PHARMACIA

Pharmacia 70(4): 927–933
DOI 10.3897/pharmacia.70.e103131

Research Article

Comparison of C-reactive protein, D-dimer, vitamin D and magnesium serum levels between migraineurs and tension-type headache sufferers

Khairul Putra Surbakti[1], Eka Mahendrayana[1], Chairil Amin Batubara[1]

1 *Department of Neurology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia*

Corresponding author: Khairul Putra Surbakti (khairul.putra@usu.ac.id)

Received 7 March 2023 ♦ **Accepted** 17 August 2023 ♦ **Published** 3 October 2023

Citation: Surbakti KP, Mahendrayana E, Batubara CA (2023) Comparison of C-reactive protein, D-dimer, vitamin D and magnesium serum levels between migraineurs and tension-type headache sufferers. Pharmacia 70(4): 927–933. https://doi.org/10.3897/pharmacia.70.e103131

Abstract

Headaches, especially migraines and tension-type headaches (TTH), are among the most prevalent problems encountered in neurology and medicine. Ongoing debate surrounds the pathophysiological mechanisms behind this condition. One of the potential ideas involves inflammation and diet. The purpose of the study was to compare the serum levels of C-reactive protein (CRP), D-dimer, vitamin D and magnesium in 23 migraineurs and 23 TTH-diagnosed sufferers. The CRP level (4.8±3.7 mg/L) was found to be significantly different between migraineurs and TTH sufferers, with a significant difference (p=0.03) between the two groups of headache sufferers. Vitamin D serum levels (19.5±7.9 ng/L) and TTH serum levels (26.7±8.4) were observed to differ significantly. Magnesium serum levels (p=0.692) did not differ significantly between the two headache patient groups.

Keywords

Migraine, tension-type headache, inflammatory markers, vitamin D

Introduction

Headaches are experienced by almost everyone around the world at least once in their lifetime. Headache included nine cases that brought sufferers to see a doctor and it was found that at least 40% of the consultations with a neurologist were due to headache. Headache is an uncomfortable sensation felt in the head area due to anything that damages or has the potential to cause structural damage. The area includes intracranial and extracranial (including the face) which indeed have many pain-sensitive structures (Rizolli and Mullally 2018).

Headaches are broadly divided into primary and secondary headaches. Primary headaches are headaches that are not caused by structural abnormalities in the intracranial, on the contrary secondary headaches indicate abnormalities in intracranial structures. Primary headaches make up most of the overall headaches and the most common are migraines and tension type headaches (TTH). Migraine has a prevalence of 15% of the entire population and the highest prevalence is owned by TTH as much as 60–80% (Ahmed 2012; Rizolli and Mullally 2018).

There is currently a view that migraine is closely related to the inflammatory process with the release of inflammatory

agents in the activation and sensitization of peripheral nociceptors. Elevated levels of inflammatory markers can provoke trigeminal nerve activation and vasoactive neuropeptide releases that contribute to inflammation (Martami et al. 2018). Inflammatory markers that are often and easily studied include C-reactive protein (CRP), neutrophil-to- lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and monocyte-to-lymphocyte ratio (MLR) and D- dimer. A study by Saricam found a significant increase in inflammatory markers such as CRP, NLR, PLR, and MLR in migraineurs compared to controls. However, no significant results were obtained on other hematological parameters such as hemoglobin, leukocytes and platelets (Saricam 2020). A study conducted by Yucel et al. in 2014 found an increase in inflammatory markers such as CRP and D-dimer in migraineurs (Yucel et al. 2014). Yildiz and Koca in 2019 found that CRP increased significantly in the migraine group compared to healthy individuals as the control group (Yildiz and Koca 2018). Geng et al. 2022 in a systematic review and meta-analysis found a higher CRP, IL-1β, TNF-α in migraine patients compared with healthy controls. In the pathophysiology of TTH, there is also a hypothesis about central and peripheral sensitization which is characterized by repeated pain and stress that will cause a decrease in the pain threshold. The effects of systemic or local inflammation on TTH are still not fully understood. Research conducted by Ozdemir and Donder in 2021 showed that there were significant differences in NLR and PLR in TTH sufferers compared to the control group. Another marker of inflammation found to be increased, namely CRP (Ozdemir and Donder 2021).

Vitamin D deficiency is associated with chronic pain, depression and several neurological disorders. The brain has many vitamin D receptors and there is evidence of a non-skeletal role for vitamin D in inflammation and neurotransmitter metabolism. Vitamin D has also been associated with severe headaches in both migraine and TTH (Song et al. 2018). Vitamin D is synthesized in the skin by the effects of sunlight. This vitamin has two forms including cholecalciferol (Vitamin D3) which is synthesized in the skin and ergocalciferol (Vitamin D2) which is ingested from food and from supplements. Adequate synthesis of vitamin D3 or adequate consumption of food is essential for lifelong muscle and bone health. Vitamin D deficiency remains a widespread health problem arising from low intake of vitamin D from the diet and from reduced sun exposure associated with a sedentary lifestyle, excessive use of sunscreen creams and seasonal variations. Serum vitamin D levels are related to sun exposure (as determined by latitude, outdoor physical activity and sun-seeking or avoiding behavior), dietary intake and genetic components (Nowaczewska et al. 2020).

Migraine sufferers tend to avoid sunlight because of photophobia during attacks and low physical activity and long working hours are reported to increase the risk of headaches. Vitamin D is thought to play an important role in many physiological activities such as regulation of the immune system and resolution of inflammation, both of which are involved in the pathogenesis of migraine. The role of vitamin D on TTH has not been widely studied. Epidemiological studies show a strong association between low serum vitamin D levels and chronic musculoskeletal pain.

Chronic TTH sufferers experience muscle pain in both other body muscles and neck muscles. This supports the speculation of a relationship between vitamin D deficiency and TTH. In a study conducted by Elsayed et al. in 2019 found a significant decrease in vitamin D levels in migraineurs (TJ et al. 2018; Elsayed et al. 2020; Maier et al. 2020). On the other hand, a study conducted by Cagac in 2019 reported that TTH sufferers had a high incidence of vitamin D deficiency (Cagac 2019).

Magnesium is an important cation in the human body and is involved in several important functions such as enzyme activity, oxidative phosphorylation, protein and DNA synthesis, neuromuscular excitability and secretion of parathyroid hormone. Approximately 99% of total body magnesium is stored intracellularly in soft tissue and muscle (~40%) or is present as a bone component on the surface of hydroxyapatite crystals (~60%). The absorption of magnesium occurs mainly in the small intestine (and to a lesser extent in the large intestine) and depends on two distinct pathways namely passive paracellular and active transcellular transport. Passive paracellular transport facilitates bulk magnesium uptake and active transcellular pathways are responsible for mediating less magnesium uptake. Of all serum electrolytes, magnesium plays an important role in the conversion of vitamin D by hepatic 25-hydroxylation and renal 1α- hydroxylation to the active form 1,25-dihydroxyvitamin D. Magnesium deficiency causes a decrease in vitamin D levels. Supplementation Magnesium has been shown to significantly reduce resistance to vitamin D treatment and has been implicated in vitamin D-resistant rickets requiring magnesium supplementation. Magnesium also plays a key role in bone mineralization by influencing the synthesis of active vitamin D metabolites. Magnesium deficiency is found in sufferers with chronic medical conditions such as kidney failure, impaired liver function, diabetes, pre-eclampsia and eclampsia. Several studies have found a link between magnesium deficiency and headaches. In a case-control study of sufferers with migraine, serum magnesium levels were found to be reduced both ictal and interictal. In a study conducted by Samaie et al. in 2012 found that total serum magnesium levels in the group with migraine headache were not significantly different from the control group (1.86±0.41 mg/dl versus 1.95±0.35 mg/dl, p=0.224). But, serum total magnesium levels were notably lower in the group with these attacks compared to the control group (1.6±0.4 mg/dl versus 2.10±0.23 mg/dl, p<0.001) (Samaie et al. 2012). This study aims to determine whether there are differences in inflammatory markers especially CRP and D-dimer as well as vitamin D and magnesium serum levels among migraineurs and TTH sufferers.

Methods

Study design

This cross sectional study was carried out over a period of 5 months from February to June 2022 in the outpatient clinic at Adam Malik General Hospital Medan and Universitas Sumatera Utara Hospital after being approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara. We studied 23 migraineurs and 23 TTH sufferers aged 18 years or older diagnosed according to International Classification of Headache Disorders, third edition beta (ICHD-3 beta) (Headache Classification Committee of the International Headache Society (IHS) 2013). All subjects agreed to participate and signed informed consent voluntarily after receiving a detailed description of the study procedures and purposes. The exclusion criteria were sufferers with a history of malignancy, renal failure, liver disease, infection and inflammation, autoimmune disease, diabetes mellitus, use of vitamin D and magnesium supplements.

Blood collection

The venous blood samples were collected under complete aseptic conditions from all subjects included in the present study. A fresh serum aliquot for each subject was used for assay of serum CRP, D-dimer, vitamin D and magnesium. The serum levels of C-reactive protein and D-dimer were measured using Cobas 6000 C 501 analyzer. Vitamin D serum levels were measured using Diasorin Liaison analyzer and magnesium serum levels using Architec analyzer.

Migraine without aura is defined as a recurrent headache with at least 5 attacks lasting 4–72 hours, having at least two of the following characteristics: unilateral location, pulsating quality, moderate or severe pain intensity, condition aggravated by routine physical activity, accompanied by one of the following: and/or photophobia and phonophobia. Tension-type headache is defined as at least 10 episodes of attacks lasting at least <1 day per month or <12 days/year. The headache lasts 30 minutes to 7 days and there are at least 2 typical headache symptoms: typically bilateral, mild to moderate pressure or tightness and pain that does not increase with routine activity and, no nausea but photophobia or phonophobia may be present (Yeh et al. 2018).

Data analysis

To determine the differences CRP, D-dimer, vitamin D and magnesium serum levels between migraineurs and TTH sufferers, Mann-Whitney test was used. Descriptive analysis was used to determine the demographic characteristics of migraineurs and TTH sufferers at Adam Malik General Hospital Medan and Universitas Sumatera Utara Hospital. All data were expressed as mean±S.D. P<0.05 was considered to be significant.

Results

Characteristics of migraineurs and TTH sufferers as the subjects in this study based on sociodemographic that included gender, age, education, occupation, ethnicity and VAS score. The mean age of migraine sufferers was 39.1±15.1 years while in TTH sufferers the mean age was 43.6±15.5 years. In migraineurs and TTH sufferers, the maximum age range is 26–45 years as many as 14 sufferers (60.9%) in migraine while in TTH sufferers 10 sufferers (43.5%) as shown in following Table 1.

Table 1. Characteristics of migraineurs and tension-type headache sufferers.

Characteristics	Migraine n=23	TTH n=23
	n (%)	n(%)
Age (year), Mean (SD)	39.1(15.1)	43.6(15.5)
≤25 years	3(13.0)	4(17.4)
26–45 years	14(60.9)	10(43.5)
46–65 years	4(17.4)	8(34.8)
>65 years	2(8.7)	1(4.3)
Gender		
Female	21(91.3)	16(69.6)
Male	2(8.7)	7(30.4)
Education		
Bachelors	9(39.1)	5(21.7)
Senior High School	11(47.8)	10(43.5)
Middle school	3(13.0)	8(34.8)
Occupation		
Civil servants	5(21.8)	3(13.0)
Private employee	4(17.4)	5(21.7)
Self employee	1(4.3)	1(4.3)
Housewife	9(39.1)	9(39.1)
Farmer	1(4.3)	1(4.3)
Student	3(13.0)	4(17.4)
Ethnic group		
Bataknese	10(43.5)	10(43.5)
Malay	6(26.1)	7(30.4)
Javanese	5(21.7)	3(13.0)
Acehnese	2(8.7)	3(13.0)
VAS, Median (min-max)	4(3–6)	4(3–4)

SD=Standard deviation..

Inflammatory marker parameters assessed in this study were levels of CRP, and D-dimer. On examination, the average CRP serum level in migraineurs sufferers was 4.8±3.7 mg/l and in TTH sufferers it was found to be 2.1±1.8 mg/l. By using the Mann-Whitney test, it was found that there was a difference in the mean CRP levels between migraineurs and TTH sufferers (p=0.003).

In the D-dimer parameter of migraine sufferers, the average was 283.5±159.6 ng/ml and 222.2±137.1 ng/ml in TTH sufferers. In the assessment of the mean difference using the Mann- Whitney test, there was no difference in the mean levels of D-dimer in the two groups (p=0.116). Table 2 presents data on the mean differences in inflammatory markers in migraineurs and TTH sufferers. Fig. 1 and Fig. 2 showed the bar graphs of the mean differences of CRP and D-dimer, respectively between migraineurs and TTH.

Table 2. Differences in inflammatory markers in migraine and tension-type headache sufferers.

	Migraine, (Mean±SD)	TTH, (Mean±SD)	P
CRP (mg/L)	(4.8±3.7)	(2.1±1.8)	0.003*
D-dimer (ng/ml)	(283.5±159.6)	(222.2±137.1)	0.116*

*Mann-Whitney test; p<0.05.

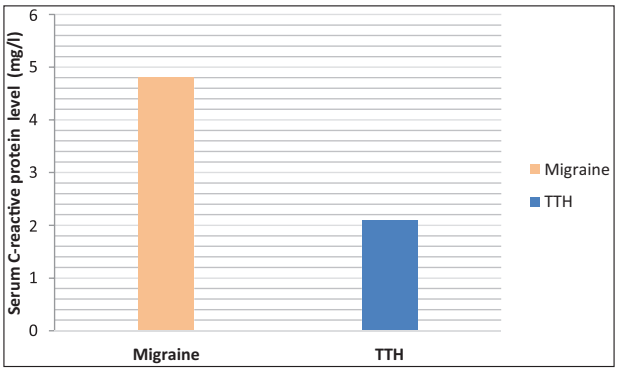

Figure 1. Serum C-reactive protein concentration (mean+S.D) in (mg/l) in migraineurs (yellow bar) was higher significantly than tension type headache patients (blue bar), using Mann-Witney test; (p<0.05).

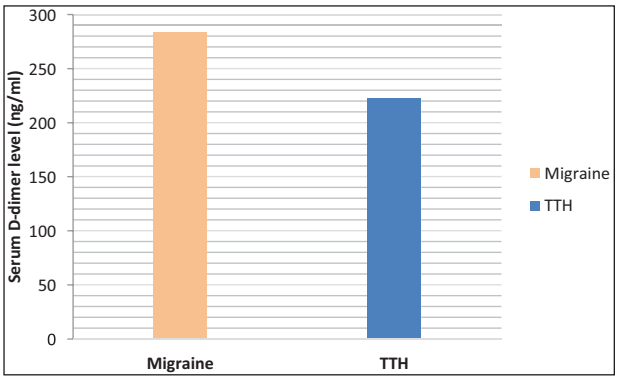

Figure 2. Serum D-dimer concentration (mean+S.D) in (ng/ml) showed no significant difference between Migraineurs (yellow bar) and tension-type headache patients (blue bar), using Mann-Whitney test analysis; p<0.05).

Examination of serum vitamin D levels in migraineurs sufferers showed an average of 19.5±7.9 ng/l, while in TTH sufferers it was found to be 26.7±8.4 ng/l. The assessment of differences in serum vitamin D levels in migraineurs and TTH sufferers used the Mann-Whitney test and the results showed that there were differences in serum vitamin D levels in the two groups (p=0.001). Data and bar graph on differences in Vitamin D levels in migraineurs and TTH sufferers can be seen in Table 3 and Fig. 3, respectively.

Examination of serum magnesium levels in migraineurs sufferers showed an average of 2.1±0.3 mEq/l and in TTH sufferers it was found to be 2.3±0.9 mEq/l. The Mann-Whitney test was used to see the difference in magnesium levels in the two groups and there was no difference in the mean magnesium content (p=0.692). Data and bar graph on differences in magnesium levels in migraine and TTH sufferers can be seen in Table 4 and Fig. 4, respectively.

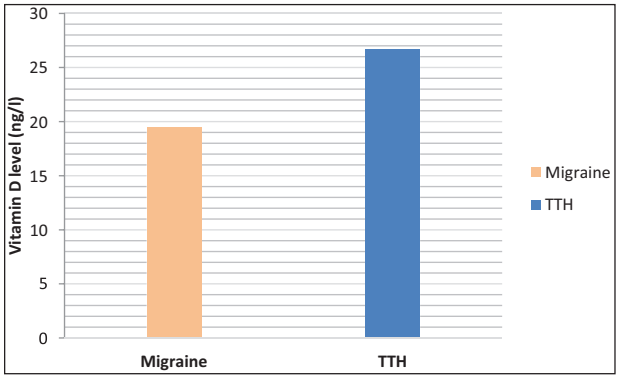

Figure 3. Serum Vitamin D concentration (mean±S.D) in (ng/l) was significantly higher in tension-type headache patients (blue bar) than in migraineurs, using Mann-Whitney test; p<0.05.

Table 3. Differences in vitamin D levels in migraine and tension-type headache sufferers.

Parameter	Migraine, Mean (SD)	TTH, Mean (SD)	p
Vitamin D (ng/L)	19.5 (7.9)	26.7 (8.4)	0.001*

*Mann-Whitney test; p<0.05.

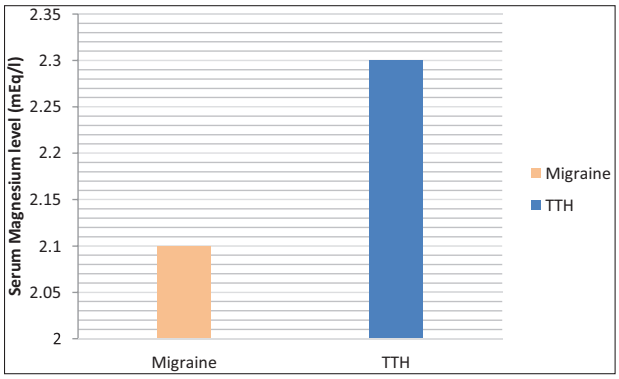

Figure 4. Serum Magnesium concentration (mean+S.D) in (mEq/l) showed no significant difference between Migraineurs (yellow bar) and tension-type headache patients (blue), using Mann-Whitney test ; p<0.05).

Table 4. Differences in magnesium levels in migraine and tension-type headache.

Parameter	Migraine, (Mean±SD)	TTH, Mean±SD)	p
Magnesium (mEq/l)	(2.1±0.3)	(2.3±0.9)	0.692*

*Mann-Whitney test; p<0.05.

Discussion

This research is descriptive analytic with cross sectional data collection method using primary data sources obtained from all migraineurs and TTH sufferers with the aim of knowing the differences in inflammatory markers of serum vitamin D and magnesium levels in migraineurs and TTH sufferers. Inflammatory marker parameters assessed were CRP levels, and D-dimer. The subjects who participated in the study were a total of 46 research subjects consisting of 23 migraineurs and 23 TTH sufferers who met the study inclusion criteria.

In terms of age characteristics, migraineurs in this study had a mean of (39.1±15.1) years, while TTH suffer-

ers had a mean of (43.6±15.5) years. The highest age range for migraineurs and TTH sufferers was at the age of (26–45) year range with 14 sufferers (60.9%) in migraineurs and 10 sufferers (43.5%) in TTH. This is in line with previous research which showed that the age of most migraine sufferers was in the (25–55) year range (Yeh et al. 2018). Migraine can appear from adolescence, young adulthood to pre-elderly age (Sproston and Ashworth 2018). Likewise, previous studies have shown the highest prevalence of TTH in the age range (30–49) years (Zivadinov et al. 2003). The prevalence of TTH can vary with age, some studies show that the prevalence increases from adolescence to around the age of 40 years and decreases thereafter and peaks in the thirty and forty years old (Yilmaz et al. 2021). The exact cause of the peak prevalence of migraine and TTH has not been ascertained but migraine and TTH are primary headaches that can arise in the presence of precipitating factors in the form of food, lifestyle, stress or other physical conditions (Sproston and Ashworth 2018).

In terms of gender characteristics, the most sufferers were found in women, both in migraineurs and TTH sufferers. This is in line with previous research conducted by Yilmaz et al. in 2021 and Arikan et al. in 2020 which showed that women suffer from migraines and TTH more compared to men (Martami et al. 2018; Yilmaz et al. 2021). Epidemiologically, both migraine and TTH are more common in women than men with a ratio of 3: 1. In a study conducted by Neumeier et al. in 2021 which highlighted the high prevalence of migraine and TTH in women, several things were found which can underlie such as the presence of comorbid diseases, response to treatment, response to pain and problems faced, anxiety and depression and hormonal factors (Neumeier et al. 2021).

Inflammatory marker parameters assessed in this study were levels of CRP and D-dimer. On examination, the average CRP level in migraineurs sufferers was (4.8±3.7) mg/l and in TTH sufferers it was found to be (2.1±1.8) mg/l. By using the Mann-Whitney test, it was found that there was a difference in the mean CRP levels between migraineurs and TTH sufferers (p=0.003). In a study that compared CRP levels in migraine sufferers to the control group and CRP levels in TTH sufferers to the control group, significant differences were found (Esa et al. 2006; Evrin and Katipoglu 2019). However, in a previous study conducted by Yilmaz et al. in 2021 found no significant difference in CRP levels in migraine sufferers and TTH (p=0.638) (Yilmaz et al. 2021). There have not been many studies comparing CRP levels in migraineurs and TTH sufferers. C-reactive protein is one of the acute phase proteins whose levels increase in the blood in acute infections as a nonspecific immune response and are also present in normal serum in very small amounts. Higher CRP concentrations may be indicative of acute infection or inflammation and are therefore often excluded in chronic inflammation studies (Luan and Yao 2018; Sproston and Ashworth 2018). Plasma CRP levels increase from about 0.1 mg/L to more than 0.5 mg/L in 24 hours - 72 hours from tissue damage such as trauma and progressive cancer (Sproston and Ashworth 2018). One of the factors underlying the occurrence of migraine is sterile inflammation of the cerebral vessels and the elevated CRP values reflect the inflammatory process. C-reactive protein also serves as an independent risk marker for cardiovascular morbidity, including ischemic stroke. Recent data suggest that migraine with aura increases the risk of ischemic stroke and myocardial infarction (Sproston and Ashworth 2018). Epidemiological studies have shown that CRP levels are slightly elevated in most populations, associated with a variety of lifestyles and diseases associated with the risk of atherosclerosis (Hagen et al. 2019).

In the D-dimer parameter of migraine sufferers, the average was (283.5±159.6) ng/ml and (222.2±137.1) ng/ml in TTH sufferers. In the assessment of the mean difference using the Mann- Whitney test, there was no difference in the mean levels of D-dimer in the two groups (p=0.116). In a study conducted by Yucel et al. in 2014 found an increase in D-dimer levels in migraine sufferers compared to controls, while research on D-dimer levels in TTH sufferers has not been found (Yucel et al. 2014). D-dimers are formed by plasmin mediated by fibrin degradation. In addition, elevated levels of fibrin degradation products, such as D-dimers, are commonly used in clinical practice as a marker of inflammation, increased coagulation activity, and a predictor of risk for thrombotic conditions (Ozdemir and Donder 2021). Normal D-dimer levels are <500 ng/ml and in this study were still within normal limits.

Migraine is associated with an increased risk of cardiovascular disease and a 2-fold increase in the risk of stroke (Avci et al. 2015). Repeated migraine attacks are also associated with arteriopathies of blood vessels, especially cranial blood vessels so that migraine is said to be a neurovascular disease associated with the occurrence of Cortical Spreading Depression (CSD), inflammation neurogenic and cranial vascular contractility dysfunction (Avci et al. 2015). C- reactive protein plays an important role in the immune response and is involved in the development and complications of atherosclerosis. Research shows that CRP is more than just a simple marker, it is also associated with possible implications in atherogenesis and directly affects vascular susceptibility through several mechanisms such as increasing local expression of adhesion molecules, decreasing endothelial nitric oxide bioactivity (Cozlea et al. 2013). The results of this study support the theory of neurovascular and inflammation in the pathophysiology of migraine which is higher than TTH.

Examination of serum vitamin D levels in migraineurs sufferers obtained an average of (19.5±7.9) ng/l, while in TTH sufferers it was found to be (26.7±8.4) ng/ml. The assessment of differences in serum vitamin D levels in migraineurs and TTH sufferers used the Mann-Whitney test and the results showed that there were differences in serum vitamin D levels in the two groups (p=0.001). In a study conducted by Elsayad et al. in 2020 found vitamin D levels in the migraineur group were significantly lower than the control group with (16.77±7.47) ng/l compared to (27.23±7.65) ng/l (p<0.001) (Elsayed et al. 2020). Likewise, in a study conducted by Song et al. (2018) which

found a deficiency of vitamin D is associated with an increase in the frequency of headaches per month in migraineurs (Song et al. 2018). While research on vitamin D levels in TTH sufferers has not been done much, however, a study by Prakash et al reported that TTH sufferers had a high incidence of vitamin D deficiency (Prakash et al. 2017). A previous study that assessed differences in vitamin D levels in migraineurs and TTH sufferers conducted by Yilmaz (2021) did not find a significant difference in the mean of vitamin D levels in migraineurs with a mean of (10.2±1.5) ng/l and in TTH sufferers of (13.3±5.8) ng/l with different results from this study (Yilmaz et al. 2021).

Serum vitamin D levels are related to sun exposure (as determined by latitude, outdoor physical activity and sun-seeking or avoiding behavior), dietary intake and genetic components. Migraine sufferers tend to avoid sunlight because of photophobia during attacks and low physical activity and long working hours are reported to increase the risk of headaches. Vitamin D is thought to play an important role in many physiological activities such as regulation of the immune system and resolution of inflammation, both of which are involved in the pathogenesis of migraine (Song et al. 2018).

Examination of serum magnesium levels in migraineurs sufferers found an average of (2.1±0.37) mEq/l and in TTH sufferers it was found to be (2.3±0.9) mEq/l. The Mann-Whitney test was used to see the difference in magnesium levels in the two groups and there was no difference in the mean magnesium content (p=0.692). In a study conducted by Samaie et al. (2012) found that total serum magnesium levels in the group with migraine headache were not significantly different from the control group (1.86±0.41 mg/dl versus 1.95±0.35 mg/dl, p=0.224). But, serum total magnesium levels were notably lower in the group with these attacks compared to the control group (1.6±0.4 mg/dl versus 2.10±0.23 mg/dl, p<0.001) (Samaie et al. 2012). Serum magnesium levels of TTH sufferers were significantly lower than control with (0.89±0.09) vs. (1.09±0.09) (p<0.001) (Maier et al. 2020). Meanwhile, no study has been conducted to compare the difference in magnesium levels between migraineurs and TTH sufferers. The average magnesium concentration in plasma is 0.75–1.0 mmol/l (1.5–2.1 mEq/l). From the results of this study, it can be seen that serum magnesium levels of headache sufferers are in the normal range. Magnesium balance in headache sufferers in the body depends on the intake and output of its metabolism. Sources of magnesium can be obtained from green leafy vegetables such as spinach and broccoli (which are rich in chlorophyll which contains magnesium), cereals, whole grains, nuts, bananas, meat, chocolate and fish. Magnesium is excreted in the urine and the kidneys play a major role in magnesium homeostasis and maintenance of plasma magnesium concentrations. The state of low magnesium intake can cause hypomagnesaemia and the state of high intake and lack of magnesium excretion can cause hypermagnesemia. Magnesium can increase with the consumption of drugs such as antacids containing magnesium or excessive laxatives, excessive salt water and kidney failure (Seo and Park 2008). The normal state of magnesium in this study may be due to adequate magnesium intake or use of antacid or laxative drugs contains magnesium oxide which may be widely used by research subjects because migraines can be accompanied by complaints of nausea and vomiting (Wakai et al. 2019).

Conclusion

In the present study, there was found a significant difference in the mean serum CRP and vitamin D levels between migraine sufferers with TTH, while the D-dimer and serum magnesium levels were not significantly different. The results of this study support the theory of neurovascular and inflammation in the pathophysiology of migraine, whereas the vitamin D is thought to play an important role in many physiological activities such as regulation of the immune system and resolution of inflammation, both of which are involved in the pathogenesis of migraine. The relationship between migraine and inflammation should be further studied, and future research should focus on anti-inflammatory drugs in the treatment of migraine in order to improve clinical symptoms of migraine patients.

References

Ahmed F (2012) Headache disorders: differentiating and managing the common subtypes. British Journal of Pain 6: 124–132. https://doi.org/10.1177/2049463712459691

Avci A, Lakadamyali H, Arikan S, Benli U, Kilinc M (2015) High sensitivity C- reactive protein and cerebral white matter hyperintensities on magnetic resonance imaging in migraine patients. The Journal of Headache and Pain 16: 1–10. https://doi.org/10.1186/1129-2377-16-9

Cagac A (2019) The relationship between vitamin D deficiency and chronic tension type headache. Eastern Journal of Medicine 2: 535–539. https://doi.org/10.1016/j.jns.2019.10.719

Cozlea D, Farcas D, Nagy A, Keresztesi A, Tifrea R, Cozlea L, Carasca E (2013) The impact of C-Reactive Protein on global vascular risk on sufferers with coronary artery disease. Current health science journal 39: 1–7.

Elsayed D, Amin K, Elsayed I, Hashim N (2020) Elucidation of the levels of vitamin D, calcium, and magnesium sufferers: a case control study. The Egyptian Journal of Neurology, Psychiatry and Neurosurgery 56: 1–9. https://doi.org/10.1186/s41983-020-00174-3

Esa T, Aprianti S, Arif M, Hardjoeno (2006) Nilai rujukan hematologic pada orang sehat berdasarkan Sysmex XT 1800 i. Indonesian Journal of Clinical Pathology and Medical Laboratory 12: 127–130. https://doi.org/10.24293/ijcpml.v12i3.875

Evrin T, Katipoglu B (2019) Evaluation of haematological parameters in migraine attack in emergency room. Annals of Medical Research 26: 1384–1387. https://doi.org/10.5455/annalsmedres.2019.04.215

Geng C, Yang Z, Xu P, Zhang H (2022) Aberration in peripheral inflammatory cytokine levels in migraine: A systematic review and meta-analysis. Journal of Clinical Neuroscience 98: 213–218. https://doi.org/10.1016/j.jocn.2022.02.026

Hagen K, Stovner L, Nilsen K, Kristoffersen E, Winsvold B (2019) The impact of C-reactive protein levels on headache frequency in the HUNT study 2006–2008. BMC Neurology 19: 1–8. https://doi.org/10.1186/s12883-019-1462-8

Headache Classification Committee of the International Headache Society (IHS) (2013) The International Classification of Headache Disorders 33: 629–808. https://doi.org/10.1177/0333102413485658

Luan Y, Yao Y (2018) The clinical significance and potential role of C-reactive protein in chronic inflammatory and neurodegenerative diseases. Frontiers in Immunology 9: 1–11. https://doi.org/10.3389/fimmu.2018.01302

Maier J, Pickering G, Giacomoni E, Cazzaniga A, Pallegrino P (2020) Headaches and magnesium: mechanisms, bioavailability, therapeutic efficacy and potential advantage of magnesium pidolate. Nutrients 12: 1–14. https://doi.org/10.3390/nu12092660

Martami F, Razeghi Jahromi S, Togha M, Ghorbani Z, Seifishahpar M, Saidpour A (2018) The serum level of inflammatory markers in chronic and episodic migraine: a case-control study. Neurological Sciences 39: 1741–1749. https://doi.org/10.1007/s10072-018-3493-0

Neumeier M, Pohl H, Sandor P, Gut H, Merki-field G, Andree C (2021) Dealing with headache: sex differencesin the burden of migraine and tension type headache. Brainsci 11: 1–11. https://doi.org/10.3390/brainsci11101323

Nowaczewska M, Wicinski M, Osinskinryk S, Kazmierczak H (2020) The role of vitamin D in primary headache–from potential mechanism to treatment. Nutrients 12: e243. https://doi.org/10.3390/nu12010243

Ozdemir H, Donder A (2021) Evaluation of neutrophil-to-lymphocyte ratio, platelets-to-lymphocyte ratio, and C-reactive protein in tension type headache patients. Journal of Neurosciences in Rural Practice 12: 566–570. https://doi.org/10.1055/s-0041-1730124

Prakash S, Rathore C, Makwana P, Dave A, Joshi H, Parekh H (2017) Vitamin D deficiency in sufferers with chronic tension-type headache: A case control study. Headache. The Journal of Head and Face Pain 57: 1096–1108. https://doi.org/10.1111/head.13096

Rizolli P, Mullally W (2018) Headache. The American Journal of Medicine 131: 17–24. https://doi.org/10.1016/j.amjmed.2017.09.005

Samaie A, Asghari N, Ghorbani R (2012) Blood magnesium levels in migraneurs within and between the headache attack: A case control study. Pan African Medical Journal 11: 1–3.

Saricam G (2020) Relationship between migraine headache and haematological parameters. Acta Neurologica Belgica: 1–8.

Seo W, Park T (2008) Magensium metabolism. Electrolyte Blood Press 6: 86–95. https://doi.org/10.5049/EBP.2008.6.2.86

Song T, Chu M, Sohn J, Ahn H, Lee S, Cho J (2018) Effect of vitamin D deficiency on the frequency of headaches in migraine. Journal of Clinical Neurology 14: 366–373. https://doi.org/10.3988/jcn.2018.14.3.366

Sproston N, Ashworth J (2018) Role of C-reactive protein at sites of inflammation and infection. Frontiers in Immunology 9: 1–11. https://doi.org/10.3389/fimmu.2018.00754

Wakai E, Ikemura K, Sugimoto H, Iwamoto T, Okuda M (2019) Risk factor for development of hypermagnesemia in sufferers prescribed magnesium oxide: a retrospective cohort study. Journal of pharmaceutical health care and science. Journal of Pharmaceutical Health Care and Sciences 5: 1–4. https://doi.org/10.1186/s40780-019-0133-7

Yeh Z, Blizzard L, Taylorq V (2018) What is the actual prevalence of migraine? Brain and Behavior 8: 1–6. https://doi.org/10.1002/brb3.950

Yildiz B, Koca T (2018) Is migraine an inflammatory event? Which inflammatory markers can we use for migraine? Annals of medical research 12: 973–975. https://doi.org/10.5455/annalsmedres.2018.12.300

Yilmaz M, Teker H, Bakkal T, Yilmaz A, Turkoglu S, Yildiz S (2021) Comparison of clinical and laboratory parameters in sufferers with migraine or tension type headaches: A case control study. Journal of Surgery and Medicine 5: 777–779. https://doi.org/10.28982/josam.948316

Yucel Y, Tunriverdi H, Arikanioglu A, Varol S, Kaplan I, Akil E (2014) Increase fibrinogen, D-dimer and galactine-3 levels in sufferers with migraine. Neurological Sciences 35: 545–549. https://doi.org/10.1007/s10072-013-1542-2

Zivadinov R, Willheim K, Sepic-Grahovac D, Jurjevic A, Bucuk M, Razmilic OB (2003) Migraine and tension type headache in Croatia: a population- based survey of precipitating factors. Cephalalgia 23: 336–343. https://doi.org/10.1046/j.1468-2982.2003.00544.x