J Biochem Tech (2019) 10(1): 51-56
ISSN: 0974-2328

The Correlation between Migraine and Some Associated Bio-markers in Saudi Females

Anbrah A. Alzubidi, Foziah A. Alshubaily*, Shuog A. Alshehri, Hala S. Sonbol, Sawsan A. Rahimuddin, Ebtihaj J. Jambi

Received: 12 November 2018 / Received in revised form: 26 February 2019, Accepted: 03 March 2019, Published online: 23 March 2019

Abstract

Background- Migraine is a common neurological disorder. It affects 11% of the world's population and 2.6-5 % of the Saudi population. Its prevalence in women is 3 times more than in men. Although the pathogenesis of migraine headache is not fully understood but there is an assumption that some nutrients may be related to headache. This study was designed to measure the levels of vitamin D, calcium, sodium, and potassium that might have a relationship with migraine in Saudi females. Methods- The sample comprised 91 previously diagnosed migraine patients and 54 healthy control subjects. We collected data regarding age, weight, height, marital status, education, medical history, and consumption of vitamin and mineral supplements for each participant. Blood sample was obtained, and serum vitamin D, calcium, sodium and potassium were measured at the chemistry lab in King Abdulaziz Hospital. For between group comparisons independent-sample t-test analysis of variance was done. Results- There were 91 migraine patients aged (mean ± SEM) 32.91 ± 1.187 years and 54 controls aged (mean ± SEM) 30.00 ± 1.320 years. No significant differences were found in migraine patients compared with the healthy controls in vitamin D, sodium and potassium concentrations ($p>0.05$). However, we found a significant difference in calcium serum level between the two groups ($p= 0.00002$). Conclusion- A higher significant difference in calcium level in migraine patients was observed compared to the healthy controls, while no significant differences were observed in the other parameters. Future studies should attempt to confirm the relationship between calcium deficiency and migraine. In addition, there is a need for well-designed clinical trials to investigate the effects of serum vitamin D, calcium, sodium and potassium serum levels on higher risk of migraine.

Keywords: Migraine Headache, Vitamin D, Calcium, Sodium, Potassium.

Anbrah A. Alzubidi, Foziah A. Alshubaily*, Shuog A. Alshehri, Hala S. Sonbol, Sawsan A. Rahimuddin, Ebtihaj J. Jambi

Biochemistry Department, Faculty of science, King Abdulaziz University, Saudi Arabia.

***Email:** falshibli@kau.edu.sa

Introduction

Migraine is the most common neurological disorder worldwide (Vos et al., 2015; Steiner et al., 2015). The headache prevalence in Saudi Arabia at 8–12% and 2.6-5 % of them is a migraine headache (Rajeh et al., 1997; Jabbar and Ogunniyi 1997; Benamer et al., 2010). Many epidemiological studies have shown the association of migraine with the social, economic and personal habits of the patients (Borsook et al., 2005; Olesen et al., 2013). Migraine causes a substantial level of disability in both males and females under the age of 50 years as it affects 15 % of patients with headaches (Borsook et al., 2005; Coppola et al., 2009; Matías-Guiu et al., 2011; Launer et al., 1999). It usually begins at childhood or adolescence and can remain with the patient for lifetime (Fukui et al., 2008; Loder et al., 2015). Migraine is more common in women than men as its prevalence is 12-18% of the general population, affecting 18%-20% of women (Fukui et al., 2008; Semiz et al., 2013).

Migraine is divided into several types but the most common types are Migraine with Aura (MA), Migraine without Aura (MO) and Chronic Migraine (CM) (Olesen et al., 2013). The migraine attack lasts from 4 to 72 hours. It is usually mild at the beginning but, in some cases, may become severe (Jay and Barkin, 2017). Symptoms which can be associated with migraine attacks include nausea, vomiting, tiredness, speak difficultly, phonophobia (sensitivity to sound) and photophobia (sensitivity to light) (Fukui et al., 2008; Silberstein 1995; Mollaoğlu 2013). Also, in some cases, neck pain can begin in the premonitory phase and continues through the postdrome phase (Ashina et al., 2015; Florencio et al., 2014; Lampl et al., 2015).

There are many internal and external factors that cause migraine, which include: fasting, sleep disturbance, stress (Fukui et al., 2008; Karli et al., 2005; Hauge et al., 2010; Kelman 2007), alcohol consumption (Taylor 2009; Littlewood et al., 1988), smoking (Kelman 2007; Rasmussen and Olesen 1995; Rasmussen 1993) and hormonal factors in women (menstruation, pregnancy, menopause and use of oral contraceptives) (Gupta et al., 2007). Foods such as bananas, peanuts (Kokavec, 2016), caffeine, citrus fruits, and dairy products can also trigger migraine (Holzhammer and Wöber, 2006). A few studies found that neck problems,

sexual problems, and travel may also cause migraine (Wöber et al., 2006).

Some researchers reported that there is a relationship between vitamin D and migraine patients (Wheeler 2008). On the other hand, other researchers found no significant difference in serum levels of vitamin D between migraine patients and controls (Zandifar et al., 2014; Mottaghi et al., 2013). Studies on the relationship of calcium and migraines have not been abundant. There was one study which found that elevated level of calcium in the blood is associated with an increased risk of migraine (Yin et al., 2016). A significant increase of cerebrospinal fluid (CSF) sodium during migraine attacks was found, but not in the sodium or total calcium of plasma (Harrington et al., 2006). A low sodium diet may also lead to a lower frequency of headache (Amer et al., 2014). A high sodium intake leads also to a lower frequency of migraine (Pogoda et al., 2016).

Migraine is a public health problem that has been widely studied over the past decades. Although multiple studies have been conducted on migraine in different countries, local studies in Saudi Arabia was limited. Therefore, the relationship between migraine in Saudi females and some basic nutrients was monitored. The purpose of the present study is to examine association between serum levels of vitamin D, sodium, potassium, calcium and migraine.

Materials and Methods

Study Participants and Design

Samples participants in this study were collected from neurology clinic in king Abdulaziz University Hospital in Jeddah City, Saudi Arabia. The study protocol was reviewed and approved by Unit of Biochemical Ethic Research Committee, King Abdulaziz University, Jeddah, KSA.

The study sample consists of 91 previously diagnosed migraine patients and 54 healthy subjects (controls). The participants were females aged between 18-65 years diagnosed with migraine according to the third edition of the International Classification of Headache Disorders (ICHD-3) and the International Headache Society (HIS). The participants with chronical illnesses such as renal disease, liver disease, thyroid disorders, diabetes and hypertension were excluded. The participants who take medications that affect bone metabolism such as steroids and antiepileptic medication, pregnant women and those of age less than 18 or more than 65 years also were exclude. Potentially eligible participants were invited to attend the research clinic for assessment. Participants were provided with verbal and written information about the study (including the patient information sheet). Eligible participants signed and filled informed consent.

Data was collected regarding age, weight, height, marital status, education, medical history, and consumption of vitamin and mineral supplements for each participant. Weight was measured by analogue scale with light clothing with accuracy of 0.5 kg. Height was measured by tape measurement accurately wearing no shoes. BMI was determined by the following equation: body weight (in kilogram) divided by height (in meter square). Volunteers were asked whether they were taking vitamin D supplements or any other drugs as well as if suffering from any other non-chronic diseases for maintain the integrity of the specifications.

Biochemical Analysis

Blood samples were obtained as a single withdrawal (5 ml) from each participant after an 8 to 12-hour overnight fasting period. Each blood sample was added to a plain tube and allowed to clot for 30 minutes at room temperature (25 ºC) and it was processed using centrifuge at 3000 rpm for 10 minutes to separate serum. Serum samples were aliquoted in Eppendorf tubes and stored at −80 °C until the measurement of biochemical variables.

In the current study, vitamin D, calcium, sodium and potassium were assessed automatically in the chemistry lab King Abdulaziz University Hospital. Two kinds of devices were used to measure the parameters: Immunoassay Analyzer (Cobas e 601) for the determination of vitamin D and Dimension Xpand (siemens) for the determination of sodium, calcium and potassium.

Statistical Analysis

All the collected measured data were assessed by using statistically package for social science software (SPSS) descriptive statistics version 21, Chicago, IL, USA. Descriptive statistics were used to analyze the demographic characteristics. Data was expressed as means ± standard error deviation (SED). Differences in means of the study parameters between migraine patients and healthy controls were assessed using independent-sample T-Test "t". A p-values less than 0.05 was considered as statistically significant.

Results

The demographic data used in this study for migraine patients and control groups are provide in Table 1. One hundred and forty-five participants with mean age of 31.83 years were included. There were 91 migraine patients aged 32.91 ± 1.187 years and 54 control subjects aged 30.00 ± 1.320 years. Statistical analysis for this study using independent t-test revealed no significant difference in age and weight between patients and control subjects. On the other hand, data showed that the BMI and height were significantly increased in patients when compared with control subjects.

The laboratory data for migraine patients and control cases are shown in Table 2. No significant differences were found in Vitamin D, sodium and potassium concentrations in migraine patients when compared with the controls ($P>0.05$). However, serum calcium concentrations ($p=0.00002$) were found to be lower in migraine patients than in controls ($P<0.001$). The prevalence of sufficient, insufficient, deficient vitamin D levels was 18.7%, 61.6% and 19.8% in migraine patients compared to 24.1%, 37% and 38.9% in controls, respectively.

Table 1: The demographic data for migraine patients and for control group.

	Patients N= 91 Mean ± SEM	Controls N= 54 Mean ± SEM	p-value
Age	32.91±1.187	30.00±1.320	0.117
Weight	65.43±2.098	60.04±1.417	0.068
Height	156.75±0.669	158.94±0.729	0.035
BMI	25.68±0.541	23.76±0.527	0.019

BMI= body mass index; SEM= standard error mean; P-value <0.05 was considered statistically significant

Table 2: The laboratory data for migraine patients and control cases.

parameters	Patients (n= 91)	Controls (n= 54)	P value
Vit. D (75-250 nmol/l)* $\bar{x}$ ± SED	48.57±2.29	51.22±4.92	0.583
Ca (2.12-2.52 mmol/l) * $\bar{x}$ ± SED	2.12 ± 0.02	2.24 ± 0.14	0.000
Na (136-145 mmol/l) * $\bar{x}$ ± SED	135.94 ± 1.59	138.78 ± 0.31	0.085
K (3.5-5.1 mmol/l) * $\bar{x}$ ± SED	4.25 ± 0.04	4.167 ± 0.05	0.240

Vit. D= vitamin D; Ca= Calcium; Na= Sodium; K= Potassium; $\bar{x}$= mean; SED= standard error mean; P-value <0.05 was considered statistically significant.

The most common symptoms reported manifestations accompanying migraine headache were nausea (73.3%), a change of mood (67.8%), difficulty in concentration (38.9%), muscle weakness (31.2%), vomiting (30%), and sleep disturbance (8.9%). Results showed that the most frequently reported migraine triggers were photophobia (78.9%), noise (67.8%), phonophobia (61.8%), stress (45.6%), and odors (34.4%).

Discussion

There is an assumption that some foods may be provocative or preventative to headaches. It is not necessary to exclude certain foods or certain components from diets, but it may require regulating certain essential components such as vitamins, ions, proteins, carbohydrates, and fats (Martin et al, 2016). According to these we hypothesized that vitamin D, calcium, sodium and potassium levels may be associated with migraine.

Recent many studies have focused on vitamin D and its relationship to many diseases, including neurological diseases. However, some studies of serum vitamin D levels correlation to migraine are still uncertain. Some of case reports have indicated the role of vitamin D in headache, including migraine. In this study, we have demonstrated no significant association between serum levels of vitamin D and migraine. In 2010, Krusz et al., reported no significant differences in vitamin D levels in patients with migraine or patients with any other pain disorders. But, this study had a limitation as it contains migraine group and pain syndrome group but lacks a control group. Zandifar et al., 2014, found no significant difference in plasma levels of vitamin D between migraine patients and controls, also no correlation between the levels of vitamin D and migraine severity. Another study has shown no significant relationship between serum vitamin D and migraine severity (Mottaghi et al., 2013). The results of the studies mentioned earlier were similar to our findings. In contrast, in 1994, Thys-Jacobs observed a significant reduction of migraine attacks, frequency and duration after two months of usage of vitamin D and calcium supplements (Thys-Jacobs 1994 and Thys-Jacobs 1994), but this study was limited because of the low number of the study cases (two premenopausal and two postmenopausal women without control group). Also, it was found that postmenopausal patients with migraine and low levels of vitamin D showed decreased frequency and duration of migraine attacks with the supplementation of vitamin D and calcium (Kjærgaard et al., 2012). In 2009, Prakesh et al., reported a positive effect of vitamin D and calcium supplements among patients with vitamin D deficiency, osteomalacia, and chronic tension-type headaches as they found an improvement or decrease in headache severity. Wheeler (2008) suggested that there is a link between vitamin D and migraines in people with vitamin D deficiency. But his study was limited because the criteria for the diagnosis of migraine were not clear and the group of patients and controls who used vitamin D supplements were not excluded from the study. In 2010, O'Brien et al. also found a high prevalence of vitamin D deficiency among pediatric patients with headaches. Togha et al (2018) observed the relationship between vitamin D and migraine that subjects who had a higher level of serum vitamin D were lower odds of migraine than others. Regional factors may also contribute to migraine attacks. There are many studies showed that more than half the population in Saudi Arabia suffer from vitamin D deficiency (Al Wossaibi and Al Howeish 2011; Kaddam et al., 2017; Siddiqui and Kamfar 2007; Ardawi et al., 2011).

The epidemiological correlation studies have not systematically studied a possible relationship between serum calcium levels and migraines. Thus, we aimed to test the hypothesis that the diagnosis of migraine is associated with low levels of calcium in the blood, diagnosed as hypocalcemia. In our analyzes, we found a significant difference in levels of calcium between migraine patients and control cases. In addition, the prevalence of decreased level of calcium concentration in migraine and control groups were 39.6% and 13%, respectively. This means that calcium levels in migraine patients are lower than others. Based on that, we concluded a relationship between levels of calcium and migraine headache disorder. As we mentioned earlier, some studies found that calcium and vitamin D supplements reduce migraine attacks, frequency and duration of the headache (Thys-Jacobs 1994a; Thys-Jacobs 1994b; Kjærgaard et al., 2012). Our results were in good agreement with those reported previously. Yin et al. found that elevation of serum calcium levels was associated with an increase in the risk of migraine (Yin et al., 2016). The results found by Yin et al were inconsistent with our findings. Some elements' concentrations in the intracellular may have an effect on the level of calcium concentration such as

magnesium; magnesium is known to play an important role in the regulation of Ca entry in neural cells (Qujeq, D., et al., 2012). Also, Serum calcium levels and migraine can be affected by genetic factors (Yin et al., 2016).

High sodium dietary is known to be associated with many diseases such as hypertension which leads to stroke, cardiac, and kidney diseases (Meneton et al., 2005). Hypertension, hypotension and obesity were associated with migraine (Tietjen et al., 2007; Blaustein et al., 2011) Moreover, the risk of cardiovascular disease is higher in migraine patients (Mancia et al., 2011; Scher et al., 2005). In our study we found that there is no relationship between migraine and sodium level in blood. In a study conducted by Harrington et al., (2006) a significant increase of CSF sodium during migraine attacks was found but not the change of sodium in plasma or in total calcium, total magnesium, and ionized calcium or potassium (Harrington et al., 2006). In 2014, Amer and colleagues found a relationship between low sodium intake and frequency of headache. The participants in the previous study were diagnosed with prehypertension. This is relatively different from the sample type selected in our research. Pogoda et al (2016), contradicted results of the study conducted by Amer, as he found that high sodium intake leads to a lower frequency of migraine. These differences in results might be explained by differences in the study design. Campbell et al (1995), reported elevated sodium blood levels in migraine patients (as distinct from our measurements that revealed no change in plasma sodium). In our analysis, there was no significant difference in potassium among migraine patients and controls. To the best of our knowledge there have been no research studies studying the relationship of potassium in people with migraines.

Conclusion

In this study, high significant difference in calcium in migraine patients compared to controls was found. The level of serum calcium is lower in migraine patients than others. However, no relationship was found between vitamin D, sodium and potassium in migraine patients in Saudi female. Regional and genetic factors may also contribute to migraine. Future studies should be performed to confirm the causal relationship between calcium deficiency and migraine. We suggest that there will be a need for a well-designed clinical trial to investigate the effects of serum vitamin D, calcium, sodium and potassium on higher risk of migraine.

References

Al Wossaibi, A. and A. Al Howeish, High prevalence of vitamin D deficiency in the sunny Eastern region of Saudi Arabia: a hospital-based study. 2011.

Amer, M., M. Woodward, and L.J. Appel, Effects of dietary sodium and the DASH diet on the occurrence of headaches: results from randomised multicentre DASH-Sodium clinical trial. BMJ open, 2014. 4(12): p. e006671.

Ardawi, M.-S., Qari, M., Rouzi, A., Maimani, A. and Raddadi, R., Vitamin D status in relation to obesity, bone mineral density, bone turnover markers and vitamin D receptor genotypes in healthy Saudi pre-and postmenopausal women. Osteoporosis International, 2011. 22(2): p. 463-475.

Ashina, S., Bendtsen, L., Lyngberg, A. C., Lipton, R. B., Hajiyeva, N. and Jensen, R., Prevalence of neck pain in migraine and tension-type headache: a population study. Cephalalgia, 2015. 35(3): p. 211-219.

Benamer, H.T., D. Deleu, and D. Grosset, Epidemiology of headache in Arab countries. The journal of headache and pain, 2010. 11(1): p. 1.

Blaustein, M. P., F. H. Leenen, L. Chen, V. A. Golovina, J. M. Hamlyn, T. L. Pallone, J. W. Van Huysse, J. Zhang and W. G. Wier., How NaCl raises blood pressure: a new paradigm for the pathogenesis of salt-dependent hypertension. American Journal of Physiology-Heart and Circulatory Physiology, 2011. 302(5): p. H1031-H1049.

Borsook, D., Maleki, N., and Burstein, R., Migraine. Elsevier, 2005.

Campbell, D.A., K. Hay, and E.M. Tonks, Salt and water balance in migraine. British medical journal, 1951. 2(4745): p. 1424.

Coppola, G., F. Pierelli, and J. Schoenen, Habituation and migraine. Neurobiology of learning and memory, 2009. 92(2): p. 249-259.

Florencio, L. L., T. C. Chaves, G. F. Carvalho, M. C. Gonçalves, E. C. Casimiro, F. Dach, M. E. Bigal and D. Bevilaqua-Grossi., Neck pain disability is related to the frequency of migraine attacks: A cross-sectional study. Headache: The Journal of Head and Face Pain, 2014. 54(7): p. 1203-1210.

Fukui, P. T., T. R. T. Gonçalves, C. G. Strabelli, N. M. F. Lucchino, F. C. Matos, J. P. M. d. Santos, E. Zukerman, V. Zukerman-Guendler, J. P. Mercante and M. R. Masruha, Trigger factors in migraine patients. Arquivos de neuro-psiquiatria, 2008. 66(3A): p. 494-499.

Gupta, S., S. Mehrotra, C. M. Villalón, M. Perusquía, P. R. Saxena and A. MaassenVanDenBrink, Potential role of female sex hormones in the pathophysiology of migraine. Pharmacology & therapeutics, 2007. 113(2): p. 321-340.

Harrington, M. G., A. N. Fonteh, R. P. Cowan, K. Perrine, J. M. Pogoda, R. G. Biringer and A. F. Hühmer, Cerebrospinal fluid sodium increases in migraine. Headache: The Journal of Head and Face Pain, 2006. 46(7): p. 1128-1135.

Hauge, A., M. Kirchmann, and J. Olesen, Trigger factors in migraine with aura. Cephalalgia, 2010. 30(3): p. 346-353.

Holzhammer, J. and C. Wöber, Alimentary trigger factors that provoke migraine and tension-type headache. Schmerz (Berlin, Germany), 2006. 20(2): p. 151-159.

Jabbar, M.A. and A. Ogunniyi, Sociodemographic factors and primary headache syndromes in a Saudi community. Neuroepidemiology, 1997. 16(1): p. 48-52.

Jay, G.W. and R.L. Barkin, Primary Headache Disorders Part I-Migraine and the Trigeminal Autonomic Cephalalgias. Disease-a-Month, 2017. 63(11): p. 308-338.

Kaddam, I. M., A. M. Al-Shaikh, B. A. Abaalkhail, K. S. Asseri, Y. M. Al-Saleh, A. A. Al-Qarni, A. M. Al-Shuaibi, W. G. Tamimi and A. M. Mukhtar, Prevalence of vitamin D deficiency and its associated factors in three regions of Saudi Arabia: A cross-sectional study. Saudi medical journal, 2017. 38(4): p. 381.

Karli, N., M. Zarifoglu, N. Calisir and S. Akgoz, Comparison of pre-headache phases and trigger factors of migraine and episodic tension-type headache: do they share similar clinical pathophysiology? Cephalalgia, 2005. 25(6): p. 444-451.

Kelman, L., The triggers or precipitants of the acute migraine attack. Cephalalgia, 2007. 27(5): p. 394-402.

Kjærgaard, M., A. E. Eggen, E. B. Mathiesen and R. Jorde, Association Between Headache and Serum 25-Hydroxyvitamin D; the Tromsø Study: Tromsø 6. Headache: The Journal of Head and Face Pain, 2012. 52(10): p. 1499-1505.

Kokavec, A., Migraine: A disorder of metabolism? Medical hypotheses, 2016. 97: p. 117-130.

Krusz, J., J. Albright, and J. Cagle, Vitamin D levels in migraine and headache patients compared to patients with pain disorders. Headache, 2010. 50: p. S24-S25.

Lampl, C., M. Rudolph, C. I. Deligianni and D. D. Mitsikostas, Neck pain in episodic migraine: premonitory symptom or part of the attack? The journal of headache and pain, 2015. 16(1): p. 80.

Launer, L.J., G.M. Terwindt, and M.D. Ferrari, The prevalence and characteristics of migraine in a population-based cohort The GEM Study. Neurology, 1999. 53(3): p. 537-537.

Littlewood, J., V. Glover, P. Davies, C. Gibb, M. Sandler and F. C. Rose, Red wine as a cause of migraine. The Lancet, 1988. 331(8585): p. 558-559.

Loder, S., H.U. Sheikh, and E. Loder, The prevalence, burden, and treatment of severe, frequent, and migraine headaches in US minority populations: statistics from National Survey studies. Headache: The Journal of Head and Face Pain, 2015. 55(2): p. 214-228.

Mancia, G., E. A. Rosei, E. Ambrosioni, F. Avino, A. Carolei, M. Dacco, G. Di Giacomo, C. Ferri, I. Grazioli and G. Melzi, Hypertension and migraine comorbidity: prevalence and risk of cerebrovascular events: evidence from a large, multicenter, cross-sectional survey in Italy (MIRACLES study). Journal of hypertension, 2011. 29(2): p. 309-318.

Martin, V.T. and B. Vij, Diet and headache: part 2. Headache: The Journal of Head and Face Pain, 2016. 56(9): p. 1553-1562.

Matías-Guiu, J., J. Porta-Etessam, V. Mateos, S. Díaz-Insa, A. Lopez-Gil and C. Fernández, One-year prevalence of migraine in Spain: a nationwide population-based survey. Cephalalgia, 2011. 31(4): p. 463-470.

Meneton, P., X. Jeunemaitre, H. E. de Wardener and G. A. Macgregor, Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. Physiological reviews, 2005. 85(2): p. 679-715.

Mollaoğlu, M., Trigger factors in migraine patients. Journal of health psychology, 2013. 18(7): p. 984-994.

Mottaghi, T., F. Khorvash, G. Askari, M. R. Maracy, R. Ghiasvand, Z. Maghsoudi and B. Iraj, The relationship between serum levels of vitamin D and migraine. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences, 2013. 18(Suppl 1): p. S66.

O'Brien, H., A. Hershey, M. Kabbouche, S. Powers, S. Cherney, S. LeCates, P. Vaughn, J. Bush, P. Manning and A. Segers, Prevalence of vitamin D deficiency among pediatric patients with recurrent headaches. in Headache. 2010. WILEY-BLACKWELL PUBLISHING, INC COMMERCE PLACE, 350 MAIN ST, MALDEN 02148 ….

Olesen, J., S. Evers, A. Charles, A. Hershey, R. Lipton, M. First, H. Bolay, M. Lante'ri-Minet and E.A. MacGregor, The international classification of headache disorders, (beta version). Cephalalgia, 2013. 33(9): p. 629-808.

Pogoda, J. M., N. B. Gross, X. Arakaki, A. N. Fonteh, R. P. Cowan and M. G. Harrington, Severe headache or migraine history is inversely correlated with dietary sodium intake: NHANES 1999–2004. Headache: The Journal of Head and Face Pain, 2016. 56(4): p. 688-698.

Prakash, S. and N.D. Shah, Chronic tension-type headache with vitamin D deficiency: casual or causal association? Headache: The Journal of Head and Face Pain, 2009. 49(8): p. 1214-1222.

Qujeq, D., M. Zandemami, A. A. Ahanger and M. E. Shahabadin, Evaluation of intracellular magnesium and calcium concentration in patients with migraine. Neurosciences, 2012. 17(1): p. 85-86.

Rajeh, S. A., A. Awada, O. Bademosi and A. Ogunniyi, The prevalence of migraine and tension headache in Saudi Arabia: a community-based study. European Journal of Neurology, 1997. 4(5): p. 502-506.

Rasmussen, B.K. and J. Olesen, Migraine with aura and migraine without aura: an epidemiological study. Cephalalgia, 1992. 12(4): p. 221-228.

Rasmussen, B.K., Migraine and tension-type headache in a general population: precipitating factors, female hormones, sleep pattern and relation to lifestyle. Pain, 1993. 53(1): p. 65-72.

Scher, A., G. Terwindt, H. Picavet, W. Verschuren, M. Ferrari and L. Launer, Cardiovascular risk factors and migraine: the GEM population-based study. Neurology, 2005. 64(4): p. 614-620.

Semiz, M., İ. A. Şentürk, H. Balaban, A. K. Yağız and Ö. Kavakçı, Prevalence of migraine and co-morbid psychiatric disorders among students of Cumhuriyet University. The journal of headache and pain, 2013. 14(1): p. 34.

Siddiqui, A.M. and H.Z. Kamfar, Prevalence of vitamin D deficiency rickets in adolescent school girls in Western

region, Saudi Arabia. Saudi medical journal, 2007. 28(3): p. 441-444.

Silberstein, S.D., Migraine symptoms: Results of a survey of self-reported migraineurs. Headache: The Journal of Head and Face Pain, 1995. 35(7): p. 387-396.

Steiner, T. J., G. L. Birbeck, R. H. Jensen, Z. Katsarava, L. J. Stovner and P. Martelletti, Headache disorders are third cause of disability worldwide. 2015.

Taylor, F.R., Lifestyle changes, dietary restrictions, and nutraceuticals in migraine prevention. Techniques in Regional Anesthesia & Pain Management, 2009. 13(1): p. 28-37.

Thys-Jacobs, S., Alleviation of migraines with therapeutic vitamin D and calcium. Headache: The Journal of Head and Face Pain, 1994. 34(10): p. 590-592.

Thys-Jacobs, S., Vitamin D and calcium in menstrual migraine. Headache: The Journal of Head and Face Pain, 1994. 34(9): p. 544-546.

Tietjen, G. E., N. A. Herial, J. Hardgrove, C. Utley and L. White, Migraine comorbidity constellations. Headache: The Journal of Head and Face Pain, 2007. 47(6): p. 857-865.

Togha, M., S. Razeghi Jahromi, Z. Ghorbani, F. Martami and M. Seifishahpar, Serum Vitamin D Status in a Group of Migraine Patients Compared With Healthy Controls: A Case–Control Study. Headache: The Journal of Head and Face Pain, 2018. 58(10): p. 1530-1540.

Vos, T., R. Barber, B. Bell, A. Bertozzi-Villa, S. Biryukov, I. Bolliger, F. Charlson, A. Davis, L. Degenhardt and D. Dicker, Global Burden of Disease Study 2013 Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet, 2015. 386(9995): p. 743-800.

Wheeler, S.D., Vitamin D Deficiency in Chronic Migraine: S33. Headache, 2008. 48: p. S52-S53.

Wöber, C., J. Holzhammer, J. Zeitlhofer, P. Wessely and Ç. Wöber-Bingöl, Trigger factors of migraine and tension-type headache: experience and knowledge of the patients. The journal of headache and pain, 2006. 7(4): p. 188-195.

Yin, P., V. Anttila, K. M. Siewert, A. Palotie, G. Davey Smith and B. F. Voight, Serum calcium and risk of migraine: a Mendelian randomization study. Human molecular genetics, 2016. 26(4): p. 820-828.

Zandifar, A., M. Banihashemi, F. Asgari, N. Manouchehri, H. Ebrahimi, F. Haghdoost and M. Saadatnia, Vitamin D status in migraine patients: a case-control study. BioMed research international, 2014. 2014.