

# An insight into migraine; a neurological disorder

## Abstract

Migraine is a major health problem in all over the world in young age especially from age 20-30 years. Migraine is the severe headache especially in female as its prevalence is much higher in females than males. Migraine affected the health of youngster in both developed such as America and US and developing country such as Pakistan, Africa, India and Afghanistan. Prevalence of migraine is higher in middle class people. As, 18% of the migraine patients belong to upper class, 81% of patients belongs to middle class and only 1% patients belongs to lower class. Prevalence of migraine is higher in middle class because people belong to middle socio-economic status take more tension of the life. Factors that can trigger the rate and frequency of migraine are smoking, consumptions of alcohol, physical exercise and dietary supplements. To find the determinants of migraine and to reduce the rate of migraine, it was essential to create the awareness among people about health issues.

**Keywords:** smoking, consumptions of alcohol, migraine, dietary supplements, manifestations, probable migraine, chronic migraine

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**Abbreviations:** TTH, tension type headaches; CTH, cluster type headaches; CM, chronic migraine; MA+, migraine with aura; MA-, migraine without aura; BMI, body mass index; IR, insulin resistance

## Introduction

Migraine is a typical neurological issue, usually beginning in adolescence and reaching out into adulthood. The headache starts in migraine affect only half of the head that is characterized by repetitive headaches that last 4-72 hours and influences patients one to fourteen times every month occasionally and more than fourteen attacks for each month in long term.<sup>1</sup> The symptoms associated with migraine are sensitivity to light, sound or smell, vomiting and nausea.<sup>2</sup> Two common types of migraine is classified as active migraine with aura, active migraine without aura<sup>3</sup> Migraine with aura is a headache that strikes along with the sensory disturbances and these disturbances include light flashes, blind spot and vision changes. Migraine without aura does not show early symptoms like Migraine with aura and its exact cause is not diagnosed.<sup>4</sup>

About one third of the total people have aura migraine. Aura migraine is a short period of disturbance that occur with little or sometimes no headache.<sup>5</sup> Migraine is the third most prevalent medical disorder worldwide. It is ranked as the 8th most disease and the seventh highest cause of disability in the world and is associated with a number of other major disorders. Despite its considerable burden, migraine is under-diagnosed and treatable.<sup>6</sup> Migraine occurs due to mixture of the environment and also due to genetic factors. Migraine occurs due to changing hormone level therefore there are more chances of migraine risk in boys rather than girls before puberty and on other hand women had a higher prevalence of migraine than males. The risk of migraine decreases at the time of pregnancy.<sup>7</sup> The prevalence ratio for females versus males was highest during the female reproductive/child-bearing years, consistent with a relationship between menstruation and migraine.<sup>8</sup> The superficial temporal artery has been believed to be the fundamental focal point of migraine, yet its diameter has never been estimated exactly.<sup>9</sup> Numerous migraine attacks are joined by tension type pain like manifestations, for example, neck torment. Mostly

their symptoms joined for example, photophobia or phonophobia and irritation by moving.<sup>10</sup> Ladies with migraine have a higher relative danger of creating hypertension contrasted with ladies without it.<sup>11</sup> There are some food substances that trigger migraine includes tyramine, phenolic flavonoids, phenylalanine, liquor, food added substances (sodium nitrate, monosodium glutamate, aspartame) and caffeine<sup>12</sup> Foods that contain high fat are one of the factors that may specifically influence migraine. Abnormal amounts of blood lipids and large amounts of free unsaturated fats are involved in activating migraine.<sup>13</sup> Some eatables in our eating routine can start off migraine in people. Some items bring an attack on through an allergic reaction. A specific number, for example, citrus, tea, espresso, pork, chocolate, drain, nuts, vegetables and cola drinks have been referred as allergens related with migraine. Other allergic reactions unrelated to diet may likewise be related with migraine.<sup>14</sup> In migraine most patients have some dietary triggers, the major one is fasting. Pre-menstrual period is also the most regular trigger. Physical exercises and some rest issues are also involved as a trigger in migraine. In the environmental factors smells are also accounted.<sup>15</sup> To treat migraine adequately it is important to make right conclusion and by keeping in mind the patient's accessibility give them appropriate options. The treatment may vary according to severity and repetition of disease. A few medications and nonpharmacological medicines are accessible to treat migraine.<sup>16</sup> Numerous ladies have migraine or pre headache happening only at the time of menstrual cycle. Long acting triptans, frovatriptan and naratriptan, taken perimenstrually all day and all night for quick relief, have been discovered beneficial in decreasing the severity of menstrual migraine. The exact mechanism of migraine is not fully understood but it is believed that nerves and blood vessels of brain are involved in this disease.<sup>17</sup> The initial treatment that can cure minute pain issue of ibuprofen and paracetamol (acetaminophen). Paracetamol is used for the treatment of headache and nausea at the time migraine and also avoid the triggers. Specific medication for example triptans and ergotamines are recommended for the patient whom has no affect with simple medications.<sup>18</sup> The further attacks of the migraine can be prevented by use of metoprolol, topiramate and valproate. For treatment, the utilization of sumatriptan, rizatriptan, and the NSAID mefenamic acid (ponstel) is proofed by the most elevated quality.<sup>6</sup>

According to a research it is claimed that about 15 percent people of the world are affected with this disease. Migraine starts at the time of puberty and with time it becomes worse such as at middle age it become severe. The word migraine comes from the Greek word that means pain of one side of head or skull. The severity of the pain, frequency of attack and duration of headache vary with patient.<sup>19</sup>

The migraine that remains for at least 72 hours is named as status migrainosus. The four possible phases that are associated with migraine are prodrome, aura, pain phase and postdrome phase. The prodrome phase occurs hours or sometimes days before headache. After this phase aura phase starts that occurs immediately after headache. Then pain phase starts that is also known as headache phase while in last postdrome phase comes which remains till the end of migraine attack.<sup>20</sup> Some other disorders are also associated with this disease such as depression, anxiety disorder, bipolar disorder and obsessive compulsive disorder. The cause of migraine is also unknown but scientists and researchers believed that some environmental and genetic factors are the major cause of this disorder.<sup>21</sup>

This disease runs in the families and there are rare chances of this disease in those people whose single gene is defective. Many things can trigger the severity, frequency and duration of pain for example fatigue, certain foods and different weather. It is believed that migraine is a neurovascular disorder but its exact mechanism is not known. Some researchers believed that neuronal mechanism play important role in migraine while some of them believed that instead of neuron, blood vessels play role in this disease. Some researchers also believed that above both mechanisms are involved in migraine.<sup>22</sup>

On theory stated that when excitability of cerebral cortex increases then pain neurons become abnormal and headache starts. The diagnosis of migraine is simple and is based on signs and symptoms. Neuroimaging tests are not used to diagnose migraine rather these are used to diagnose other causes of headache.<sup>23</sup>

The International Headache Society presents a criterion that can be used to diagnose the migraine without aura. According to that criteria, if a person experiences two or more attacks in a day then there are more chance of migraine and if duration of attack remains for four hours to three days then migraine is confirmed. Some other symptoms include unilateral (pain of half head or skull), pulsating, severe pain especially at the time of physical activity.<sup>24</sup>

According to International Headache society there are seven further subtypes of migraine that are migraine with aura (classic migraine), migraine without aura (common migraine), childhood periodic syndrome, retinal migraine, probable migraine, chronic migraine and abdominal migraine. The attacks of migraine can be prevented by some medication, alteration of lifestyle, nutritional supplements and surgery.<sup>25</sup>

The goal of treatment is to reduce the painfulness, frequency and duration of pain in those patients whose headache remains for few days and pain cannot be tolerated. Approximately one billion of total people are diagnosed with migraine in all over the world.

The researcher is aimed to determine the underlying causes of migraine with dietary habits among students so that awareness could be created through extensive nutritional education. As if not addressed well on time, the burden of disease would be increased in the society.

## Review of literature

Evans EW et al.<sup>26</sup> in USA during 2015 examined the dietary intake patterns and its quality among women with and without migraine. For the review 3096 women's of age 20-25 were selected. A questionnaire including food frequency table and 24 hour recall was used to collect the data. Analysis revealed that dietary patterns did not differ in women with migraine and without it and normal weight has lower quality diet than women who don't suffer from migraine.

Rist PM et al.<sup>27</sup> conduct a cross sectional study in USA during 2014 to analyze dietary patterns and its relation with migraine and how food triggers migraine. A logistic regression was used to evaluate the association. Results showed that migraine with aura were having low intake of chocolate, hot dogs, ice creams and processed meat. People suffering from migraine were taking low fat milk and wine at least one per week. The research concluded that dietary triggers varied according to the aura status and frequency of attacks in migraine.

A case control study was conducted by Nazari F et al.,<sup>28</sup> in Iran during 2010 to examine relation between migraine and lifestyle of women. Total 170 patients were chosen randomly using poison sampling. Women with and without migraine living in a same area and lifestyle were selected for the study. Interview method and questionnaires were used. Results showed that there was a relation of diet, sleeping habits, rest and drug usage with migraine but no relation was found between smoking, stress and exercises with migraine. Some changes in lifestyle may decrease the side effects of migraine.

A cross sectional study was conducted by Rockett FC et al. in Brazil during 2012 to evaluate triggers of migraine and the role of diet. For the study 123 adult patients of both genders were chosen using convenience sampling. The data were collected by interviews. Results showed that in dietary triggers fasting was the most frequent and the second most common was stress and consumption of alcohol. Hormonal and environmental factors were also act as a trigger which includes sleep, stress, odor, noise and menstruation. A large number of triggers were found in the study and its avoidance could be beneficial for patients of migraine.<sup>29</sup>

Sun-Edelstein in New York during 2008 reviewed the evidence for supplements in migraine treatment. The results showed that to identify food triggers in migraine, food dairies the easy and cheapest way and for the relief of migraine the use of the supplements coenzyme Q10, riboflavin, alpha lipoic acid and magnesium is beneficial. According to them Most patients are sensitive to aspartame, monosodium glutamate, nitrates, nitrites, alcohol, and caffeine.<sup>30</sup>

A case control study was conducted by Gludekin B et al.<sup>31</sup> in turkey during 2008. The aim of the study was to evaluate leptin levels in patients with migraine and without it and to investigate its relation to vascular risk factors. 61 patients with migraine and 64 healthy individuals were chosen for the study. Leptin levels were calculated by test ELISA in serum taken after fasting of one night. Results showed that leptin levels were found significantly lower in migraineurs than controls although BMI did not differ between 2 groups but fat mass and its percentages were significantly lower in migraine patients. The study concluded that migraine patients had lower low leptin levels and fat mass which could be related to pathogenesis of migraine.

Saint R in Israel during 2014 reviewed the association between migraine and obesity. According to him obesity is a modifiable

risk factor for migraine and it also increases the frequency of attacks. Obesity as a pro-inflammatory state may be associated with neurovascular inflammation in individuals with migraine and increased levels of plasma calcitonin gene-related peptide (CGRP) in obese people may play a role as an important post-synaptic mediator of trigeminovascular inflammation in migraine. Further, dysregulation in the hypothalamic neuropeptide, orexin, in obese persons may be associated with increased susceptibility to neurogenic inflammation causing migraine attacks and leptin and adiponectin can activate proinflammatory cytokine release that is involved in the pathogenesis of migraine. Whereas rapid weight loss helps in the reduction and frequency of attacks. He concluded that weight control should be included as a part of the treatment and BMI should be calculated.<sup>32</sup>

A cross-sectional study was conducted in a private university of southern Brazil in 2010. The aim of the study was to check the prevalence of headaches. Headaches were further divided into 6 types that is migraine, probable migraine, tension-type headache, probable tension-type headache, non-classifiable headache, no headache. Migraine Disability Assessment Questionnaire (MIDAS) was used as a tool to assess the disability. In all undergraduate students 74.5% had at least one headache attack in the last three months. Regarding disability, there was a significant difference between the headache types ( $p < 0.0001$ ) migraine was the headache type with most reported disability. They concluded headache as a highly prevalent condition among the students at the University of Caxias do Sul.<sup>33</sup>

A cross-sectional study was conducted by Fava *et al.*, in Italy during 2013. The aim of the study was to assess serum glucose, insulin levels and insulin resistance (IR) in a sample of episodic migraineurs, chronic migraineurs and healthy individuals. Eighty-three women with episodic migraineurs, 83 with chronic migraineurs and 83 healthy controls were chosen. Waist circumference, body mass index (BMI) and blood pressure were measured and metabolic parameters included fasting glucose, oral glucose tolerance test, serum HbA1c, blood lipid profile, C-reactive protein and prolactin were measured. The homeostasis model assessment formula was used to calculate IR. Results showed significant prevalence of IR in chronic migraine ( $P = 0.002$ ). No significant associations were found with fasting glycaemia, the blood lipid profile, C-reactive protein, prolactin and waist circumference. Obesity (BMI  $> 30$  kg/m<sup>2</sup>) was associated with an increased risk of chronic migraine. This may suggest that chronic migraine is associated with IR status, particularly when it combines with obesity.<sup>34</sup>

A study was conducted by Okumura *et al.*, in a clinic in Japan during 2010. The aim of the study was to characterize patients with headache in an outpatient unit. Each parameter such as age, sex or diagnosis was investigated. Results showed that out of 4693 patients, 418 patients visited hospital because of headache. Primary headache was found in 167 patients (39.9%). The rate of tension-type headache (TTH) (30.8%) was highest, followed by migraine (9.1%). The rate of migraine was 3 times higher in female patients than in male patients. In female patients, migraine was observed more rapidly in younger patients, TTH rate peaks between the ages of 40 and 49 years in both sexes. They concluded that tension type headache is highly observed among all headaches in the clinic.<sup>35</sup>

A study conducted by Fukui *et al.*, in 2008 in Brazil. To analyse the precipitating factors in a sample of Brazilian migraine patients. Two hundred consecutive migraine patients were interviewed about possible factors for migraine attacks. Results showed some dietary

trigger, fasting was the most common one, include alcohol and chocolate. Hormonal factors appeared in 53%, pre-menstrual period is the most regular trigger. Physical exercises caused migraine in 13%, sexual activities in 2.5% and 64% revealed stress trigger factor. 81% related some sleep problem as a trigger factor. Regarding environmental factors, smells were reported by 36.5%. Trigger factors were frequent in migraine patients its avoidance may decrease headache frequency and also improve patient's quality of life.<sup>36</sup>

A study conducted by Faraji *et al.*, in Iran during 2017 to assess dietary intake of thiamine in migraine patients and its association with frequency of attacks. A demographic questionnaire was used to collect the data. Results showed that people with migraine have low levels of thiamine than people who don't have migraine but the study failed to find the association of thiamine with migraine and the frequency of attacks.<sup>37</sup>

A study conducted by Finocchi *et al.* in Italy during 2012 to assess food as a trigger. A questionnaire is used to collect the data. Results of the study showed that there were some dietary items which can be a trigger for migraine; the most frequent one has fasting, increased consumption of chocolate, cheese and alcohol. For the reduction of the frequency of attacks it is important to identify the environmental factors which also include dietary factors but the biological research was still missing. The study concluded that dietary factors may trigger migraine and helpful to reduce frequency of attacks.<sup>38</sup>

A study conducted by Mitchell *et al.*, in York city, England during 2011 to evaluate the effectiveness of ELISA test. An ELISA (Enzyme Linked Immuno-Sorbent Assay) test was done by eliminating different foods from the diet. Results showed a small decrease in the headaches over 12 weeks. They concluded that there is a little reduction in migraine and its frequency after 4 weeks diet but not a significant change after 12 weeks of diet.<sup>39</sup>

Kurth *et al.*<sup>40</sup> conducted a case-control study to determine the association of migraine with risk of stroke in the women. To perform this study 39,754 health professionals of US participate of age 45. The incident stroke was confirmed by the review of medical report. During study total 385 strokes were occurred from which 309 cases were ischemic, 72 were hemorrhagic and 4 were undefined. The results indicated that patients of migraine with aura and migraine without aura did not have increased risk of stroke type. It was also indicated that with migraine there are increase risk of ischemic stroke while there is no association of migraine with any other type of stroke.

A Population-based study of migraine was conducted by Cesar Fernandez *et al.*,<sup>41</sup> at April 2010 in adults to find the relation of socio-demographic factors and life style with migraine and other types of headache. In this study the prevalence of migraine in Spanish population was estimated and its association with socio-demographic factors, life style, self-reported health status and co-morbidity was conducted. The data was obtained from the adults of age 16 years or older than 16. The result was collected by home based interviews of civilians who participate in study. Socio-demographic factors such as gender, age, educational level, marital and occupational status and monthly income and habits of life style and obesity were analyzed. The prevalence of diagnosed migraine was 11.02 percent which was higher in female (15.94 percent) as compare to male (5.91 percent) and the age group at which risk of migraine attack is high ranges from 31-50 year. Depression and poor health status was associated with migraine.<sup>41</sup>

Cheryl D Bushnell et al.<sup>42</sup> conducted a study in 2009 to determine the association in between the migraine and cardiovascular diseases at the time of pregnancy. The study was conducted in US and its design was population based case-control study. Almost 18,345,538 women participate in the study. The women with migraine were identified by ICD-9code 346 and 346.1 while women with cardiovascular disease or stroke were identified by standard ICD-9 code. The data collected from study indicated that migraine was not associated with any non-vascular disease such as pneumonia, postpartum infection or hemorrhage. It was concluded that in sample of pregnant women who were admitted in hospital had a strong relation between peripartum migraine and vascular diseases at time of pregnancy. Study was unable to define that whether migraine come first or vascular disease.

In 2011 Han Le et al.<sup>43</sup> conducted a study to check the relationship between migraine, lifestyle and other social factors. To check this association a population-based cross-sectional study was conducted in which sex related factors were also investigated. In this study Han Le et al distinguished between two subtypes of migraine, migraine with aura and migraine without aura. The questionnaire contains questions about lifestyle and socioeconomic factors was prepared and sent to almost 46,418 twin individuals who were lived in Denmark. Between those people 31,865 twin individuals were aged 20-71 When migraine with aura (MA) and migraine without aura (MA) were compared it was investigated that with low education and intake of alcohol the risk of MA as compared to MO decrease.

Nathalie Jette et al.<sup>44</sup> conducted a National Population-based study to investigate comorbidity of migraine and Psychiatric disorders in 11 January 2008. The objective of study was to determine the prevalence of psychiatric conditions that are associated with migraine and to determine the pattern of association of those conditions with health related outcomes. Data was collected from the Canadian Community in which interview was conducted of 36,884 subjects. The results show that from 36,984, 15.2 percent patients were female while 6.1 percent were male. It was also determined that migraine was mostly diagnosed in people whose age ranges from 25 to 44 and were taking low income. Migraine was associated with depression disorder, bipolar disorder, social phobia and panic disorder and people with these disease experiences twice chances of migraine attack than people without these diseases. It was investigated that people with both conditions migraine and psychiatric disorders experiences worse attack of migraine as compare to people with alone condition.

In 13 July 2010, Astrid Milde-Busch et al.<sup>45</sup> conducted a cross-sectional study to check the association of diet and lifestyle with severity, frequency and duration of attack ofmigraine. The study showed that diet and life style greatly influence the headache regarding with migraine in adults. The study checked the association of life style with both type of headache such as migraine and tension-type headache. Total 1260 students were collected of grade 10 and 11 of high class schools. Questionnaire was prepared in which questions about different physical activities, intake of meals, alcoholic and non-alcoholic drinks, coffee and smoking were included. The data was collected and multiple logistic regression models were calculated that were adjusted according to sex and grade. The results indicated that the students with high intake of cocktails have 6 percents chances of migraine while lack of physical activity includes 3.7 percent chances.

In January 2014 a case control study was conducted by Dr Tony et al. to find the efficacy and tolerability of new oral antagonist of calcitonin gene related peptide receptor named telcagepant as compare

to zolmitriptan for the treatment of acute migraine. Calcitonin gene related receptor play an important role in the pathophysiology of migraine and it is believed that its antagonist might give the treatment without vasoconstrictor effect. The objective of the study was to check the efficacy and availability of that drug. For this study a placebo controlled treatment was conducted in 81 sites of different countries such as USA and Europe. The patients were classified into four groups and oral telcagepant of 150 mg and 300 mg, zolmitriptan 5mg and placebo treatment was given to different groups to check the efficacy. The data collected from the study indicated that telcagepant 300 mg is most effective drug for the treatment of migraine disorder as compare to zolmitriptan 5 mg but it was also find that telcagepant have more adverse effects than other drugs.<sup>46</sup>

A Verroti et al, conducted a cross sectional study to determine the effect of weight on the migraine in adolescent in 2013. This investigation was done by taking obese people as sample. In this method almost 135 people were taken of about 14018 years old whose body index was 97.it was 12-month program and people were investigated before and after treatment. After a detailed study it was investigated that less weight is useful and can decrease the frequency and duration of attack in migraine.<sup>47</sup>

Silvia Jimenez-Sanchez et al.,<sup>48</sup> conducted a cross-sectional study to determine the effect of sociodemographic factors in migraine in 2013. The prevalence of migraine headache in Romany population was compared with prevalence of Spanish population. The life style of both the population was checked by interviewing them separately. The result showed that prevalence of migraine is much higher in Romany population than Spanish because of their life style.

In 2014 Amy Elphick et al.<sup>49</sup> conducted a case control study to find the relationship between epistaxis, migraine and triggers in this condition. A nonbiased questionnaire was prepared in which 17 questions were added. The questionnaire contains question about duration and frequency of attack and questions similar to it. It was concluded that there is an unexpected association between nosebleeds and migraine.

Roland B Walter *et al*, conducted a cross sectional study to determine the effect of over the counter drug on the treatment of migraine. For this purpose 64,839 men and women were taken and groups were identified to investigate the effect of drug. One group was treated with NSAIDs while other was treated with non NSAIDs and then data was collected about frequency of attack and headache. It was investigated that NSAIDs are useful for the treatment of hematological migraine.<sup>50</sup>

In 2013 Elizabeth Donovan et al.,<sup>51</sup> conducted a population based cross sectional study to determine the rate of migraine in people. Almost 67,345 people were taken as sample and were tested that either they have migraine problem or not. A questionnaire of 16 question was prepared and distributed in the sample to find the result. The data was collected and concluded. The result indicated that 6 percent people were suffered with this disease and were undiagnosed. It showed that migraine is a disease that mostly remains undiagnosed

## Conclusion

Study concluded that, female gender, eating habits, caffeinated foods, low socioeconomic status, low family income and depression were the risks factors of migraine. There are many factors that can trigger the rate and frequency of migraine such as smoking,

consumptions of alcohol, physical exercise and dietary supplements. Physical exercises and some rest issues are also involved as a trigger in migraine. In the environmental factors smells are also accounted. To treat migraine adequately it is important to make right conclusion and by keeping in mind the patient's accessibility give them appropriate options.

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## Conflicts of interest

The authors have no conflicts of interest to declare.

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