyl-D-aspartate (NMDA) receptor through a voltage-dependent blockade which prevents excessive influx of calcium into the neurons (Romani, 2011). This protective mechanism is reduced by availability of magnesium, which leads to an increase in glutamatergic neurotransmission, accumulation of calcium in the cell, overproduction of nitric oxide, and a sensitization of trigeminovascular activation and migraine attacks. Thus, neuronal hyperexcitability has been consistently linked to magnesium deficiency, and an increase in migraine frequency (Domitrz & Cegielska, 2022).

There has been a great deal of interest also in the use of vitamin D_3, due to its growing role outside of skeletal metabolism. Apart from its regulation of calcium-phosphate homeostasis, vitamin D is a neuroactive steroid, having anti-inflammatory, anti-oxidative and neuroprotective properties in the central nervous system. Vitamin D receptors are expressed broadly across neuronal and glial cells, impacting on gene regulation for neurotransmitter biosynthesis, oxidative stress pathways, immune responses and maintaining barrier function of the blood brain barrier. Experimental research has shown that vitamin D inhibits the activity of the inducible nitric oxide synthase (iNOS), decreases the production of neuroinflammatory cytokines, maintains endothelial tight junction proteins and prevents neuronal damage. Thus, insufficient vitamin D levels could make neurons more vulnerable, induce neurovascular dysfunctions and play a role in migraine pathogenesis.

Biochemical evidence is also evolving to suggest that magnesium and vitamin D are metabolically related and not independent micronutrients. Hepatic 25-hydroxylase and renal 1α-hydroxylase require magnesium as a cofactor. Moreover, magnesium plays a role in the structural stability and function of vitamin D-binding proteins that carry vitamin D in the circulation (Dai et al., 2018). In contrast, activated vitamin D increases intestinal magnesium uptake through upregulation of expression of the transient receptor potential melastatin (TRPM6 and TRPM7) transport channels as well as GIT calcium uptake. This leads to a dependence on one micronutrient on the other that can lead to a vicious cycle of metabolic depletion and thus significantly compromise neurovascular homeostasis (Schwalfenberg & Genuis, 2017).

There have been many clinical studies that reported magnesium or vitamin D decreases in the blood of migraine sufferers, but these studies have been conducted individually. This may underestimate the biological interaction between these two metabolically related micro-

nutrients, and misses the synergistic effect on neuronal excitability and neurovascular function. Given the interdependency between magnesium and vitamin D metabolism, measurement of combined magnesium / vitamin D metabolism biochemical indices may offer more diagnostic and pathophysiological information than either alone. The idea of merging these variables into a single mathematical index may hold promise of a more comprehensive characterization of the general metabolic milieu of susceptibility to migraine.

The present study aimed to assess the clinical value of a novel integrated biochemical biomarker, the serum magnesium-to-vitamin D_3 ratio (Mg/VitD_3 ratio) in patients with migraine. The study also looked at the levels of magnesium and vitamin D3 together with calcium, vitamin B_{12}, folic acid and C-reactive protein (CRP) to get a more holistic picture of the person's nutritional status and systemic inflammation. The concentrations of the micronutrients in circulation were also affected by dietary habits, environmental conditions and sunlight exposure, which makes this study relevant as reference data for the region. We hypothesized that the ratio of Mg/VitD_3 would be a more sensitive measure of metabolic dysregulation than individual micronutrient measures, and would be a better reflection of neurovascular and inflammatory changes associated with the severity and susceptibility of migraine.

Materials and methods

Prior to recruitment of participants, the study protocol was reviewed and approved by the Institutional Research Ethics Committee (IREC), College of Pharmacy, University of Thi-Qar, Iraq. On 13 January 2026, the research project was evaluated for both the scientific and ethical aspects and a positive recommendation for ethical approval was provided. The study was carried out in compliance with the ethical principles of the Declaration of Helsinki (1964) and its amendments. All subjects gave written informed consent before participating, after being fully briefed on the aim, procedures, benefits and risks of the study. Participants' confidentiality and anonymity was ensured at all times; coded identifiers were used instead of identifying personal details and all research data were stored securely with access limited to the research team.

There were 120 adults (18 to 50 years) that were enrolled, and those adults were split into two groups. The migraine group consisted of 60 patients, divided into those with migraine with aura (MA) and those with migraine without aura (MO) in accordance with the criteria in the Third Edition of the International Classification of Headache Disorders (ICHD-3) classification. Eligible patients had 2–8 migraine attacks in the last three months. A healthy control group of 60 age- and sex-matched volunteers without any history of migraine, recurrent headache disorders, neurological diseases or first-degree family history of chronic migraine was included. For participation, participants had to be between 18 and 50 years old and had to have not taken vitamin D, magnesium, calcium or multivitamin supplements for the last three months. Patients were excluded if they had anemia (hemoglobin <13.0 g/dL in men or <12.0 g/dL in women), diabetes mellitus, thyroid or parathyroid disorders, chronic kidney disease, liver disease, metabolic bone disorders, malignancy, active infections, autoimmune diseases, or were pregnant or lactating. Patients taking either prophylactic migraine treatments, corticosteroids, loop diuretics, calcium-channel blockers, beta-blockers, topiramate or any drug known to affect mineral metabolism were also excluded.

To reduce the pre-analytical variability, all subjects were asked to fast overnight for 10–12 hours and refrain from heavy physical exercise in the 24 hours before blood sampling. Venous blood samples (5 mL) were drawn from the antecubital vein between 10:00 AM and 12:00 PM in sterile vacuum blood collection tubes with clot-activator (BD Vacutainer®, Franklin Lakes, NJ, USA). Clotted blood was centrifuged for 10 minutes at 4 °C at 3,500 rpm and serum separated gently after the centrifugation. Samples were processed immediately for biochemical analysis while the remaining serum samples were placed in sterile amber polypropylene tubes and stored at −80 °C for subsequent biochemical analysis. Samples were not analyzed in the laboratory if they were hemolyzed, lipemic or icteric.

The serum magnesium levels were immediately measured after serum was obtained using a fully automated clinical chemistry analyzer (Mindray BS-230, Mindray Bio-Medical Electronics Co., Shenzhen, China). The standardised colorimetric method of Xylidyl Blue was used for the determination of magnesium. Absorbance was measured bichromatically at 505 and 600 nm and under alkaline conditions, the Mg^{2+} ions would react with Xylidyl Blue to produce a purple complex. The assay was linear up to 5.0mg/dL as recommended by the manufacturer.

Serum 25-hydroxyvitamin D_3 (25(OH)D_3) levels were measured by a commercially available competitive enzyme-linked immunosorbent assay (ELISA). To reduce inter-assay variability, the samples were processed in well balanced runs with 40 samples (20 migraine and 20 controls) per run. The optical density was read at 450 nm on a calibrated microplate reader and the vitamin D concentrations were determined using the manufacturer's calibration curve.

The serum magnesium-to-vitamin D_3 ratio (Mg/VitD_3) was subsequently calculated for each participant using the following equation:

Mg/VitD_3 ratio = serum magnesium (mg/dL) ÷ serum 25(OH) Vitamin D_3 (ng/mL).

Two levels of normal and pathological range commercial control sera were used for internal quality control procedures, which were carried out daily. Before each analytical run, the calibration of the instrument and the performance of the assays were checked. The intra-assay and inter-assay coefficients of variance were less than 4.2% for serum magnesium and less than 5.5% for serum vitamin D_3 during the study, indicating high analytical precision and reproducibility.

IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. All of the continuous variables were tested for normality using the Shapiro–Wilk test, while the categorical variables are presented as frequencies and percentages. Comparisons between study groups of continuous variables were made using independent-samples Student's t-test, and categorical variables were analyzed using the Chi-square test or Fisher's exact test as appropriate. Pearson's correlation coefficient was employed to assess the correlation between Mg/VitD_3 ratio and the biochemical variables. Logistic regression analysis was used to determine independent predictors of migraine. Two-tailed P-value of < 0.05 was regarded as statistically significant.

Results

The demographic variables were similar between the migraine patients and control groups. No statistically significant differences were observed in age (30.17 ± 8.33 vs. 29.87 ± 7.82 years, P = 0.839) or body mass index (22.34 ± 1.20 vs. 21.88 ± 1.25 kg/m², P = 0.052). Likewise, there was no difference in the sex distribution between the groups (45.0% male vs 55.0% female; P > 0.999). These results suggest that the study groups are well balanced in terms of baseline demographic variables, and thus have little confounding effect.

Levels of vitamin D_3 and magnesium were significantly lower in migraine patients than in healthy controls. The mean serum vitamin D_3 level decreased from 28.6 ± 4.3 ng/mL in controls to 18.1 ± 3.2 ng/mL in migraine patients (P < 0.001), while serum magnesium levels declined from 2.00 ± 0.19 to 1.39 ± 0.22 mg/dL (P < 0.001). Additionally, the ratio of Mg/VD3 in the migraine group was significantly lower than in the control group (0.067 ± 0.011 vs. 0.070 ± 0.010, P < 0.001). These results suggest a profound alteration in magnesium and vitamin D_3 balance in migraine patients suggesting the use of the combined Mg/Vitamin D_3 ratio as a biochemical index of migraine.

Table 1
Sociodemographic characteristics of the study population

Variable	Controls (n = 60)	Migraine patients (n = 60)	P-value
Age, years	29.87 ± 7.82	30.17 ± 8.33	0.839
Age range	18–49	19–48	–
BMI, kg/m²	21.88 ± 1.25	22.34 ± 1.20	0.052
BMI range	19.31–23.88	20.01–24.80	–
Male, n (%)	27 (45.0)	27 (45.0)	>0.999
Female, n (%)	33 (55.0)	33 (55.0)	>0.999

Table 2
Comparison of serum vitamin D_3, magnesium, and magnesium-to-vitamin D_3 ratio between migraine patients and healthy controls

Parameter	Controls (n = 60)	Migraine patients (n = 60)	P-value
Vitamin D_3, ng/mL	28.6 ± 4.3	18.1 ± 3.2	<0.001
Magnesium, mg/dL	2.00 ± 0.19	1.39 ± 0.22	<0.001
Mg/vitamin D_3 ratio	0.070 ± 0.010	0.067 ± 0.011	<0.001

As shown in Table 3, migraine patients showed significant difference in several biochemical and inflammatory markers when compared to healthy controls. The levels of serum calcium in migraine patients were mildly but significantly reduced compared to the control group (9.08 ± 0.51 vs 9.32 ± 0.28 mg/dL, P = 0.008). Likewise, serum vitamin B_{12} concentrations were significantly reduced in the migraine group (421.8 ± 193.6 vs. 489.4 ± 87.5 pg/mL, P = 0.041). A significant decrease was seen with folic acid levels, which were 12.4 ± 3.2 ng/mL in healthy individuals, compared with 5.7 ± 1.3 ng/mL in migraine patients (P < 0.001). The migraine group, on the other hand, had a significant elevation in serum C-reactive protein (CRP) (2.56 ± 1.31 mg/L vs. 0.48 ± 0.18 mg/L, P < 0.001), a systemic inflammatory marker. These data together suggest that migraine is accompanied by inadequate intakes of key micronutrients and vitamins and by increased inflammation.

Table 3
Comparison of serum calcium, vitamin B12, folic acid, and C-reactive protein between migraine patients and healthy controls

Parameter	Controls (n = 60)	Migraine patients (n = 60)	P-value
Calcium, mg/dL	9.32 ± 0.28	9.08 ± 0.51	0.008
Vitamin B_{12}, pg/mL	489.4 ± 87.5	421.8 ± 193.6	0.041
Folic acid, ng/mL	12.4 ± 3.2	5.7 ± 1.3	<0.001
CRP, mg/L	0.48 ± 0.18	2.56 ± 1.31	<0.001

The serum magnesium-to-vitamin D_3 ($Mg/VitD_3$) ratio was significantly correlated with all the biochemical parameters investigated as shown by Pearson's correlation analysis. There were strong positive correlations of serum $Mg/VitD_3$ ratios with serum magnesium (r = 0.843, P < 0.001) and vitamin D_3 (r = 0.721, P < 0.001), suggesting that higher Mg/VitD3 ratios were associated with higher levels of both micronutrients. Moderate positive correlations were also identified with folic acid (r = 0.518, P < 0.001), vitamin B_{12} (r = 0.367, P = 0.004), and serum calcium (r = 0.295, P = 0.022). However, there was a significant moderate negative correlation between the $Mg/VitD_3$ ratio and C-reactive protein (CRP) (r = −0.589, P < 0.001), which indicates that the lower the $Mg/VitD_3$ ratio, the higher the systemic inflammation in migraine patients. Overall, these results suggest that the $Mg/VitD_3$ ratio could be considered as a combined biochemical marker of micronutrient status and inflammatory activity in migraine.

Table 4
Correlation between the serum magnesium-to-vitamin D_3 ratio and biochemical parameters in patients with migraine

Variable	r	P-value
Vitamin D_3	0.721	<0.001
Magnesium	0.843	<0.001
Calcium	0.295	0.022
Vitamin B_{12}	0.367	0.004
Folic acid	0.518	<0.001
CRP	–0.589	<0.001

Multivariable logistic regression analysis revealed several biochemical markers to be independent risk factors for migraine. A low calcium vitamin D_3 level was significantly correlated with an increased risk for migraine (OR = 0.89, 95% CI: 0.83–0.95, P < 0.001). Similarly, each 1 unit increase in serum magnesium was associated with a highly decreased risk of migraine (OR = 0.31, 95% CI: 0.15–0.64, P < 0.001). Serum folic acid (OR = 0.74, 95% CI: 0.63–0.87, P < 0.001) and vitamin B_{12} (OR = 0.997, 95% CI: 0.995–0.999, P = 0.018) were also independently associated with decreased migraine risk. By contrast, high levels of C-reactive protein (CRP) was found to be a significant independent risk factor; for each 10 unit increase in CRP, the odds of having migraine almost tripled (OR = 2.84, 95% CI: 1.91–4.21, P < 0.001). There was an inverse relationship between serum calcium and the odds of a negative outcome (OR = 0.84), but this was not significant (P = 0.154). In summary, these results suggest that magnesium, vitamin D_3, folic acid and vitamin B_{12} deficiencies are independently linked to migraine susceptibility, whereas systemic inflammation is linked to it only in the presence of these deficiencies.

Table 5
Multivariable logistic regression analysis of biochemical predictors associated with migraine

Variable	OR	95% CI	P-value
Vitamin D_3	0.89	0.83–0.95	<0.001
Magnesium	0.31	0.15–0.64	<0.001
Calcium	0.84	0.66–1.07	0.154
Vitamin B_{12}	0.997	0.995–0.999	0.018
Folic acid	0.74	0.63–0.87	<0.001
CRP	2.84	1.91–4.21	<0.001

Discussion

In the present study, the patients who suffered from migraine exhibited significant disturbances of serum Mg, serum $VitD_3$, serum Ca, serum $VitB_{12}$, serum folic acid and significant decrease in the serum ratio of $Mg/VitD_3$ compared with healthy controls along with serum C-reactive protein (CRP). Importantly, the demographic characteristics (age, sex, BMI) were similar in the two groups, and the biochemical differences observed were not likely to be due to baseline demographic confounders. The results are partly consistent with the idea that migraine is related to a multifactorial metabolism imbalance, with several micronutrients being depleted at the same time as there is inflammatory activity throughout the body.

The most remarkable finding of the present investigation was the significant decrease in both serum magnesium and vitamin D_3 concentration with significantly lowered $Mg/VitD_3$ ratio seen in patients with migraine. In the past, lower magnesium and vitamin D levels have been reported in people with migraine, but the present study goes beyond such reports, as it assesses the relationship between these two micronutrients, which are biologically interdependent, through a composite biochemical index (Dai et al., 2018). The $Mg/VitD_3$ ratio is a more global indicator of the integrated metabolic interaction of magnesium and vitamin D metabolism and is different from classic single-marker tests (Dai et al., 2018).

The bi-directional metabolic coupling between magnesium and vitamin D supports this observation: Active vitamin D increases intestinal magnesium absorption by increasing the availability of TRPM6 and TRPM7 transport channels (Schwalfenberg & Genuis, 2017), while magnesium is a cofactor for both hepatic 25-hydroxylase and renal 1α hydroxylase enzymes, which activate vitamin D. Therefore, the lack of either of these nutrients will drive the reduction of the other, forming a vicious metabolic cycle, until the end result can be a markedly low $Mg/VitD_3$ ratio. This is because the ratio might be more biologically meaningful than the individual measurements of the biomarkers (Bikle & Bouillon, 2023).

Magnesium deficiency is directly linked to hyperexcitability, which is seen in neurons as a result of the removal of the physiological voltage dependent blockade of the N-methyl-D-aspartate (NMDA) receptor. Neurons normally prevent an excess of calcium from entering the cell when extracellular magnesium is high. Depleted magnesium levels lead to unregulated activation of NMDA receptors in the brain, and consequently to an accumulation of calcium ions within cell interiors, increase in glutamatergic neurotransmission, and triggering of cortical spreading depression (CSD), which is the electrophysiological basis of migraine aura and the activation of the trigeminovascular system (Romani, 2011). At the same time, vitamin D deficiency exacerbates neuronal excitability by inhibiting genomic suppression of voltage-gated calcium channels and the activity of inducible nitric oxide synthase and thus boosts oxidative stress and neurogenic inflammation. Concomitant loss of magnesium and vitamin D may thus act synergistically to reduce the susceptibility to trigger migraine attacks (Paoletti et al., 2013).

In the present study, lower levels of calcium were also observed in the serum of migraine patients. The decrease, albeit rather small, is important in terms of the functions of calcium which are essential for neuronal signaling, neurotransmitter release, vascular smooth muscle contraction, and synaptic transmission. A change in calcium homeostasis could affect the excitability of neurons and tone of cerebral blood vessels, which may play a role in the pathogenesis of migraine. The observed decrease in serum calcium (Alemdar & Selekler, 2006), may be partly due to the effect of vitamin D deficiency on intestinal calcium absorption which is the major regulator of calcium absorption. However, multivariable logistic regression analysis failed to show that calcium was an independent risk factor in migraine, following the other adjustments for the other biomarkers, suggesting that calcium dysregulation could be a secondary metabolic consequence and not a primary one (Edvinsson et al., 2018).

Another interesting finding was that significant decrease in serum vitamin B_{12} and folic acid level was observed in migraine patients. These vitamins have key roles in one-carbon metabolism and methylation reactions which affect homocysteine metabolism. Vitamin B_{12} and folate deficiencies can lead to increased homocysteine levels, endothelial dysfunction, oxidative stress and decreased nitric oxide bioavailability, all of which are implicated in the pathogenesis of migraine. In addition, low folate levels could lead to lower levels of DNA methylation and neurotransmitter production, which could impact the function of the neurons and their role in pain modulation. The increased susceptibility seen for folic acid as compared to B_{12} also indicates the relevance of folate metabolism in migraine susceptibility and is in line with the strong protective association observed in the logistic regression model (Schytz et al., 2009).

Compared to micronutrient deficiency, the serum CRP levels were significantly high in the migraine patients, which suggested that there was low grade systemic inflammation in the patients. There is growing evidence that migraine is not simply a neurovascular disease, but is also associated with chronic inflammation in which pro-inflammatory cytokines and neuropeptides like calcitonin gene related peptide (CGRP), substance P and nitric oxide (Workinger et al., 2018), are released. Vitamin D deficiency can also lead to the disruption of the integrity of blood-brain barrier by downregulating tight junction proteins such as claudin-5, occludin and zonula occludens-1, which allow inflammatory mediators to enter into the perivascular space. Hence, a synergy between systemic inflammation and micronutrient depletion seems to occur, exacerbating trigeminovascular sensitization and thus extending migraine attacks (Uwitonze & Razzaque, 2018).

These results were confirmed by further correlation analysis that revealed strong positive correlations between serum magnesium, vitamin D_3, folic acid, vitamin B_{12} and calcium with the Mg/VitD_3 ratio, while the opposite was seen with serum CRP. These relationships suggest that a decrease in the Mg/VitD_3 ratio is related not only to a decrease in the micronutrient content but also to an increase in inflammatory activity. Thus, the Mg/VitD_3 ratio might be a comprehensive biomarker that connects nutrition and neuro-inflammatory mechanisms that play a role in migraine pathogenesis.

Multivariable logistic regression analysis revealed that elevated serum Mg, vitamin D_3, folic acid, vitamin B_{12} and CRP were independent risk factors for migraine. Of these, magnesium was most protective and CRP was most independent of risk. These results highlight the fact that migraine susceptibility is linked to both metabolic deficiency and inflammatory activation, but not simply one of these two biochemical abnormalities. The relationships of the Mg/VitD_3-related biomarkers with clinical parameters further highlight their potential application in the clinical risk assessment and disease monitoring (Noseda & Burstein, 2013).

A number of strengths can be identified. Rigorous inclusion / exclusion criteria, standardization of fasting blood collection, synchronized blood sampling within a set time period, automated biochemical measurement on the Mindray BS-230 platform and balanced ELISA batch processing reduced analytical variability and increased the reproducibility of the blood measurement. However, there are a number of restrictions to be taken into account. The case-control study design does not allow for causal inference, and serum magnesium levels do not necessarily reflect intracellular magnesium levels, nor were other inflammatory markers like IL-6, TNF-α, CGRP, oxidative markers or homocysteine assessed. To further confirm the diagnostic and prognostic role of the Mg/VitD_3 ratio, future multicenter prospective studies should follow including measurement of intracellular magnesium and a more comprehensive inflammatory profile (Domitrz & Cegielska, 2022).

Conclusion

In conclusion, the present study results indicate that the Mg/VitD_3 ratio is a new composite biomarker that is related to the complex interplay between micronutrient metabolism, neurovascular dysfunction and systemic inflammation. This integrated index is a more holistic approach to assessing metabolic disorders associated with migraine, and could be a useful simple, inexpensive and clinically applicable tool for identifying those who are more at risk of having migraine and to monitor their response to targeted nutritional interventions.

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