International Journal of Basic & Clinical Pharmacology
Banday MS et al. Int J Basic Clin Pharmacol. 2020 Aug;9(8):1191-1198
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20203135

Original Research Article

Impact of trigger factors on clinical profile of migraine patients

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Received: 25 May 2020
Revised: 02 July 2020
Accepted: 03 July 2020

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ABSTRACT

Background: Migraine is a primary headache disorder. The study was designed to provide a better understanding of the potential role of triggers in the cause of migraine and their impact on its clinical profile and treatment protocol.
Methods: A prospective study was conducted between June 2018 to May 2020 in 323 patients suffering from migraine in out-patient department of neurology. Patients were labelled as migraine on the basis of simplified diagnostic criteria for migraine. A structured questionnaire was used to interview patients about triggers and correlated with various clinical variables.
Results: All patients had migraine without aura with males 30 (9.3%) and females 293 (90.7%). Episodic migraine found more than chronic daily headache. Trigger factors were present in 234 (72.4%) and absent in 89 (27.6%) patients. Common triggers were hot climate, emotional stress, lack of sleep and fasting. Common foods to precipitate an attack are tomatoes, cheese and collard greens. Mean duration of headache in patients with trigger factors is 5.67±4.99 years with a significant p value ($p<0.02$). Mean frequency of headache in trigger positive patients is 15.22±8.28 (days/month). Clinical symptoms significant in trigger positive patients are nausea ($p<0.0001$) (OR=3.94;95% CI=2.02-7.68),vomiting ($p=0.0001$) (OR=2.62;95% CI=1.50-4.59), photophobia ($p<0.0001$) (OR=2.69;95% CI=1.56-4.64), phonophobia ($p<0.0001$) (OR=5.16; 95% CI=2.54-47), pulsating headache ($p=0.006$) (OR=2.09; 95% CI=1.22-3.56), unilateral location ($p<0.0001$) (OR=2.88; 95% CI=1.74-4.77).
Conclusions: Triggers are not easily modifiable, and avoiding triggers may not be realistic. Healthy life style like exercise, adequate sleep, stress management and eating regularly may prevent triggers and transformation to chronification over time.

Keywords: Migraine, Headache, Trigger factors

INTRODUCTION

Migraine is a primary headache disorder. It is the second most common painful and incapacitating disorder in the world, afflicts approximately 15% of women and 6% of men over a one year period.[1] It has a global prevalence of around one in seven people.[2] According to global burden of disease study, it ranks as the seventh most common cause of disability worldwide, rising to the most common cause in the age of under 50.[3] Migraine is an important cause of reduced health related quality of life and has a significant and negative personal, societal and economic burden and is often underdiagnosed, misdiagnosed (e.g. in sinusitis) and undertreated in both primary and secondary care perhaps in part because there are no biological markers to confirm the diagnosis.[4-8] The latest version of the international headache society's international classification of headache disorders

ICHD-III (beta) (headache classification committee of the international headache society, 2013 classifies migraine as migraine without aura, migraine with aura, chronic migraine, complications of migraine, probable migraine, and episodic syndrome that may be associated with migraine.[9] A simplified diagnostic criteria for migraine is quite reproducible which mentions as repeated attacks of headache lasting 4-17 hours in patients with a normal physical examination, no other reasonable cause for the headache and at least 2 of the these features as unilateral pain, throbbing pain, aggravation by movement, moderate or severe intensity plus at least one of the features like nausea/vomiting, photophobia and phonophobia.[1]

Clinical understanding and the definition of chronic migraine (CM) have evolved over time. In ICDH-3b, CM is broadly defined as migraine experienced greater than or equal to 15 days/month for more than 3 months with migrainous features, whereas in episodic migraine (EM) headache frequency lasts less than 15 days/month.[9] Migraine attacks usually occur in response to identifiable triggers.[10] Headache triggers have been defined as factors that alone or in combination, induce headache attacks in susceptible individuals.[11] Triggers (also called precipitating factors) usually precede the attack by less than 48 h. Headache can be initiated or amplified by various triggers, including stress and negative emotions; hormonal factors for females; flicker, glare and eyestrain; noise; odours; hunger and consumption of certain foods and alcohol; weather; fatigue; and lack of sleep. The knowledge about migraine triggers is important for proper management of the patients. Trigger avoidance is sometimes referred to as 'headache hygiene'. There is paucity of studies in different ethnic populations of India to identify various triggering factors depending on diverse dietary habits.[12] The study was designed with an objective to provide a better understanding of the potential role of triggers in the cause of migraine and to emphasize strategy of avoiding or coping with dietary and other migraine triggers before initiating long term drug therapy. In addition, migraine triggers were correlated with various clinical variables to understand the link between the trigger factors and headache in order to yield evidence based therapeutic approach in management protocol.

METHODS

A prospective study was conducted between June 2018 to May 2020 in 323 patients suffering from migraine in outpatient department of neurology in Sheri Kashmir Institute of Medical Sciences Soura, a 750 bedded multispecialty tertiary care teaching hospital. The study received an approval from Institutional Ethics Committee. Patients were labeled as migraines on the basis of simplified diagnostic criteria for migraine adapted from international headache society classification (headache classification committee of the international headache society 2013) patients were enrolled in the study after an informed written consent. A structured self-designed questionnaire was used to interview the patients clinically diagnosed as migraine for evaluation of endogenous (stress, negative emotions; hormonal factors for females) and exogenous (flicker, glare, eyestrain, noise, odour, hunger and consumption of certain foods and alcohol, weather, fatigue, and lack of sleep) triggers. Inclusion criteria included subjects aged 18-65 years with migraine without aura and migraine with aura. In exclusion criteria subjects with medication overuse headaches and other type of headaches were excluded. Detailed clinical history was taken in all patients and a clinical examination with specific reference to central nervous system (CNS) examination like Romberg's sign, tandem gait, drift of outstretched hands, finger-nose test, finger dexterity, binocular visual fields, to confrontation, eye movements, facial weakness, pupillary responses and Horner's syndrome, tendon reflexes and plantar responses and fundoscopy was carried out. The location of headache, total duration of migraine, its frequency per month and associated clinical presentation were also noted. Investigations like CT head and MRI brain was advised in some patients who did not respond to the initial treatment.

Statistical analysis

The data was analyzed by using statistical package for social sciences 22 program (SPSS Inc, Chicago, IL, USA). Fisher's exact test is used to identify the significant clinical symptoms with respect to trigger. The odds ratios (OR) and 95% confidence intervals (CI) were calculated to evaluate the measure of association between clinical variables and trigger factors. Descriptive statistics of clinical symptoms, triggering factors and other numeric variables is reported for an overview description of parameters. Independent sample t-test is employed, to assess the significance of age of patients (years), duration (years) and frequency of headache (days/month) between trigger positive and trigger negative patients. The level of significance was set at less than 0.05 for all analyses. Results were given as mean±SD.

RESULTS

The study included 323 patients of migraine among which males were 30 (9.3%) and females were 293 (90.7%). The mean age of males is 38.80±17.53 years and of females 35.38±13.29 years, with a p value of 0.307. Most of them were in 21-30 years age group 26%, followed by 31-40 years 24.45%. Table 1 summarizes the clinical symptoms, location, frequency of attacks and quality of headache in migraine patients. All the patients had migraine without aura and presented most commonly with phonophobia 88.2%, nausea 87%, photophobia 76.8%, vomiting 56.9%, light headedness 38.1%, relief after vomiting 21%, scalp tenderness 4.6% and vertigo 2.8%. Patients presented with episodic migraine more frequently 62.2% than chronic daily headache 37.8%.

Table 1: Clinical symptoms, location of pain, frequency of attacks and quality of headache in migraine patients (n=323).

Clinical symptoms	Present/absent	Frequency	%
Nausea	No	42	13
	Yes	281	87
	Total	323	100
Vomiting	No	119	43.1
	Yes	157	56.9
	Total	276	100
Relief after vomiting	No	252	79
	Yes	67	21
	Total	319	100
Light headedness	No	200	61.9
	Yes	123	38.1
	Total	323	100
Scalp tenderness	No	308	95.4
	Yes	15	4.6
	Total	323	100
Photophobia	No	75	23.2
	Yes	248	76.8
	Total	323	100
Phonophobia	No	38	11.8
	Yes	284	88.2
	Total	322	100
Vertigo	No	314	97.2
	Yes	9	2.8
	Total	323	100
Frequency of headache (days/month)	Episodic migraine (EM)	201	62.2
	Chronic daily headache (CDH)	122	37.8
	Total	323	100
Pulsating quality headache	No	95	30.7
	Yes	214	69.3
	Total	309	100
Unilateral/hemi-cranial	No	132	40.9
	Yes	191	59.1
	Total	323	100
Global/holo-cranial	No	201	62.2
	Yes	122	37.8
	Total	323	100
Occipital/nuchal	No	291	90.1
	Yes	32	9.9
	Total	323	100
Bilateral	No	318	98.5
	Yes	5	1.5
	Total	323	100
Bitemporal with supraorbital	No	307	95
	Yes	16	5
	Total	323	100
Frontal	No	305	94.4
	Yes	18	5.6
	Total	323	100

Classical pulsating headache was found in 69.3% of patients while others presented with pain of mild to moderate severity with no pulsating quality. With regards to location of headache, unilateral was found in 59.1% of patients followed by holo-cranial 37.8%, occipital 9.9%, frontal 5.6%, bitemporal with supraorbital 5% and bilateral 1.5%. The mean duration of headache was 5.3±4.7 years and the frequency of attacks was 14.74±8.2 (days/month).

Trigger factors were present in 234 (72.4%) and absent in 89 (27.6%) patients as shown in (Figure 1).

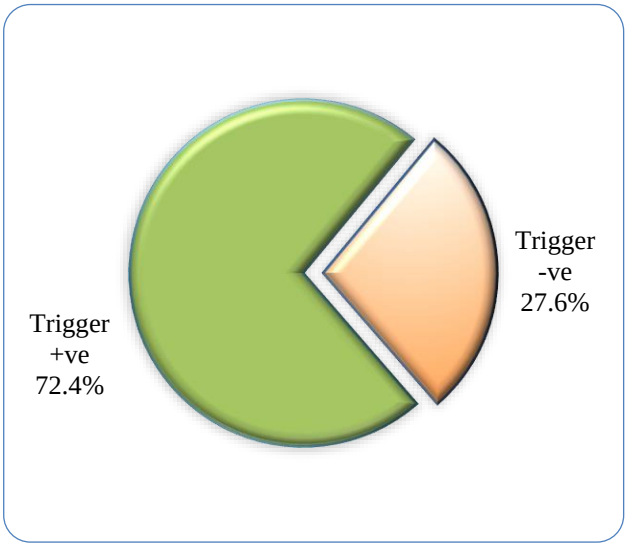

Figure 1: Percentage of presence and absence of trigger factors in migraine patients.
–ve = trigger absent, +ve = trigger present.

Table 2: Trigger factors in migraine patients (n=323).

Trigger factors	Number of patients	%
Tomatoes	35	10.8
Cheese	24	7.4
Onions	2	0.6
Collard greens/Kale (Haak)	21	6.5
Hot climate	118	36.5
Fasting	78	24.1
Lack of sleep/sleep deprivation	86	26.6
Emotional stress/anxiety	118	36.5
Spicy junk food	4	1.2
Exposure to cold	3	0.9
Pickles	4	1.2
Turnips and radish	5	1.5
Pulses and beans	5	1.5
Workload	2	0.6
Menstrual cycle	3	0.9
Total	508	157.3

Most common trigger factors observed in our ethnic population are depicted in (Table 2). The common food items which are seen to precipitate an attack are tomatoes 35 (10.8%), cheese 24 (7.4%), collard greens/kale (Haakh) 21 (6.5%), (in Kashmir valley collard greens popularly known as Haakh in local parlance are included in most of the meals and both the leaves and roots are consumed. It belongs to species *Brassica oleracea*) turnips and radish 5 (1.5%), pulses and beans 5 (1.5%), pickles 4 (1.2%) and onions 2 (0.6%).

Majority of patients had multiple trigger factors varying from nil to maximum of seven. Figure 2, depicts the percentage of patients with none, one or more than one trigger factors responsible for precipitating an attack.

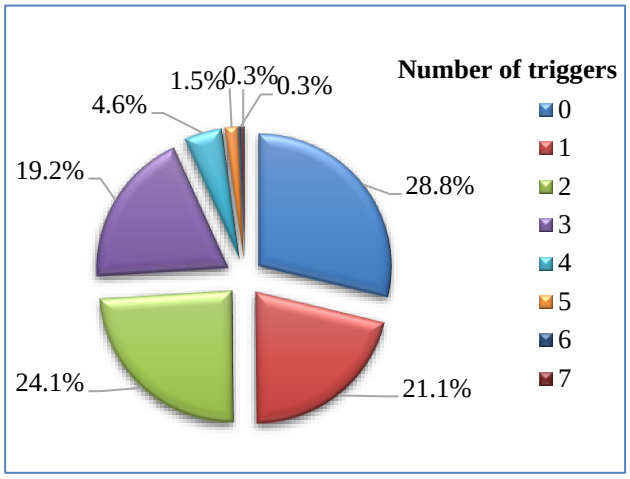

Figure 2: Percentage of zero to seven trigger factors in migraine patients.

Table 3: Relationship of age, duration of headache and frequency of attack in migraine patients with and without trigger.

Trigger factor		N	Mean ±SD	P value
Age of subjects (years)	Trigger -ve	82	35.659± 15.736	0.974
	Trigger +ve	233	35.717± 13.028	
Duration of headache (years)	Trigger -ve	78	4.397± 3.822	0.020
	Trigger +ve	232	5.672± 4.998	
Frequency of headache (days/month)	Trigger -ve	79	13.342± 8.184	0.081
	Trigger +ve	231	15.225± 8.288	

*****Results are given as mean ±SD. Independent T-test was used to compare groups with significance of p<0.05, –ve = absent, +ve = present, N frequency.

Table 3 represents the relationship between mean age of patients, duration of headache and frequency of attack with patients presenting with or without trigger factor in the neurology clinic. The mean duration of headache in patients who present with a history of trigger factor or factors is 5.67±4.99 years with a significant p value (p<0.02). The mean frequency of headache in trigger positive patients is 15.22±8.28 (days/month) and the p value is 0.081. Table 4 summarizes the correlation between the clinical symptoms, location of pain, frequency of attacks and quality of headache with the trigger factors associated with migraine patients.

Table 4: Correlation of clinical symptoms, location of pain and frequency of attacks and nature of pain in patients with and without trigger.

Clinical symptoms		Triggering factor		Total	P value	Odds ratio (OR)	95% Confidence interval	
		Trigger -ve	Trigger +ve				Lower limit	Upper limit
Nausea	No	23	19	42	<0.0001	3.943	2.023	7.685
		54.8%	45.2%	100.0%				
	Yes	66	215	281				
		23.5%	76.5%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Vomiting	No	42	77	119	0.001	2.626	1.501	4.596
		35.3%	64.7%	100.0%				
	Yes	27	130	157				
		17.2%	82.8%	100.0%				
Total		69	207	276				
		25.0%	75.0%	100.0%				
Relief after vomiting	No	74	178	252	0.218	1.574	0.823	3.010
		29.4%	70.6%	100.0%				
	Yes	14	53	67				
		20.9%	79.1%	100.0%				
Total		88	231	319				
		27.6%	72.4%	100.0%				

Continued.

Clinical symptoms		Triggering factor		Total	P value	Odds ratio (OR)	95% Confidence interval	
		Trigger -ve	Trigger +ve				Lower limit	Upper limit
Light headedness	No	57	143	200	0.628	1.134	0.683	1.881
		28.5%	71.5%	100.0%				
	Yes	32	91	123				
		26.0%	74.0%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Scalp tenderness	No	86	222	308	0.768	1.550	0.427	5.626
		27.9%	72.1%	100.0%				
	Yes	3	12	15				
		20.0%	80.0%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Photophobia	No	33	42	75	<0.0001	2.694	1.563	4.644
		44.0%	56.0%	100.0%				
	Yes	56	192	248				
		22.6%	77.4%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Phonophobia	No	23	15	38	<0.0001	5.166	2.548	10.476
		60.5%	39.5%	100.0%				
	Yes	65	219	284				
		22.9%	77.1%	100.0%				
Total		88	234	322				
		27.3%	72.7%	100.0%				
Frequency of headache (days/month)	EM	55	138	193	0.139	1.544	0.894	2.668
		28.5%	71.5%	100.0%				
	CDH	24	93	117				
		20.5%	79.5%	100.0%				
Total		79	231	310				
		25.5%	74.5%	100.0%				
Pulsating headache	No	34	61	95	0.006	2.093	1.228	3.567
		35.8%	64.2%	100.0%				
	Yes	45	169	214				
		21.0%	79.0%	100.0%				
Total		79	230	309				
		25.6%	74.4%	100.0%				
Unilateral/hemi-cranial	No	53	79	132	<0.0001	2.889	1.747	4.775
		40.2%	59.8%	100.0%				
	Yes	36	155	191				
		18.8%	81.2%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Global/holo-cranial	No	48	153	201	0.073	0.620	0.377	1.018
		23.9%	76.1%	100.0%				
	Yes	41	81	122				
		33.6%	66.4%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Occipital/nuchal headache	No	82	209	291	0.536	1.401	0.583	3.365
		28.2%	71.8%	100.0%				
	Yes	7	25	32				
		21.9%	78.1%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				

Continued.

Clinical symptoms		Triggering factor		Total	P value	Odds ratio (OR)	95% Confidence interval	
		Trigger -ve	Trigger +ve				Lower limit	Upper limit
Bilateral headache	No	88	230	318	0.703	1.530	0.169	13.882
		27.7%	72.3%	100.0%				
	Yes	1	4	5				
		20.0%	80.0%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Bitemporal with supraorbital	No	85	222	307	0.815	1.149	0.360	3.660
		27.7%	72.3%	100.0%				
	Yes	4	12	16				
		25.0%	75.0%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
Frontal headache	No	84	221	305	0.983	0.988	0.342	2.857
		27.5%	72.5%	100.0%				
	Yes	5	13	18				
		27.8%	72.2%	100.0%				
Total		89	234	323				
		27.6%	72.4%	100.0%				
		27.6%	72.4%	100.0%				

ve = trigger absent, +ve = trigger present, EM: episodic migraine, CDH: chronic daily headache.

Nausea was present in 281 patients out of which 215 (76.5%) presented with history of one or more trigger factors with a p value of (p<0.0001), (OR=3.94; 95% CI=2.02-7.68). Vomiting in 130 (82.8%) patients with trigger factors with a p value of (p=0.0001), (OR=2.62; 95% CI=1.50-4.59). Photophobia was seen in 192 (77.4%) patients with trigger with a p value of (p<0.0001), (OR=2.69; 95% CI=1.56-4.64). Phonophobia in 219 (77.1%) patients with trigger with a p value of (p<0.0001), (OR=5.16; 95% CI=2.54-10.47). Pulsating nature of headache was seen in 169 (79.0%) patients with history of one or more trigger factors, with a p value of (p=0.006, (OR=2.09; 95% CI=1.22-3.56). The pain was most commonly perceived as unilateral/hemi-cranial in 155 (81.2%) patients with triggers and a p value (p<0.0001), (OR=2.88; 95% CI=1.74-4.77). Other clinical symptoms, frequency of headache (days/month) and other locations of headache did not show significant values with respect to presence or absence of different trigger factors.

DISCUSSION

The present study observed that in our ethnic population all the patients had migraine without aura and most frequently reported symptoms were phonophobia, nausea, photophobia, vomiting, lightheadedness, relief after vomiting, scalp tenderness and vertigo. Pulsatile pain was found in 69.3% and unilateral pain in 59.1% of migraineurs (Table 1). Similar findings have been observed in a US population based survey conducted by Lipton et al which shows photophobia (80% of migraineures), phonophobia (76% of migraineures), nausea (73%), vomiting (29%), pulsatile pain (85% of migraineures) and unilateral pain in 59%.[13] Our study shows trigger factors were present in 72.4% of patients. The commonest trigger factors which have been identified are hot climate, emotional stress/anxiety, lack of sleep/sleep deprivation and fasting. Common food items identified as triggers were tomatoes, cheese and collard greens (Table 2). Majority of patients had multiple trigger factors, with no trigger in 28.8% of migraineures, one in 21.1%, two in 24.1%, three in 19.2%, four in 4.6%, five in 1.5%, six in 0.3% and seven in 0.3% of patients. According to study conducted by Martin et al, anxiety emerged as one of the most common triggering factors of migraine.[14] Predominantly individuals react to the headache in the form of anxiousness, related to cause of headache, how to manage it and it impact on them. The anxiety reaction creates negative feedback loops, thereby increasing the perception of pain and exacerbates anxiety trigger factor. A clinical study by Kelman found that 76% of migraineures responded affirmatively when asked whether they had triggers for migraine attacks.[15] Moreover, Berg et al, indicated that migraineures reported a median of 3 triggers with a range from 1 to 12.[16] These studies are consistent with our study where triggers range from nil to 7. Fasting was one of the common triggers in our study 24.1%. In our ethnic population fasting is commonly observed as a religious obligation especially in the holy month of Ramdhan. Missing a meal due to occupational reasons is yet another reason for fasting. Similar findings have been reported in a study conducted by Yadav et al, in India.[17] Stress hormone release and hypoglycemia has been implicated to trigger a migraine attack due to fasting.[18] Water deprivation has also been attributed to trigger migraine attack.[19] Diet can play an important role in the precipitation of headaches in children and adolescents

with migraine. The list of foods, beverages, and additives that trigger migraine includes cheese, chocolate, citrus fruits, hot dogs, monosodium glutamate, aspartame, fatty foods, ice cream, caffeine withdrawal, and alcoholic drinks, especially red wine and beer.[18,20] In our study the dietary triggers which have been implicated to trigger headaches are tomatoes, cheese, collard greens, pickles and junk food. A study carried by Spierings et al reported the factors indicated most frequently as precipitating headache by the patients with migraine were stress/tension 84%, not eating on time/fasting 82%, fatigue 79%, and lack of sleep 74%.[21] These studies are consistent with our study except for certain dietary items which are native to our ethnic population. In current study clinical symptoms have been correlated in patients in without precipitating factors for migraine attacks. Very little studies have been so far conducted where the influence of trigger factors on clinical presentation has been studied. In our study clinical symptoms like nausea, vomiting, photophobia, phonophobia, pulsatile and unilateral location of headache show significant p-values in patients who have established precipitating factors. The study has paved way for further research with a robust data to establish a link between intensity and degree of occurrence of clinical symptoms and presence of trigger factors in patients of migraine.

CONCLUSION

Both EM and CDH are significant health issues, cause much suffering, adversely effects an individual's functional capacity and has a high societal cost. Headaches are precipitated by triggers and advice to avoid triggers is a standard feature of clinical management. But currently the concept of "coping with triggers should replace the idea of avoiding triggers". A behavioral management involves graded exposure to desensitize the headache sufferers to some triggers, whilst reserving avoidance only for selected ones with an increased potential for eliciting headache with a secondary benefit of less restricted lifestyle, encouragement of a well-balanced diet and enhanced self-efficacy for preventing headache. This may be preferable to long-term prophylactic drug treatment with attending adverse reaction.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Banday MS, Wani M, Para BA, Qureshi S. Impact of trigger factors on clinical profile of migraine patients. Int J Basic Clin Pharmacol 2020;9:1191-8.