



## Clinical profile and management of migraineurs in north India

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### Abstract

This cross-sectional study was carried out six months period in Department of Neurology, Guru Gobind Singh Medical College and Hospital (GGSMCH), Faridkot. 300 Patients who were diagnosed with migraine of within the age of 18-75yrs were enrolled in our study after taking their written consent. Disability was assessed using Migraine Disability Assessment Score (MIDAS). Among the total study population 22.7% were male and 77.3% were female. Many patients were from the rural area 65.3%. By the occupation majority of the patients were housewife 61.3%. Location of the headache in majority of the patients was Unilateral changing sides, constricting and pulsatile i.e. up to 21.3%. Significantly higher combined precipitating factors that are responsible for migraine are physical activity/humidity/dust/smell/lack of sleep and depression. The regimen for migraine treatment was constituted mostly of NSAIDs, antidepressants and proton pump inhibitors which was given to the 53.3% of the patients. In prophylaxis of migraine, monotherapy was used most commonly in 55.3% patients followed by dual therapy and poly therapy. In our study the occurrence of migraine was more in females as compared to their male counterparts apart from this the rural population and married individuals developed migraine often. More studies are needed for identification of associations between symptoms, signs, and pathology and treatment based strategies in the Indian population.

**Keywords:** headache disorders, migraine, drug utilization review, prescription pattern, clinical characteristics of migraine

### 1. Introduction

Drug utilization studies are great exploratory tools to ascertain the role of drugs in the society, they generate a sound socio-medical and health economics basis to make health care decision<sup>[1, 2]</sup>. Drug utilization research is a collection of descriptive and analytical methods for the quantification, understanding and evaluation of the processes of prescribing, dispensing, and consumption of medicines, and for the testing of interventions to improve the quality of these processes<sup>[3]</sup>. Drug utilization research was defined by World Health Organisation (WHO) in 1977 as the marketing, distribution, prescription and use of drugs in a society, with special importance on the resulting medical, social and economic consequences<sup>[4]</sup>. It also provides unique approach for insight into the efficacy of drug use i.e. whether a certain drug therapy provides value for money. Drug utilization research can therefore help to set priorities for the rational allocation of health care budgets.

Migraine is a common, complex, incapacitating malady. Migraine is the 3rd most prevalent and 7th leading cause of disability worldwide. According to the International Headache Society (IHS), Migraine is a throbbing or pulsating headache that is experienced on one side of head usually accompanied with nausea, vomiting and sensitivity to light, sound and smell. A migraine attack can very last anywhere from 4-72 hours during which the sufferer may want to rest in a silent and dark place<sup>[5]</sup>. Population- based studies have shown that approximately 6% of men and 18% of women suffer migraine attacks<sup>[6]</sup> and over 80% of these suffer some degree of headache-related disability<sup>[6-8]</sup>. Despite of the high prevalence, migraine is under-recognized and undertreated<sup>[8]</sup>.

Long-term management of migraine is often a major challenge primarily because it is a chronic condition with frequent episodic attacks, with varying characteristics among patients and even within attacks in the same patient. Migraine attacks vary not only in severity but also in occurrence.

In case of Indian set-up migraine is highly prevalent in India, and associated with considerable disability, especially among women and rural populations. It's prevalence was reported in 2014 as 25.2% in South India and 14.12% in East India<sup>[9, 10]</sup>. From an urban headache clinic in India found that 47% of patients were found to have migraine without aura and only 4% had migraine with aura; Indian data for the incidence of migraine with aura appear to be lower when compared with data from other parts of the world. Most migraine patients get habituated to living with headache as an integral part of their day-to-day life. Unlike in many developed countries, figures for the economic burden due to unpredictable absenteeism, frequent consultations, extensive investigations, repeated prescriptions, and ineffective over-the-counter medications, are unfortunately not available for India. Although there is as yet no biological marker to confirm the diagnosis, there have been a number of advances in diagnosis and treatment of migraine. Effective treatments are now available which are changing the way migraine is managed. Yet most patients with migraine are never diagnosed by a physician or treated with prescription medications<sup>[11]</sup> and those who do receive care are treated in so many different ways that they are finally dissatisfied with the results and keep on to suffer<sup>[12]</sup>.

#### 1.1 Pathophysiology of Migraine

The pathophysiology of migraine has historically been

acknowledged to be a process of vasoconstriction resulting in ischemia of brain tissue, followed by vasodilation of the cerebral arteries. This theory was believed to be supported by the focal neurologic changes often seen in migraine [13]. Activation of trigeminal sensory nerves triggers the release of vasoactive neuropeptides, including calcitonin gene-related peptide, neurokinin A, and substance P from perivascular axons. Vasodilation of dural blood vessels may occur with extravasation of dural plasma resulting in inflammation [14]. These neurochemicals produce inflammation, extravasation of plasma and vasodilatory changes which lead to a pulsatile headache. Initial vasoconstriction of intracranial and extracranial arteries causes a transient ischemia that may lead to prodrome symptoms such as confusion, vertigo, and hemiparesis [15].

Serotonin (5-hydroxytryptamine or 5-HT) is believed to play a significant role in mediating cerebral dilatory changes and inflammation. Release of serotonin triggers the stimulation of pain fibers [16]. Manipulation of 5-HT levels impacts perceived pain, but does not influence vasoconstriction or dilation [17]. Menstrual and postpartum migraines are believed to be initiated by rapidly falling levels of estrogen which trigger a vasospasm. This theory may help explain the higher prevalence of migraine in the female population. Some theorists have proposed that a decrease in estradiol and estrone may be the trigger for perimenopausal headaches [18].

## 2. Materials & methods

This was a descriptive cross-sectional study approved by Institutional Human Ethical Committee of ISF College of Pharmacy Registration no: ISFCP/IEC/2017-17/P-06. All relevant details of the enrolled patients were obtained from various data sources and documented in data collection form. Our study was conducted on a patient pool of 300 from August 2017 to December 2017 period in Department of Neurology, Guru Gobind Singh Medical College and Hospital (GGSMCH), Faridkot. Patients who were diagnosed with migraine of within the age of 18-75yrs and who were willing to participate were enrolled in our study after taking their written consent. The patient who are not willing to participate

in the study, Pregnant and lactating mothers and patients with major neurological disorders (e.g. epilepsy, space occupying lesions, neurodegenerative disorders) were excluded from the study. Diagnosis was made on the basis of medical history and physical examination, and, if necessary, tests to rule out other diseases or conditions causing the headache were done. Disability was assessed using Migraine Disability Assessment Score (MIDAS).

A diagnosis of migraine is usually made on the basis of repeated attacks (at least 5) that meet the following criteria [5]:

- Attacks of headache last for 4 - 72 hours.
- Headache having atleast 2 of the following characteristics: Location on one side of the head; throbbing pain; moderate or severe pain intensity; pain worsened by normal physical activity (such as walking or climbing stairs).
- During the headache, the patient has one or both of the following characteristics: Nausea or vomiting; extreme sensitivity to light or sound.
- The headache cannot be attributed to another disorder.
- The study was approved by the institutional ethics committee and informed consent was obtained from all the study subjects. Specially designed data collection form (was developed). It includes demographic details like name, age, gender, medical history, height, weight, clinical data such as diagnosis, therapeutic details such as dose, type of treatment given, outcome, and management.

## 3. Results

The study enrolled 300 patients. Among the total study population 22.7% of the patients were male and 77.3% of patients were female. The mean age (mean±S.D) of the patients was 40.07±12.61 years with range 10-80 years. Out of the 300 studied patients, most of them were from the rural area 65.3%. By the occupation majority of the patients were housewife 61.3%. From the point of education a large number of the patients were 37.3% of patients were 10th passed while the smallest number were post graduate, 1.3%. Most of the patients 86.7% were married. Many patients 84% were having no family history. Large number of the patients 88% were non addict [Table 1].

**Table 1:** Socio-Demographic characteristics of the study population (n=300)

Variable	No. of Patients (n=300)	Percentage (%)
Age (Years)		
10-20	20	6.7
21-30	48	16.0
31-40	88	29.3
41-50	96	32.0
51-60	32	10.7
61-70	12	4.0
71-80	04	1.3
Gender		
Male	68	22.7
Female	232	77.3
Residence		
Rural	196	65.3
Urban	104	34.7
Marital status		
Married	260	86.7
Unmarried	40	13.3

Occupation		
Housewife	184	61.3
Agriculture	32	10.7
Teacher	28	9.3
Student	24	8.0
Armyman	08	2.7
Other	24	8.0
Education		
Illiterate	44	14.7
10th	112	37.3
12th	84	28.0
Graduate	56	18.7
Post graduate	04	1.3
Family history		
Yes	48	16.0
No	252	84.0
Addiction		
Alcoholic	20	6.7
Smoker	04	1.3
Other	12	4.0
None	264	88.0

On examining the characteristics of migraine headache in study population it was found that the location of the headache in majority of the patients was Unilateral changing sides, constricting and pulsatile that is up to 21.3%. The major Central nervous system (CNS) symptoms experienced by the patients were sensitivity to noise, photophobia and ringing in ears 18.7% however 30.7% of the patients were having no

central nervous system symptoms.

In case of Gastrointestinal system (GIT) symptoms experienced by the patients up to 24% of the patients were having nausea while 52% of the patients were having no gastrointestinal system symptoms. The major symptom other than the CNS, GIT symptoms was weakness which was experienced by the 53.3% patients [Table 2].

**Table 2:** Characteristics of migraine headache in study population

Parameter	Number (n=300)	Percentage (%)
<b>Location:</b>		
Strictly unilateral	12	4.0
Unilateral changing sides	20	6.7
Bilateral	28	9.3
Constricting	04	1.3
Unilateral changing sides + constricting + Pulsatile	64	21.3
Strictly unilateral+ Pulsatile	44	14.7
Bilateral + Pulsatile	56	18.7
Bilateral + Constricting	36	12.0
<b>Associated features</b>		
<b>CNS Symptoms:</b>		
Sensitivity to noise + Photophobia+ Ringing in ears	56	18.7
Sensitivity to noise + Photophobia+ Numbness	36	12.0
Phonophobia	08	2.7
Ringing in the ears + Numbness + Weakness+ Sensitivity to noise	48	16.0
Blurred vision	32	10.7
Numbness	28	9.3
No CNS symptoms	92	30.7
<b>Gastrointestinal system:</b>		
Nausea	72	24.0
Vomiting	36	12.0
Nausea+Vomiting	156	52.0
No GIT symptoms	36	12.0
<b>Other symptoms:</b>		
Weakness	160	53.3
Sweating	20	6.7
Weakness+Sweating	60	20.0
No other symptoms	60	20.0

On examining the distribution of precipitating factors for migraine in study population test of proportion showed most of the patients were significantly higher combined precipitating factors that are responsible for migraine are 14.7% i.e. (physical activity, humidity, dust, smell, lack of

sleep and depression), (travel, physical activity, lack of sleep), (dust, travel, physical activity, humidity, crowd, smell, watching TV, lack of sleep and depression), 1.3% of the patients were having least precipitating factors lack of sleep, physical activity respectively as shown in [Table 3].

**Table 3:** Distribution of precipitating factors for migraine (n=300)

Precipitating factors	No. of the patients (n=300)	Percentage (%)
Travel+Crowd+Smell+Lack of sleep +depression	40	13.3
Physical activity+Humidity +Dust+ Smell+ Lack of sleep+Depression	44	14.7
Travel+Dust+Crowd	36	12.0
Humidity+Physical activity +Crowd + Smell+Watching TV+Depression	32	10.7
Travel+Physical activity+Lack of sleep	44	14.7
Travel+Crowd+Smell	24	8.0
Dust+Travel+Physical activity+ Humidity + Crowd+ Smell+ WatchingTV +Lack of sleep +Depression	44	14.7
Travel +Physical activity + Chocolates + Crowd + Dust +Watching TV+Lack of Sleep	24	8.0
Physical activity	04	1.3
Lack of sleep	08	2.7

On assessing Migraine Disability Assessment Score (MIDAS) of the study participants test of proportion showed most of the patients were having higher 42.7% mild disability, 2.7% of the patients were having severe disability, 13.3% of the patients were having little or no disability and 41.3% of the patients

were having moderate disability. Headache was severe enough to hamper daily work only 8 cases (2.7%), while majority of the score was mild 42.7%. Migraine without aura was the commonest presentation 66.66 % while only 33.33% had migraine with aura [Table 4].

**Table 4:** Migraine Disability Assessment Score (MIDAS)

Migraine Disability Assessment Score of the patients	No. of the patients (n=300)	Percentage (%)
I Little or No Disability(0-5)	40	13.3
II Mild Disability(6-10)	128	42.7
III Moderate Disability(11-20)	124	41.3
IV Severe Disability(21+)	08	2.7

The regimen for migraine treatment was constituted mostly of NSAIDS, antidepressants and proton pump inhibitors which was given to the 53.3% of the patients. In prophylaxis of migraine, monotherapy was used most commonly in 55.3%

patients followed by dual therapy and poly therapy. In our study polytherapy was used most commonly in 53.3% patients [Table 5].

**Table 5:** Regimen for Migraine

Regimen for Migraine	No. of the patients (n=300)	Percentage (%)
NSAIDS+Antidepressants+PPI+Betahistime+Antipsychotic agents	08	2.7
NSAIDS+Antidepressants+PPI+ARB	08	2.7
NSAIDS+Antidepressants+PPI	160	53.3
NSAIDS+Antidepressants+PPI+Piperidine derivatives+Anticonvulsants	24	8.0
NSAIDS+PPI+Antidepressants+Anticholinergics	24	8.0
Antipsychotic agents+CCB+ARB+Antivertigo+Anticonvulsants	04	1.3
NSAIDS+Antipsychotic agents+Anticonvulsants	12	4.0
Anticonvulsants+NSAIDS+Beta Blockers+Antidepressants	12	4.0
Corticosteroids+Anticholinergics+NSAIDS+PPI+Antidepressants	12	4.0
NSAIDS+PPI+Antidepressants+Antipsychotic Drugs	20	6.7
NSAIDS	16	5.3

### Abbreviations

NSAIDS (Non Steroidal Anti-inflammatory Drugs), PPI (Proton pump inhibitor), CCB (Calcium Channel Blocker), ARB (Angiotensin II receptor blocker)

On examining the which drugs were most prescribed each drug classes. It was found that the Naproxen was mostly

prescribed in 78.7% of the patients in NSAIDS class, Domperidone in 86.7% Selective Dopamine D2 receptor antagonist class, Escitalopram and Clonazepam were 58.7% prescribed together most often in Antidepressants class, While in Proton pump inhibitors class Pantoprazole Sodium was prescribed mostly in 73.3% of the study population. Details

are which types of drugs were prescribed are shown in [Table5].

**Table 5:** Types of drugs which were prescribed

Drugs	No. of Patients (n=300)	Percentage (%)
<b>Non Steroidal Anti-inflammatory Drugs</b>		
Naproxen	236	78.7
Aceclofenac + Paracetamol	36	12.0
Aspirin	04	1.3
Diclofenac	08	2.7
Mefanamic acid	04	1.3
Naproxen + Mefanamic acid	04	1.3
Not given	08	2.7
<b>Selective dopamine d2 receptor antagonist</b>		
Domperidone	260	86.7
Not given	40	13.3
<b>Antidepressants</b>		
Escitalopram	36	12.0
Clonazepam	12	4.0
Escitalopram+Clonazepam	176	58.7
Amitriptyline	28	9.3
Escitalopram+Clonazepam+Amitriptyline	12	4.0
Sertraline	04	1.3
Not given	32	10.7
<b>Proton pump inhibitors</b>		
Pantoprazole sodium	220	73.3
Rabeprazole sodium	40	13.3
Not given	40	13.3
<b>Antivertigo</b>		
Betahistimine	16	5.3
Not given	284	94.7
<b>Antipsychotic agents</b>		
Prochlorperazine Maleate	24	8.0
Olanzapine	08	2.7
Levosulpride	08	2.7
Not given	260	86.7
<b>Piperidine derivative</b>		
Tolperisone	24	8.0
Not given	276	92.0
<b>Anticonvulsants</b>		
Pregabalin	16	5.3
Topiramate	28	9.3
Divalproex	08	2.7
Not given	248	82.7
<b>Corticosteroids</b>		
Dexamethasone	12	4.0
Not given	288	96.0
<b>Anticholinergics</b>		
Dicyclomine	36	12.0
Not given	264	88.0
<b>Beta Blockers</b>		
Propranolol	08	2.7
Not given	292	97.3
<b>Calcium Channel blockers</b>		
Amlodipine	08	2.7
Not given	292	97.3

#### 4. Discussion

In our set up, the commonest complaint with which patient comes to the neurology OPD was headache. The study population had female preponderance (77.3%) more than the male patients. The Female to male ratio is 3.1:1 in this study which is similar to previous study. The literature from various

studies also suggests migraine is more frequent in the female population [9-11, 19]. Housewives were more likely to suffer from migraine than the other professionals. Test of proportion showed most of the patients 32% were significantly higher in the age group 41-50 years which was also reported in other studies [20, 21]. The majority of the patients in this study

suffered from migraine without aura with a prevalence of 66.66 %. Migraine without aura is the common presentation reported in Indian studies [22, 23]. The prevalence of migraine was higher in rural patients than the urban patients which is quite the opposite as reported in another studies conducted in India and western countries [24], however lifestyle and ethnicity can be a major factor in this difference. The married patients were more likely to suffer from migraine than the unmarried patients similar finding was reported in a study conducted in Finland [25].

Trigger factors are important for migraine as these may be helpful as indicators to treat the cause & severity of migraine attack. The most common precipitants can be tension, hunger/skipped meal/ fasting, insomnia, depression etc. Some interesting but unrelated stress factors also were observed during other studies such as fish, vegetables, fast foods etc. and changing weather (even taking a bath). Certain other factors associated with migraine include frequent & more television, strong light, computer, eating citrus fruits [26-28]. In current study common precipitate factors that are responsible for migraine were (14.7%) Dust/ Travel/Physical activity/ Humidity / Crowd / Smell / Watching TV / Lack of sleep / Depression. Association of migraine with allergic and psychiatric disorders was seen in our study population, such as migraineurs with significantly more asthma and chronic musculoskeletal pain compared to non- migraineurs (5% versus 3.2% and 39% versus 25%, respectively) [29].

Unilateral type of headache (59.8%) was much more common than bilateral type (40.2%). Headache was throbbing (71.5%) in nature in a majority of migraineurs which was consistent with various previous studies [30, 31]. Some other studies from India showed strictly unilateral pain in 40.5% patients [32]. Our study showed photophobia, phonophobia, nausea, and vomiting as the most common accompanying symptoms as the previous reports [33]. Other reported symptoms were dizziness, allodynia, and neck stiffness. In current study unilateral changing sidetype of headache (21.3%) was more common than bilateral type (9.3%). Headache was constricting and pulsatile in nature. Sensitivity to noise, photophobia, ringing in ears, blurred vision, numbness, nausea, vomiting, weakness are the most common symptoms in migraine patients. Migraine is more commonly associated with anxiety disorder than with depression [34]. It was observed that migraine was under diagnosed & management was insufficient affecting quality of life. Avoidance of trigger factors is important in management of migraine. In our study, for acute attack, NSAIDs alone were prescribed in 44.6% of cases and in combination with ergots and triptans 33.8% cases. For acute therapy ergotamine and sumatriptan alone were used in 9.8% and 11.1% cases, respectively. NSAIDs are a usual first-line therapy for mild to moderate migraine. A 2007 meta-analysis of ibuprofen for moderate to severe migraine showed that 200mg and 400mg doses were effective for short-term pain relief [35]. In our current study about 78.7% of the patients were received NSAIDs, 58.7% of the patients were received antidepressants, 73.3% of the patients were received proton pump inhibitors. Higher use of NSAIDs in this study could be due to easy availability and less cost. Triptans are considered first-line therapy for moderate to severe migraine or mild to

moderate attacks unresponsive [19, 36]. In prophylaxis of migraine, monotherapy was used most commonly in 55.3% patients followed by dual therapy and poly therapy. Beta-blockers were most common drugs (57.1%) followed by, antidepressants and calcium channel blockers. Studies have shown Beta blocker (60-80%) were effective in reducing attack frequency by more than 50% [37-40]. In our study polytherapy was used most commonly in 53.3% patients.

## 5. Conclusion

In our study the occurrence of migraine was more in females as compared to their male counterparts apart from this the rural population and married individuals developed migraine than urban population and unmarried individuals. The occurrence of migraine was more in the least literates but it was low in patients with higher education. The familial history shown no significance in connection with disorder. Surprisingly people who were non addict was higher in numbers as compared to non addict. NSAIDs, antidepressants and proton pump inhibitors were more prescribed to the patients than the other class of drugs. More studies are needed for identification of associations between symptoms, signs, and pathology and treatment based strategies in the Indian population.

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