

DETERMINANDO ENXAQUECA COM FATORES DESENCADEANTES DE AURA PARA MELHORAR A PRÁTICA: UM ESTUDO TRANSVERSAL DA ARÁBIA SAUDITA

DETERMINING MIGRAINE WITH AURA TRIGGER FACTORS TOWARD IMPROVING THE PRACTICE: A CROSS-SECTIONAL STUDY FROM SAUDI ARABIA

تحديد عوامل إثارة نوبات الصداع النصفي المصحوب بهالة لتحسين الممارسة العملية:
دراسة مقطعية على المملكة العربية السعودية

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RESUMO

Introdução: A cefaleia primária é uma das doenças mais comuns tratadas nas clínicas de neurologia. Globalmente, estima-se que a prevalência atual de transtorno de cefaleia em adultos sintomáticos, pelo menos uma vez no último ano, é de cerca de 50%. De acordo com o estudo do *Global Burden of Disease*, em 2015, a enxaqueca foi classificada como a terceira causa mais comum de deficiência em todo o mundo. Uma das enxaquecas significativas é a enxaqueca com aura, uma dor de cabeça frequente que ocorre após ou com distúrbios sensoriais. **Objetivo.** Este estudo teve como objetivo identificar e comparar os gatilhos em pacientes previamente diagnosticados com enxaqueca com aura (MwA) com aqueles que não foram identificados com enxaqueca com aura antes, mas diagnosticados de acordo com um questionário distribuído no Reino da Arábia Saudita (KSA). **Métodos:** Adultos com idade entre 18 e 50 anos foram selecionados aleatoriamente no Reino da Arábia Saudita para participar deste estudo transversal não intervencionista multicêntrico. Os dados do estudo foram coletados por meio de um questionário online usando os critérios de diagnóstico da Classificação Internacional de Distúrbios de Cefaléia 2018 e o questionário de cefaléia da Cleveland Clinic Canada. **Resultados e Discussão:** Dos 4.140 indivíduos potencialmente elegíveis, 302 não foram previamente diagnosticados com enxaqueca com aura, mas foram diagnosticados com um questionário (Grupo A), enquanto 71 participantes já foram diagnosticados (MwA) (Grupo B). Uma relação significativa foi encontrada entre MwA e estresse e ansiedade, distúrbios do sono, lugares barulhentos, exposição a muitas luzes, trabalho prolongado no computador, fome, jejum, estudo para exames e menstruação no Grupo A. O Grupo B experimentou todos os gatilhos anteriores além das mudanças climáticas, certos odores e o consumo de queijo, banana e cachorro-quente. **Conclusões:** Os fatores desencadeantes são comuns em indivíduos com MwA. O conhecimento desses gatilhos é essencial para prevenir as complicações graves de MwA, portanto, melhora a qualidade de vida dos pacientes.

Palavras-chave: enxaqueca com aura, dor de cabeça, Reino da Arábia Saudita, dor de cabeça primária, fatores desencadeantes

ABSTRACT

Background: Primary headache is one of the most common disorders treated in neurology clinics. Globally, it has been estimated that the current prevalence of headache disorder in adults symptomatic, at least once within the last year, is about 50%. According to the Global Burden of Disease Study 2015, migraine was ranked as the third most common cause of disability worldwide. One of the significant migraines is migraine with aura, a frequent headache that occurs after or with sensory disturbances. **Aim:** This study aimed to identify and compare triggers in previously diagnosed patients with migraine with aura (MwA) to those who have not been identified with migraine with aura before but diagnosed according to a questionnaire survey distributed in the Kingdom of Saudi Arabia (KSA). **Methods:** Adults aged 18–50 years were randomly selected in the Kingdom of Saudi Arabia to

participate in this non-interventional, multicentre, cross-sectional study. The study data was collected via an online questionnaire using the diagnostic criteria of the International Classification of Headache Disorders 2018 and the Cleveland Clinic Canada headache questionnaire. **Results and Discussion:** Of the 4.140 potentially eligible individuals, 302 were not previously diagnosed with migraine with aura but were diagnosed with a questionnaire (Group A), while 71 participants were already diagnosed (MwA) (Group B). A significant relationship was found among MwA and stress and anxiety, sleep disturbance, noisy places, exposure to lots of lights, prolonged computer work, hunger, fasting, studying for exams, and menstruation in Group A. Group B experienced all of the previous triggers in addition to weather changes, certain odors, and the consumption of cheese, bananas, and hotdogs. **Conclusions:** The trigger factors are common in individuals with MwA. Awareness of these triggers is essential for preventing the severe complications of MwA, hence, enhance the quality of life of patients.

Keywords: *migraine with aura, headache, Kingdom of Saudi Arabia, primary headache, trigger factors.*

الملخص البحثي:

مقدمة: يعد الصداع الأولي أحد أكثر الأمراض شيوعًا التي يتم علاجها في عيادات طب الأعصاب. على الصعيد العالمي، تشير التقديرات إلى أن معدل الانتشار الحالي لمرض الصداع لدى البالغين الذين تظهر عليهم الأعراض، مرة واحدة على الأقل خلال العام الماضي، يبلغ حوالي 50٪. وفقًا لدراسة العبء العالمي للأمراض لعام 2015، تم تصنيف الصداع النصفي على أنه ثالث أكثر أسباب الإعاقة شيوعًا في جميع أنحاء العالم. يعد الصداع النصفي المصحوب بالهالة أحد أهم أنواع الصداع النصفي، وهو صداع متكرر يحدث بعد أو مع اضطرابات حسية.

الهدف: هدفت هذه الدراسة إلى تحديد ومقارنة المحفزات في المرضى الذين تم تشخيصهم سابقًا بالصداع النصفي المصحوب بالهالة مع أولئك الذين لم يتم تشخيصهم بالصداع النصفي المصحوب بالهالة من قبل ولكن تم تشخيصهم وفقًا لاستبيان تم توزيعه في المملكة العربية السعودية.

الطريقة: تم اختيار البالغين الذين تتراوح أعمارهم بين 18 و 50 عامًا بشكل عشوائي في المملكة العربية السعودية للمشاركة في هذه الدراسة المقطعية غير التدخلية متعددة المراكز. تم جمع بيانات الدراسة عبر استبيان عبر الإنترنت باستخدام معايير التشخيص الخاصة بالتصنيف العالمي لاضطرابات الصداع 2018 واستبيان كليفلاند كلينك كندا.

النتيجة: من بين 4.140 فردًا، لم يتم تشخيص 302 شخصًا سابقًا على أنهم مصابون بالصداع النصفي المصحوب بالهالة، ولكن تم تشخيصهم عن طريق الاستبيان (المجموعة أ)، بينما تم بالفعل مشاركة 71 مشاركًا بالاستبيان وهم مشخصين سابقًا بالصداع النصفي مع هالة (المجموعة ب). تم العثور على علاقة كبيرة بين الصداع النصفي المصحوب بالهالة والتوتر والقلق واضطراب النوم والأماكن الصاخبة والتعرض للكثير من الضوء وعمل الكمبيوتر لفترات طويلة والجوع والصيام والدراسة للامتحانات والحيز في المجموعة الأولى. بالإضافة إلى التغيرات المناخية وبعض الروائح واستهلاك الجبن والموز والهوت دوج.

الختام: العوامل المحفزة للصداع النصفي شائعة لدى الأفراد المصابين بالصداع النصفي مع هالة. يعد الوعي بهذه المحفزات أمرًا ضروريًا لمنع المضاعفات الشديدة للصداع النصفي المصحوب بالهالة، وبالتالي تحسين نوعية حياة المرضى.

1. INTRODUCTION:

A primary headache is one of the most common disorders treated in neurology clinics (Wöber and Wöber-Bingöl, 2010). Globally, it has been estimated that the current prevalence of headache disorder in adults symptomatic, at least once within the last year, is about 50%. Worldwide, half to three-quarters of adults aged 18-65 had a headache, and at least 30 percent of these individuals, reported migraines. A primary headache is diagnosed depending on the defined standards in the International Headache Society categorization (Zenebe *et al.*, 2020 and Breslau *et al.*, 2001). According to data published by the World Health Organisation, tension headaches are considered the most common headaches. However, migraine constitutes the primary reason behind a large number of visitors to the neurology clinic. Various headaches cohabit among some sick people who do not meet the diagnostic

standards, while in some cases, they are concealing a secondary headache. Owing to this reason, consulting a doctor is recommended to apply the correct diagnosis and the suitable identified treatment (Andrasik *et al.*, 1982). As a result, the case does not apply to all patients.

In respect of tension headache, which is considered the most common type of headache, it has resulted from muscular tension on both napes of the neck and the forehead in general. And usually concurrent with stress periods. Such headaches lead to continuous tension or pressure (Amiri *et al.*, 2007; Wachholtz *et al.*, 2017). It resembles a helmet in terms of its primary occurrence on nape of the neck and the forehead, i.e., in both sides of the head. In many cases, palpation of the affected muscles might alleviate the pain. Generally speaking, the severity of the pain in tension headaches is frequently less disabling and reasonable than headache resulting from either migraine or secondary headaches

(Siegel *et al.*, 2017; Dueland, 2015). In general, the pain starts throughout the day, but its intensity increases in the afternoon. However, it might become acute, and it might last for a couple of days (Dwyer, 2018; Blumenfeld and Siavoshi, 2018).

Recurrent or repeated episodes of headache distinguish between migraine or acute headache. The severity might differ in the different episodes, but might be acute, when the patient asks for medical care. In general, the pain starts with one or other part of the head (hemicranial) until it covers the entire head. It is usually vibrant such as heartbeats and might be associated with vomiting, nausea, and a discomfort that becomes worse with noise (phonophobia), smells (osmophobia), and light (photophobia), (Matar *et al.*, 2015). The pain becomes worse with physical activity, enhances with rest, and might be caused by stress periods, climate changes, menstruation, fasting, some foods, hunger, or changes in sleep pattern (sleepless, or even more than usual) (Moghaddassi *et al.*, 2016).

2. REVIEW OF LITERATURE

2.1. Migraine

It might be caused by genetic heritage because it is commonly acceptable to notice that such a disease is associated with a migraine family history. An aura usually precedes a migraine attack, but it may also occur during the attack. It may appear without a headache and last for only four hours or several days. It might be provided as aura migraine (20%) — preceded by sensory, visual, motor, speech, or motor symptoms, or as migraine without aura (80%). Aura migraine patients might suffer from headache episodes with no aura (Wöber and Wöber-Bingöl, 2010; Silberstein *et al.*, 2016).

Migraine or severe headache is attributed to either recurrent or repeated episodes of headache. The severity might differ in the different episodes, but might be extreme, when the patient claims for medical care. In general, the pain starts with one or other side of the head (hemicranial) until it covers the entire head (Jackson *et al.*, 2015). Its speed resembles heartbeat and may be associated with both vomiting and nausea, besides the feeling of discomfort that becomes worse with noise (phonophobia), smells (osmophobia), and light (photophobia). It may become worse when the patient does exercise. Still, it enhances when the person takes a rest and might be stimulated by stress periods, sleep

pattern changes that is characterized by either taking insufficient amount of sleep or oversleeping, women period, fasting, climate changes, some foods, or hunger (Schain *et al.*, 2017).

It is worth mentioning that chronic disease occurs when a patient suffers from severe headache that lasts more than fifteen days each month might have tension or migraine. To clarify, eight patients meet migraine standards (Barnes, 2015). Approximately a small proportion of patients, 2.5% their case changes from episodic to the chronic form. The following points clarify the underlying reasons that develop this chronic disease, namely non-modifiable reasons - low economic status, a history of head traumas, or being a Woman -, and modifiable factors, such as the existence of 'fibromyalgia' or other painful symptoms, obesity, an increased frequency of stress, abuse of analgesic, stress, medication, depression, anxiety, caffeine abuse (Levy *et al.*, 2019; Jahromi *et al.*, 2018).

2.2. Trigeminal autonomic cephalalgia

Various cases with common clinical characteristics are unified together: one-sided pain existed in the area nourished by the trigeminal nerve and independent cranial symptoms, such as red-eye, watery eyes, nasal packing, congestion, facial sweating, or flow of liquid from the nose or rhinorrhea (Ashina *et al.*, 2015). They last for a short period and very severe headaches and have various episodes a day. The pain and the independent symptoms result from the activation of the trigeminal nerve and the parasympathetic nervous system due to the facial-trigeminal reflex in the brainstem or the pathological activation (Moghaddassi *et al.*, 2016). The hypothalamus is the brain region that acts as a producer that enhances such reflex.

2.3. Migraine with Aura

Migraine headache, either with or without aura, is considered the most common type of primary headache. Migraine considers a complicated disorder that involve various pathophysiological mechanisms like hypothalamic dysfunction revealed by a chronobiologic dysregulation, and a probable hyperdopaminergic state. In general, it starts from childhood or adolescence and might last for a long time. According to World Health Organization (2001) roughly 2–15% of the population of the world is influenced by Migraine with aura (MwA) and Migraine without aura (MA). Migraine is a common neurological disorder that is preceded by an aura

in approximately 20–30% of migraine patients. Migraine without aura (MA) is a phenomenon whose manifestations coincide with a wave of cortical spreading depolarization/depression (CSD) through the cerebral cortex. It is considered the most frequent one. Incidence figures revealed that severe migraine is commonly found among women of child-bearing age, primarily because of MwA.

The determination of stimulating factors is commonly recommended as a primary strategy in the treatment of migraine. Several external and internal factors engaged in migraine attacks. Various studies are compatible with: fasting, lack of sleep, and stress as the most common stimulator factors. However, other factors should be considered, such as excessive caffeine consumption, hormonal factors in women, and alcohol usage (Rocella *et al.*, 2019). Various stimulating factors might enhance headache attacks, such as milk and dairy products, sexual activity, head trauma, exhaustion, neck problems, traveling, posture, smoking, vegetables, nuts, and fruits. but there is not much scientific evidence on this issue (Hadjikhani and Vincent, 2019; Munjal *et al.*, 2018). Identifying stimulating factors might enable health professionals to manage the migraine headache and enhance the patient's quality of life (Vianna-bell *et al.*, 2019; Santangelo *et al.*, 2018). It is significant for patients with migraines to be well educated about all stimulating factors of migraine and management (Sen *et al.*, 2018). The health professional role in headache management might contain providing patients with information, headache history taking; and engaging with patients to make sure their compliance with their care program, complete an effect questionnaire, and to express and spread headache diaries (Lebedeva *et al.*, 2018; Ghanizada and Al-karagholi, 2019; Hospitalario *et al.*, 2020). Stimulating factors are significant in controlling migraine management because any negligence of these factors might reduce the frequency of headaches and increase patients' quality of life. Regardless of its significance, a minority of people aware of migraine stimulating factors in the Society (Frank *et al.*, 2020; Yeh *et al.*, 2018).

A widespread debilitating primary headache condition is called a migraine headache. It was ranked as the third most common cause of disability in both men and women under 50 years worldwide in the Global Burden of Disease Report 2015. Migraine patients with migraine without aura (MwoA) are usually characterized by unilateral position, pulsating

quality, mild to extreme strength, which can be exacerbated by routine physical activity and are correlated with nausea/or photophobia and phonophobia. It presents as chronic headaches lasting from 4 to 72 hours. Migraine with aura is characterized mainly by repeated attacks lasting only minutes, is accompanied by unilateral, entirely reversible symptoms of the visual, auditory, or another central nervous system that typically develop progressively, followed by migraine-related headache and symptoms. Common migraine triggers include extended periods of fasting, hypoglycemia, sleep disturbances, psychological stresses, hormonal changes, and certain medications. It is essential to know the triggers for a migraine headache so that attacks can be prevented. If left untreated, migraines can lead to serious complications, including stroke. A large-scale prospective epidemiologic study of the association between migraine and stroke in women found a non-random association of severe headaches and migraines with stroke. Furthermore, another study showed that women with MwA who take combined hormonal contraception had a 6-fold increased risk of ischemic stroke (Mph *et al.*, 2017),

The goal of this research was to identify trigger factors in patients previously diagnosed with MwA and compare them to patients in the Kingdom of Saudi Arabia (KSA). They were not diagnosed with MwA in the hospital but were diagnosed through the questionnaire.

3. MATERIALS AND METHODS:

This cross-sectional study included adults aged 18–50 years of both sexes who were randomly selected from the KSA population between 2018 and 2019. In total, 4,140 individuals were identified as potentially eligible study participants. Each individual was assessed for MwA Using the International Classification of Headache Disorders 2018 diagnostic guidelines and the type of the Cleveland Clinic Canada headache questionnaire (Appendix 1) with the comorbidity and secondary headache exclusion criteria at the start of the questionnaire. The patients were divided into two groups. The patients were divided into two groups. In group A, a total of 302 participants who were not MwA screened but whose health condition was diagnosed through questionnaire; And group B, a total of 71 participants patients with previous medical examination, who knew cases of MwA.

3.1. The Delphi approaches

The Delphi approach contains a questionnaire or interview schedule (Appendix 1) to a panel of 'informed people' in a particular field of application for taking their opinion or judgment on a specific issue. After that, the data are gathered, and another questionnaire (Appendix 1) is designed depending solely on the findings taken from the first application (Harteis and Hertrampf, 2010). Such a second questionnaire will be given to each participant required (in respect of the first phases findings), to retake their previous opinion and return their answers to the researcher. The purpose behind repeating the phases is to arrive at the final conclusion, i.e., the consensus of opinion, or a point of diminishing returns might be reached. As a result, the Delphi technique considers a multistage approach in which every stage depends on the previous one's findings (Harteis and Hertrampf, 2010). It resembles a highly organized meeting of experts, managed by a chairperson who is skilled in outlining the emotions of the meeting by clarifying the participants perspectives back to them in such a way that they enable them to improve further; the only variable is that the responses of the individuals are unfamiliar to one another (Harteis and Hertrampf, 2010; James and Cathain, 2019). There is crucial evidence in the literature that in the first phase of any Delphi investigation, a wide discrepancy of person's perspective is typical. However, after several repetitions, the subjects of the study are inclined to intersect towards unanimous. Regarded this as almost unavoidable, taking into account the use of the feedback-response loop. A significant issue among researchers thinking to employ the Delphi technique lies in comprehending the meaning behind 'unanimous.' It is recommended that this should be commensurate with 51% agreement among participants.

3.2. Ethics

This study was approved by the university Institutional Review Board (IRB) and was conducted in alignment with the ethical principles of the 1975 Declaration of Helsinki (as revised in 2000). The respondents supplied informed written consent. A special code for data storage protected by a password was provided to every respondent for data management and protection. It guaranteed the privacy of all data. Employing the Windows Statistical Kit for Social Sciences, statistical research was performed. Employing the chi-squared test, also categorical variables were contrasted.

3.3. Instruments

Generally speaking, the study employed two tools, namely: The List of Trigger Factors of Migraine (LTFM) and the Personal Information Form (PIF) (Appendix 1). Concerning the contents of the second tool so-called 'PIF' contained the cure for patients with migraine, headache characteristics, and sociodemographic. The study recorded the following: lifestyle data, biographic data, headache characteristics, medication, and general medical history, and the patients were asked about potential trigger factors of migraine. The following issues were covered in respect of lifestyle data: sleep, physical activity, consumption of alcohol, chocolate, smoking habits, and caffeine. On the other hand, biographic data covered the following issues: gender, age, number of children, marital status, profession, and education level.

3.4. Data Analysis

To analyse the demographic characteristics, descriptive statistics were used. Besides, the use of SPSS is essential for both statistical analyses and calculations. Data were presented as standard deviation (SD), means, range, and median. The essential statistical tests were used on the data revealing a normal distribution. The percentage was employed for tackling the distribution of stimulating factors among patients with migraines. The Chisquare test was employed to define the precise relationships that occur between the parameters of gender, age, migraine types, and stimulating factors. As a result, the p values of <0.05 were considered as significant.

3.5. Other relevant information

This research focused on undiagnosed cases of MwA among Saudis. Many trigger factors are common across multiple studies, but they may differ from between countries; thus, it is important to identify them to prevent serious complications. A general description about demographics including all parameters Region: (Eastern province Northern province, Central province, Western province, Southern province) and, sex (male and female), age (18-50), social status (Single and Married), job (Students, Ordinary Employee, Shifts worker/night-time worker, Unemployed), and alcohol, smoke, drugs, Beta-, propranolol, timolol, metoprolol, venlafaxine, amitriptyline, anticonvulsants, paracetamol and aspirin were also investigated.

Besides, trigger factors parameters as stress and anxiety, sleep, noisy place, lights, computer work, hungry, fasting, exams and menstruation were also investigated (supplementary material upon request).

4. RESULTS AND DISCUSSIONS:

4.1. Results

Of the 4.140 individuals enrolled in the study, 2.678 were excluded due to the presence of chronic disease or being on specific medication that could cause a secondary headache. A further 128 were excluded because a neurologist had already diagnosed them to have a primary headache other than MwA (Table 1).

In Group A, 302 participants have not previously been diagnosed with MwA by Questionnaire, they have MwA. In Group B, 71 participants had known cases of MwA and were diagnosed in hospital. The demographical data for both Groups A and B are shown in (Table 2). The Pearson correlation coefficient indicated a significant relationship between MwA in Group A, stress and anxiety, sleep disturbance, noisy places, exposure to lots of lights, prolonged computer work, hunger, fasting, studying for exams, and menstruation (Table 3). The Pearson correlation coefficient also revealed a significant relationship between MwA in Group B, studying for exams, stress and anxiety, sleep disturbance, noisy places, exposure to lots of lights, prolonged computer work, hunger, fasting, menstruation, weather changes, certain odors, and the consumption of cheese, bananas, and hotdogs (Table 4).

Concerning specific triggers for Group A, the Pearson correlation indicated no significant relationship with use of any drugs, being on a low-calorie diet, relaxation after a period of stress, weather changes, eating oranges, cheese, bananas, smoked fish, fast foods, hotdogs, chocolate, spicy foods, exposure to certain odors, smoking, sexual activity, drinking alcohol, decrease or increase the daily dose of caffeine, and exercise (all >0.05).

On the other hand, with Group B, the Pearson correlation indicated no significant relationship with use of drugs, being on a low-calorie diet, relaxation after a period of stress, eating oranges, smoked fish, fast foods, chocolate, spicy foods, smoking, sexual activity, drinking alcohol, decrease or increase daily dose of caffeine, and exercise (all $p > 0.05$).

Among the 373 subjects, 28% percent

reported using But it was diagnosed through a questionnaire. Group B, participants had a previous diagnosis of migraine with aura. When taking the drug, MwA lasted for only minutes in 53.9% of cases in group A and 70.4% of cases in group B, respectively. 18% reported receiving emergency injections, and 28% reported using naproxen to treat their MwA (Figure 1). When medication is taken, the MwA only lasted for minutes in 53.9% of cases in Group A and 70.4% of cases in Group B, respectively (Figure 2).

In this study, the common triggers for MwA in the KSA in Group A are: stress and anxiety, sleep disturbances, noisy places, exposure to lots of lights, prolonged computer work, hunger, fasting, studying for exams, and menstruation; and in Group B, they are: Study for exams, stress and anxiety, sleep disturbances, noisy places, exposure to lots of lights, prolonged computer work, hunger, fasting, menstruation, certain odors, and eating cheese, bananas, and hotdogs. Based on the data, it appears that those diagnosed with MwA are more likely to be aware of their trigger factors than someone who is undiagnosed. Therefore, clinical diagnosis and awareness of MwA are crucial to avoid the trigger factors to prevent serious complications of MwA that can affect one's quality of life.

4.2. Discussion

This study identified some trigger factors for MwA in the KSA. Earlier studies have focused on migraines in general but have not differentiated between the trigger factors associated with MwA and those associated with MwOA. The patients were divided into two groups: Group A, which included patients who have not been diagnosed with MwA but were diagnosed by the questionnaire, and Group B, which included patients who have known cases of MwA.

This study found no significant relationship between MwA in Group A and eating any kind of food. Still, on the other hand, there was a significant relationship between MwA in Group B and the consumption of cheese, bananas, and hotdogs. Previous studies have identified chemical triggers for migraines Theobromine, phenolic amines, octopamine, nitrites, nitric oxide, allergenic proteins, linoleic and oleic fatty acids, onosodium glutamate, tartrazine, aspartame, histamine, tyramine, and sulphites, including tyramine, phenylethylamine, theobromine. In certain forms of foods which can lead to migraines, these chemical causes have been identified (Zencirci, 2010; Al-shimmery, 2010). There are

also food allergies in some patients, which may explain why some foods act as triggers for MwA, especially because there has been a correlation between migraines and food allergies.

In this study, 185 patients from Group A and 55 patients from Group B developed MwA when fasting, with a significant relationship between fasting and MwA in both groups. Previous studies have shown that headaches after fasting are more common in patients with a history of chronic migraine (Zencirci, 2010; Al-shimmery, 2010). Fasting leads to changes in serotonin and norepinephrine levels, hypoglycemia, and increased stress hormone levels. Migraines are rarely associated with insulin-induced hypoglycemia in patients with diabetes; therefore, the role of decreased blood glucose has been questioned (Health, 2018).

Menstruation is a leading trigger factor for some patients. In this study, Group A and Group B both showed a significant relationship between having MwA and menstruation. In the literature, reports are suggesting that hormonal changes and a decrease in plasma oestradiol are triggers for migraine (Bergh, Amery, Ph, and Waelkens, 1987), (Lebedeva *et al.*, 2018). It was found that some patients are susceptible to MwA after sexual activity; however, there was no relationship between sexual activity and Group A and Group B, which is consistent with a previous finding that the prevalence of headache associated with sexual activity is more significant in patients with migraine. Some studies have shown that a low percentage of migraine patients consume alcohol due to previous experiences of alcohol acting as a trigger (Robbins *et al.*, 1993; Sen *et al.*, 2018). However, this study found no significant relationship with Group A or B; however, this may be due to the low number of patients who drink alcohol and not on a regular basis in our study.

It was observed no significant relationship between environmental triggers (weather and odors) and having MwA in Group A. On the other hand, Group B showed a significant relationship between environmental triggers. Previous research has suggested that patients who develop migraines after exposure to certain odors may have olfactory hypersensitivity (Biehl *et al.*, 2007; Ghanizada and Al-karaghali, 2019). A total of 143 and 46 patients in Group A and Group B, respectively, developed MwA after exposure to certain odors. One study showed that after the provocation of MwA using natural trigger factors, no patient developed attacks following photostimulation alone.

The literature has reported an association between weather and migraine changes in some patients (Tafari *et al.*, 2015). This research further corroborates this as 122 and 61 patients in Group A and B, respectively, developed MwA after exposure to weather changes, with a significant relationship in Group B.

Environmental noise is an essential trigger in some patients who have MwA. This study found that 225 and 54 patients in Group A and Group B, respectively, developed MwA when they are in noisy places, which aligns with another study that reported an increased risk of migraine in adults who experienced severe annoyance as a result of traffic and neighborhood noise (Academy *et al.*, 2013; Vianna-bell *et al.*, 2019).

This study found no significant relationship between exercise and having MwA in Group A and Group B, with only 35 patients from Group A and 39 patients from Group B developing MwA. However, a previous study has suggested that MwA can be triggered by physical activity in some patients (Munjal *et al.*, 2018).

There was also no significant relationship between water consumption in Group A and Group B and the development of MwA. Other researchers have shown that insufficient fluid intake could trigger MwA in some patients but could not explain the mechanism behind water intake and migraines (Silberstein *et al.*, 2016). Furthermore, there was significant relationship between sleep disturbance in Group A and Group B developing MwA. Previous studies have recognized a relationship between sleep and migraines. For example, in one study, 527 subjects developed MwA. They reported sleep disturbance as a trigger finding as 272 patients from Group A and 59 patients from Group B noticed a relationship between MwA and sleep disturbance.

Previous research suggests the relationship between stress and migraine (Hauge, Kirchmann, and Olesen, 2010). In the present study, 234 patients from Group A and 60 patients from Group B reported stress and anxiety to trigger MwA, with a significant relationship found in Group A. There was no significant relationship between relaxation after a period of stress and having MwA in Group A and Group B.

In regards to medication, one study stated that acute medication tends to be more effective if administered early in the attack (Jia *et al.*, 2017). While Group B patients are aware of their condition and may also be aware of their own trigger factors, they can take medication upon MwA onset, which may prevent its development.

However, Group A patients are not aware that they have a migraine so taking medication may be delayed.

The limitations of this study are the relatively small number of subjects who were diagnosed with MwA and small number of individuals who responded to certain triggers (e.g. drinking alcohol). Further studies are needed to examine each trigger factor individually with a larger sample size of patients with MwA in the Saudi population and compare it with MwoA.

5. CONCLUSIONS:

The recognition of headache stimulating factors in migraine patients might be an efficient strategy to avoid the improvement of migraine headaches from a global perspective. Patients treated for migraine are more prone to engage in disease self-management, implement promising findings, and have better life quality. The strategies of management strategies are available to deal with and avoid such headaches, and some headache sufferers achieve satisfactory management. Therefore, nurses and other health-care providers have to be prepared to evaluate and interfere in preventing or controlling the headache from patients with migraines, particularly those with MwA and MA. Medical staff might support patients to be well acquainted with all stimulating factors of migraine and management. The necessary self-management behavior is embedded in reducing headache stimulators to avoid migraine attacks, and patient-centered education has been revealed to manage acute disease efficiently.

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Table 1. The frequency and percentage of normal people and participants with headache

		Frequency	Percentage
Normal		961	65.7%
Unknown and diagnosed with migraine with aura by the questionnaire*		302	20.6%
Previously known case of headache	migraine with aura	71	4.8%
	migraine without aura**	61	4.1%
	Tension headache	67	4.5%
Total		1462	100%

* Group A, ** Group B

Table 2. Demographics in participants not previously diagnosed with Migraine with Aura but diagnosed by questionnaire (n=302) and participants previously diagnosed with Migraine with Aura (n=71)

Demographics		Group A (n=302)		Group B (n=71)	
		Frequency	Percent	Frequency	Percent
Region	Eastern province	92	30.5%	29	40.8%
	Northern province	43	14.2%	11	15.5%
	Central province	68	22.5%	10	14.1%
	Western province	64	21.2%	14	19.7%
	Southern province	35	11.6%	7	9.9%
Sex	Male	108	35.8%	19	26.8%
	Female	194	64.2%	52	73.2%
Age	18-25	163	54%	36	50.7%
	26-30	52	17.2%	15	21.1%
	31-35	41	13.6%	6	8.5%
	36-40	24	7.9%	8	11.3%
	41-45	14	4.6%	2	2.8%
	46-50	8	2.6%	4	5.6%
Social status	Single	190	61.3%	37	52.1%
	Married	112	37.1%	34	47.9%
Job	Students	142	47%	32	45.%
	Ordinary Employee	76	25.2%	16	22.5%
	Shifts worker/night-time worker	23	7.6%	7	9.9%
	Unemployed	61	20.2%	16	22.5%
Drink Alcohol	Yes	8	2.6%	3	1.4%

	No	294	97.4%	68	95.8%
Are you a smoker?	Yes	46	15.2%	10	14.1%
	No	256	84.8%	71	85.9%

Table 3. Trigger Factors for Group A participants (n = 302)

Trigger Factors	Number of patients who notes that		P-values
	There is a relationship	No relationship	
Stress and anxiety	234 (77.5%)	68 (22.5%)	< 0.0001
Sleep disturbance	272 (90.1%)	30 (9.9%)	< 0.0001
When you are in a noisy place	225 (74.5%)	77 (25.5%)	< 0.0001
When you see a lot of lights	209 (69.2%)	93 (30.8%)	< 0.0001
Prolonged computer work	229 (75.8%)	73 (24.2%)	< 0.0001
When you are hungry	168 (55.6%)	134 (44.4%)	0.006
When you are fasting	185 (61.3%)	117 (38.7%)	< 0.0001
Study for exams	139 (75.1%)	46 (24.9%)	< 0.0001
Menstruation	130 (67%)	64 (33%)	< 0.0001

Table 4. Trigger Factors for Group B participants (n = 71)

Trigger Factors	Number of patients who notes that		P-values
	There is a relationship	No relationship	
Stress and anxiety	60 (84.5%)	11 (15.5%)	< 0.001
Sleep disturbance	59 (83.1%)	12 (16.9%)	< 0.001
Study for exams	26 (81.3%)	6 (18.8%)	< 0.001
When you are in a noisy place	54 (76.1%)	17 (23.9%)	< 0.001
When you see a lot of lights	58 (81.7%)	13 (18.3%)	< 0.001
Weather changes	61 (85.9%)	10 (14%)	< 0.001
When you eat cheese	57 (80.3%)	14 (19.7%)	< 0.001
When you eat banana	62 (87.3%)	9 (12.7%)	< 0.001
When you eat hotdog	63 (88.7%)	8 (11.3%)	< 0.001
When you eat eggs	56 (78.8%)	8 (21.1%)	< 0.001
Menstruation	37 (71.2%)	15 (28.8%)	< 0.002
Prolonged computer work	50 (70.4%)	21 (29.6%)	< 0.001
Certain odors	46 (64.8%)	25 (35.2%)	< 0.001
When you are hungry	49 (69%)	22 (31%)	< 0.001
When you are fasting	55 (77.4%)	16 (22.5%)	< 0.001

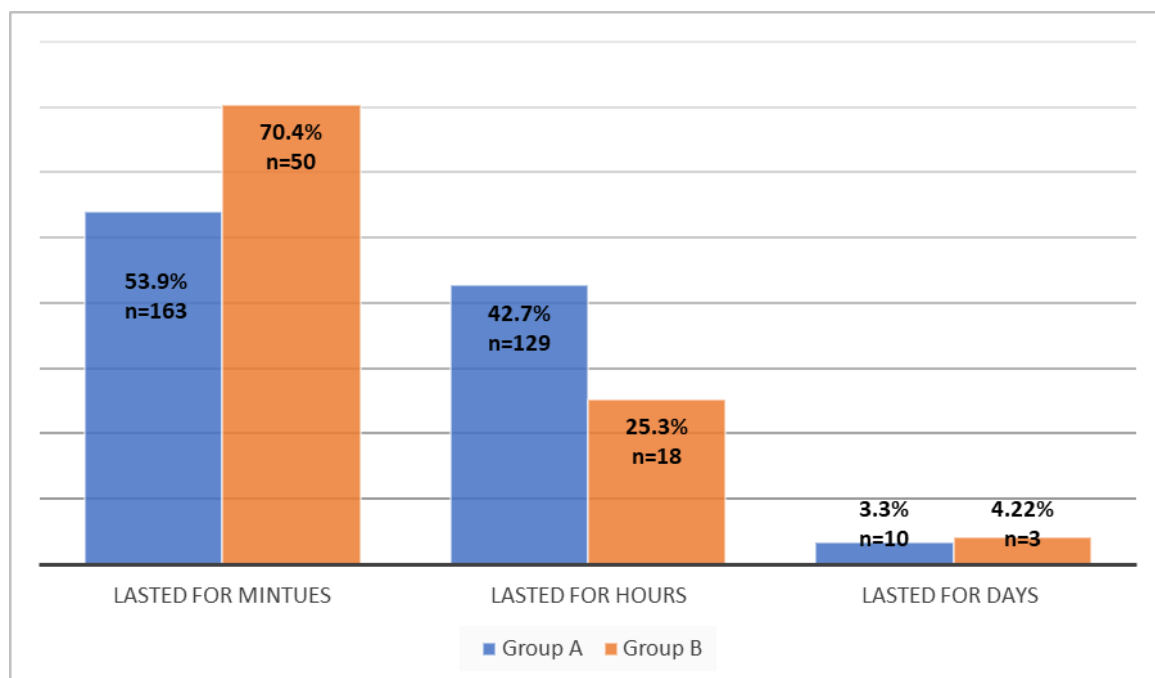


Figure 1. A comparison of headaches duration when a medication was used between groups A and B. Notes: Group A, participants were not previously diagnosed with migraine with aura but diagnosed by reseach questionnaire. Group B, participants with a previous diagnosis of migraine with aura.

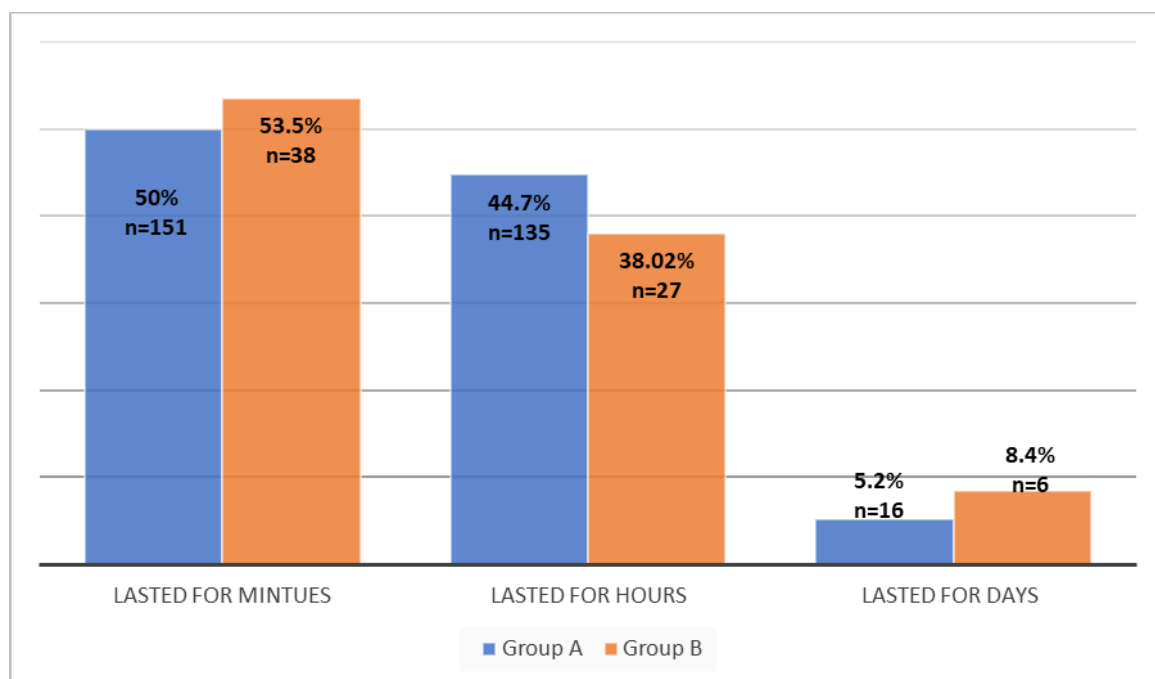


Figure 2. A comparison of headaches through medication was used between groups A and B. Notes: Group A, participants not previously diagnosed with migraines with aura but diagnosed by a research questionnaire. Group B, participants with a previous diagnosis of migraine with aura.

APPENDIX 1

Determining Migraine with Aura Trigger Factors, toward improving the practice: A cross-sectional study from Saudi Arabia (Questionnaire)

Do you agree to participate in this study? (all your information will be private)

- ☐ Yes
- ☐ No

Data collector name:

Region:

- ☐ Eastern province
- ☐ Northern province
- ☐ Central province
- ☐ Western province
- ☐ Southern province

Gender:

- ☐ Male
- ☐ Female

Age:

- ☐ 18-25
- ☐ 26-30
- ☐ 31-35
- ☐ 36-40
- ☐ 41-45
- ☐ 46-50

Social status:

- ☐ Single
- ☐ Married
- ☐ Divorced
- ☐ Widow

Your weight?

- ☐ My weight has been fairly stable (within 10 lbs) in my adult life

- My weight has been increase over the years
- My weight has gradually declined over the years
- My weight tends to fluctuate up and down

Your height?

Do you diagnosed before in neurology clinic with any of the following?

- Migraine headache without aura
- Migraine headache with aura
- Tension headache
- No I didn't diagnosed before

Did you suffer from headaches when you were younger?

- Child
- Teenager
- 20s-40s year of age
- 50s - 60 year of age

Was there a precipitating event or trigger for your current headache problem?

- None known
- Specific stress (mention it below and when)
- Injury (mention the type of injury and when below)
- motor vehicle accident (mention when below)
- Illness (mention what type of illness and when below)
- Menarche (first period)
- Pregnancy (mention how many children do you have and in which pregnancy you developed the headache below)
- Birth control pills (mention what type and when you start using it below)
- Hormonal replacement therapy (mention for how long you are using it)
- Other (mention it)

Do you have first degree family history of chronic headaches?

- Yes
- No

If yes mention the relative relation

Job:

- Students
- Ordinary Employee

- Shifts worker/night time worker
- Unemployed

Mention your job or your college:

How many hours you work daily?

- 2-6 hours
- 6-8 hours
- More than 8 hours
- More than 12 hours

How many hours you sleep daily?

- Between 2-5 hours
- Between 6-8 hours
- More than 9 hours

What's the pattern of your sleep?

- Regular sleep pattern
- Delayed or insufficient sleep / insomnia (including Intermittent sleep pattern)

Approximately, How many cup of water you drink daily?

- 1-2
- 3-4
- 5-6
- 6-9
- More than 10

How many main meals you eat daily?

- 1
- 2
- 3
- More than 3

How many cup of tea or coffee you drink daily?

- Nothing
- From 1-2
- From 3-4
- More than 5

Are you smoker?

- Yes
- No

If yes, how many cigarette per day?

Do you use any illegal drugs?

- Yes, daily
- Frequently
- No

Do you drink alcohol?

- Yes, daily
- Frequently
- No

If yes, how many glass per day?

How many times you go for exercise per week?

- No attacks
- 1-5 attacks
- 6-12 attacks
- More than 12 attacks

Do you have any chronic diseases? (You can choose more than 1)

- Diabetes
- Hypertension
- Asthma
- Sinusitis (pressure on your forehead, behind your eyes, on your cheeks, nasal discharge, fever)
- IBS or any GI problems
- Autoimmune diseases
- Congenital diseases
- Thyroid problems
- Psychiatric problems
- Cardiac problems
- Neurological problems
- Vision problems (having refractive errors without correction? Dryness?)

If yes, mention it please

Do you use any medication for long term in the last 6 months?

- Contraceptive pills

- Steroid
- Medications to enhance Weight loss medications
- Antidiabetic medications
- Antihypertensive medications
- Antacid or PPI
- Thyroid medications
- Antihistamine
- Hormonal replacement therapy

Others? Mention it please

Is your headache?

- Transit, in attacks
- Persistent

For how long you have headache attacks?

- Less than 1 month
- Less than 6 months
- More than 6 months
- More than 1 year
- More than 2 years
- More than 3 years

Headaches typically begin:

- Gradually
- Suddenly
- Varies

They usually begin in the

- Night
- Evening
- Afternoon
- Morning

How long before they reach maximal intensity

- Minutes
- Hours

Headaches usually last (with medication)

- Minutes
- Hours

- Days

Headaches usually last (without medication)

- Minutes
- Hours
- Days

Approximately How many attacks you have in the last 6 months:

- 5-7 attacks
- More than 8 attacks
- More than 15 attacks
- Less than 3 attacks
- No attacks

During your last 5 attacks, the headache was localized as:

- Left side
- Right side
- May be either side right or left
- Temple
- Behind eye(s)
- Back of head
- Neck
- Bilateral headache
- Start unilateral then bilateral
- Localized more in your forehead like a band

Do you have any of the following symptoms before 5-50 minutes from starting of the headache attack?

- Mood changes
- Personality changes
- Change in appetite
- Neck pain
- Food cravings
- Fatigue
- Numbness in any parts of you body
- Weakness in any part of your body
- Since of pin or niddle moving from part of your body, tongue, or face
- Seeing zigzag figure near your eyes, or stars
- Seeing points moving in front of you
- Nausea / vomiting

- Dizziness or vertigo
- Partial loss of vision / blurry vision / blindness (circle applicable)
- Paralysis
- No, I don't have these

How you can prescribe the nature of your headache?

- Pulsating
- tightening
- Stabbing
- Throbbing
- Pressure
- Burning
- Dull ache
- None of the above (mention it)

Do you experience any of the following during the attack? (you can choose more than one):

- Nausea
- Vomiting
- Photophobia (sensitivity to light)
- Phonophobia (sensitivity to sounds)
- Strong smells/odors bother you
- Dizziness / lightheadedness / vertigo (circle applicable description)
- Numbness or tingling
- Increased sensitivity of Scalp / Hair / Ears
- Eye tears
- Difficulty concentrating
- Runny or stuffy nose
- Mood changes / irritability

During a headache, what makes you feel the most comfortable

- Lying down / sleeping
- Keeping physically active
- Massage your head
- Cold pack on your head/neck
- Being in a dark quiet room
- Pacing back-and-forth
- Tying something around your head
- Hot pack on your head/neck

Duration of your headache attacks last for:

- ☐ Less than 4 hours
- ☐ 4-72 hours
- ☐ More than 72 hours

How it affects your daily life?

- ☐ Aggravated by routine physical activity such as walking or climbing stairs
- ☐ NOT Aggravated by routine physical activity such as walking or climbing stairs

Does it prevent you from doing your job?

- ☐ Yes
- ☐ No

How sever you can rate your pain?

- ☐ Mild – moderate in intensity
- ☐ Moderate – sever

What are you doing usually to relive your attacks and it works with you?

- ☐ Taking paracetamol
- ☐ Taking ibuprophen
- ☐ Emergency injection

If you take paracetamol or ibuprophen mention how many tablets you need to relive your headache attack

Rate the following from (0 to 2): 0 means no relationship, 1 means sometimes you notice, 2 means you usually notice that this thing trigger your headache).

Triggers	0	1	2
Stress and anxiety			
Sleep disturbance			
Study for exams			
Use any of the drugs mentioned above			
When you use low calorie diet			
When you in a noisy place			

When you see a lot of lights			
Relaxation after a period of stress			
Change in weather			
When you drink alcohol			
When you drink so much caffeine			
When you decrease your daily dose of caffeine			
When you increase your daily dose of caffeine			
When you eat hotdog			
When you are hungry			
When you eat fast food			
When you eat eggs			
When you eat spicy food			
When you eat smoked fish			
When you eat chocolate			
When you eat cheese, banana, orange			
Menstruation			
Exercise			
Prolonged computer work			

Certain oddrs			
Alcohol			
wine			
Sexual activity			
coughing			
Weather changes			

Do you have any other triggers didn't mention above?

- ☐ Yes
- ☐ No

If yes, mention it please

Thank you