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Prospective Study on Prevalence, Risk Factors, Treatment Outcome and Assessment of Quality of Life in Patients with Migraine at Various Hospitals, Palakkad



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ABSTRACT

Background/ Aim: Migraine is a common, multifactorial, disabling, recurrent, hereditary neurovascular headache disorder whose principal symptom is episodic intense throbbing pain in the head which is often accompanied by photophobia, phonophobia, nausea and vomiting. The main objective of this study is to assess the prevalence and risk factors of migraine and to evaluate the treatment outcome and assess the quality of life of Migraineurs. **Design:** A prospective observational study. **Subject and Methods:** A total of 204 patients with migraine were included whose age ranged between 18 to 65 years of both gender. Quality of life and migraine disability were assessed. **Results:** The study included 83.82% females and 16.18% males. 36.6% of the included patients have a normal body weight and the study concluded that majority (90%) have O positive blood group. Symptoms are experienced mostly during the attack stage and the major trigger was emotional stress affecting 53% of study population. Anti-hypertensives are mostly prescribed 272(57.14%). The study shows that migraine populations have a least quality of living on physical health domain (57.82±13.936). Patients have lessened their disability due to migraine with a difference of 9.65±5.241. **Conclusion:** Prevalence of migraine is high among females. Younger age and female sex are other contributory factors as prevalence of migraine. Emotional stress is mediating as the major trigger of migraine and excluding the normal eight subjects, pre-obese patients have higher risk for migraine. The co-morbidities didn't suggest any apparent relation with migraine, though hypothyroidism was observed in a few populations. The study demonstrates a less quality of living in physiological health domain of Migraineurs followed by psychological health domain. Majority of the study population have severe disability due to migraine, that impacts on their households and work.



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INTRODUCTION

Migraine is a common, complex, debilitating malady. Population based studies have shown that approximately 6% of men and 18% of women suffer migraine attacks¹ and over 80% of these suffer some degree of headache-related disability^[1]. According to GBD study of 2010, migraine contributes as a 3% of disability that is attributable to a specific disease worldwide and it is one among the most disabling neurological disease^[2]. Migraine is a common and often debilitating neurological condition characterized by primary recurrent headaches lasting 4 to 72 h with at least two of the following pain characteristics: unilateral, pulsating, moderate or severe intensity, or aggravated by routine physical activity. In addition, migraine attacks are often accompanied by nausea, vomiting, and sensitivity to light (photophobia) and sound (phonophobia)^[3]. Migraine has been placed 19th in the World Health Organization (WHO)'s list of diseases ranked by years lived with disability^[4,5].

Headache is one of the commonest symptoms, and primary headache disorders are among the most ubiquitous disorders, affecting people in all countries. India appears to be no exception. The Global Burden of Disease Study 2010 (GBD2010) found a tension-type headache (TTH) and migraine to be the 2 and 3rd most prevalent disease worldwide^[6].

Several studies have assessed the associations between a migraine and underweight, pre-obesity or obesity, with conflicting results^[7]. Obesity and headache are both associated with a substantial personal and societal impact, and epidemiologic studies have consistently identified a positive association between obesity and headache in general, as well as obesity and migraine specifically^[8].

The ABO blood type, an easily accessible factor in patient's genetic make-up has been associated with many diseases, though the explanation for the association between ABO blood groups and some diseases is still unclear. Blood cellular genes and gene aberrations may be associated with the diseases. The frequency of occurrence of migraine was found to be highest in group O. The incidence for migraine was highest in group B in case of Rh+ve individuals and lowest in group AB. In case of Rh-ve individuals, maximum incidence for the disease was found in group A and minimum were in group AB. The absence of both the antigens and presence of both A and B antibodies may be responsible for higher incidence of migraine. When any of the two antigens or antibodies are absent the chances for the occurrence of the disease may decrease. As both the antigens are present or both the

antibodies become absent the chances for the disease may decrease. Thus, both the antibodies i.e. A and B antibodies may have a cumulative effect on the occurrence of migraine^[9].

Migraine is known to be associated with psychiatric comorbidities, with reported prevalence of 20-40% for anxiety and 10-15% for depression^[10]. Migraine has been reported to be associated with psychiatric comorbidities such as depression, anxiety, bipolar disorder, panic disorder, and suicide. A recent large, population-based, cross-sectional study reported a higher prevalence of headache, including migraine, in individuals with reflux symptoms, diarrhea, constipation, or nausea than in individuals without such complaints^[11]. Hypothyroidism may exacerbate primary headaches in some of the patients and it can be a risk factor for the occurrence of new daily persistent headache. Based on the second edition of the International Classification of Headache Disorders, it is considered as a headache related to homeostasis.

A number of intrinsic or extrinsic factors can trigger migraine attack. The important triggers are stress, weather changes, fatigue, food and beverages, sleeplessness, hunger, and menstruation. Social and cultural factors in different regions can vary thereby influencing the significance of triggering factors. The knowledge about migraine triggers is important for proper management of the patients^[12].

Quality of life has been defined as the ability of an individual to play a role in society and to enjoy fully their role as a citizen, with an independent social status^[13]. HRQoL is a subset of overall quality of life representing the overall effect of illness and its therapy on a patient. It encompasses an individual's health state, functional status (both physically and mentally), as well as the individual's overall well-being^[14]. Migraine patients are phasing severe impairment in various fields including their physical, psychological, social and environmental relations. The WHOQOL-BREF has been developed to provide a short form quality of life assessment that looks at Domain level profiles. In clinical practice, the WHOQOL assessments will assist clinicians in making judgments about the areas in which a patient is most affected by disease, and in making treatment decisions. Together with other measures, the WHOQOL-BREF will enable health professionals to assess changes in quality of life over the course of treatment^[15].

MATERIALS AND METHODS

Patients from the outpatient and inpatient department, fulfilling the diagnostic criteria for migraine, were recruited for the study from District Co-operative Hospital, Ascent ENT Hospital and Welcare Hospital, Palakkad, Kerala [December 2016 to May 2017]. Ethical clearance was obtained from the institutional ethics committee. All participants provided written informed consent. The identity of the patients and their family was concealed.

A total of 204 patients of both genders are selected. Patients who were presented with migraine of age 18-65 and of both gender included for this study. And Patient who are not willing to give inform consent and not interested to participate in the study and Patient with malignancies are excluded. Patients, demographics, social history, educational level, past medical history and known allergies were collected from patients prescriptions, interviews with patient and/or their caretakers in a pre-designed data entry form. All patients fulfilling the diagnostic criteria for migraine were enrolled and their characteristics noted. The migraine triggers were inquired by evaluating endogenous (menstruation, emotional stress) and exogenous (fasting, physical strain, sleep deprivation, change in weather, specific foods and drinks) triggers during the interview. Patients were further interviewed to obtain the impact of migraine on their quality of living and recorded using WHOQOL-BREF questionnaire. The migraine disability was evaluated and scored using MIDAS.

Questionnaires

WHOQOL-BREF

The WHOQOL-BREF produces a quality of life profile. It is possible to derive four domain scores. There are also two items that are examined separately: question 1 asks about an individual's overall perception of quality of life and question 2 asks about an individual's overall perception of their health. The four domain scores denote an individual's perception of quality of life in each particular domain. Domain scores are scaled in a positive direction (i.e. higher scores denote higher quality of life). The mean score of items within each domain is used to calculate the domain score. Mean scores are then multiplied by 4 in order to make domain scores comparable with the scores used in the WHOQOL-100. The first transformation method converts scores to range between 4-20, comparable with the WHOQOL-100. The second transformation method converts domain scores to a 0-100 scale.

MIDAS

The MIDAS is a seven item questionnaire developed to measure headache disability. It measures disability in three domains of daily activity during the past three months. Items 1 to 5 measure disability in relation to these three domains, namely paid work or school work, household work, and leisure. Two items (A and B) enquire about the number of headache days in the last three months and the severity of the headache on a scale ranging from 0 to 10, respectively.

Statistics: Statistical Analysis was conducted using SPSS for windows.

RESULTS

A total of 204 subjects with diagnosis of migraine were enrolled in the study. Our results are based patients with migraine whose mean age was 35.2 (range 18-65) years and 171 were females. The demographic features of the study population are given in Table 1.

Table 1. Prevalence of migraine

Variable	Male	Female
Gender (%)	33(16%)	171(84%)
Mean age (\pm SD, year)	36.27 \pm 10.935	33.46 \pm 11.287

Risk factors of migraine

The factors that make more prone to having migraine include family history, age, sex and hormonal changes. The study shows high prevalence of female (84%) than males. The mean age of male was found to be 36.27 \pm 10.935 and female was found to be 33.46 \pm 11.287.

Table 2. Age wise distribution of study population

	Frequency	Prevalence
18-19	17	8.3%
20-39	127	62.25%
40-64	57	27.94%
65	3	1.4%

The age group with high prevalence of migraine was found to be between 20 and 39(62.25%) [Table 2]. Table 3 shows the hereditary link and incidence of migraine. Majority of the population have no family history and among the 50% population with the hereditary incidence of migraine have 38.72% maternal inheritance.

Table 3. Family history of migraine

Family history	Frequency	Prevalence
Father	5	2.4%
Mother	79	38.72%
Mother, Siblings	10	4.90%
Nil	102	50%
Siblings	8	3.9%

The hormonal imbalance was analyzed by collecting the menstrual characteristics of female population and grouping the thyroid status of the total population. The study reveals only 11.76% prevalence of hypothyroidism with migraine. Majority of participants are Euthyroid (74.51%) [Table 4].

Table 4. Thyroid status

Thyroid status	No. of patients	Percent
Euthyroid	152	74.51%
Hypothyroidism	24	11.76%
No data	28	13.73%

Table 5 shows the menstrual characteristics of female patients. Major group has normal menstruation (63.725) whereas a least are menopause women (7%), pregnant women (1%) and with irregular menstrual status (11.27%).

Table 5. Menstrual status

Menstrual status	Frequency	Prevalence
NORMAL MENSTRUATION	130	63.72%
INCORRECT MENSTRUATION	23	11.27%
MENOPAUSE	10	4.9%
MENOPAUSE-UTERUS REMOVED	6	2.9%
PREGNANT PATIENTS	2	0.98%
NA [MALE PATIENTS]	33	16.18%

Body Mass Index distribution in study population

Body Mass Index wise distribution of the enrolled study population is included in Table 6. The study shows a greater prevalence of migraine in normal weight groups 75(36.6%) followed by pre-obese 66(32.55), obese 33(16.4%) and underweight 30(14.6%).

Blood group prevalence

Table 7 shows that in migraine patient's maximum incidence were found in blood group O and minimum in Rhesus negative patients. Among all the Rhesus positive patients, the trend for prevalence was O (43.9 %)>B (31.7 %)>A (17.6 %)>AB (4.9%).

Table 6. BMI distribution among study population

BMI_CLASS		
Variable	Frequency	Prevalence
Underweight	30	14.6
Normal weight	75	36.6
Pre-obese	66	32.5
Obese	33	16.4
Total	204	100

Table 7. Blood group prevalence in migraine

BLOOD GROUP		
Variable	Frequency	Prevalence
A+	36	17.6
B+	65	31.7
AB+	10	4.9
O+	90	43.9
A-	1	0.5
B-	1	0.56
AB-	1	0.56
Total	204	100

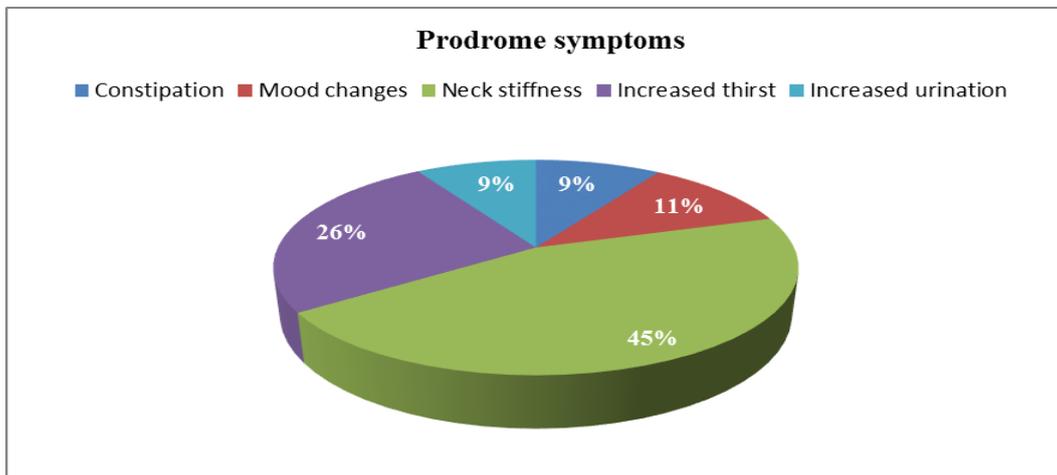


Fig 1. Prodrome symptoms of migraine

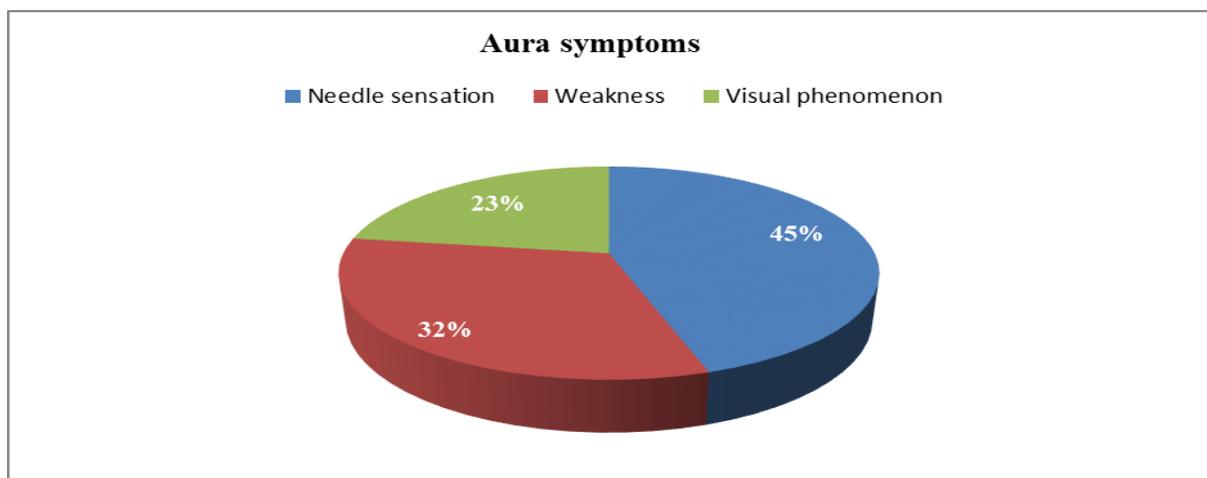


Fig . Symptoms just before attack 2

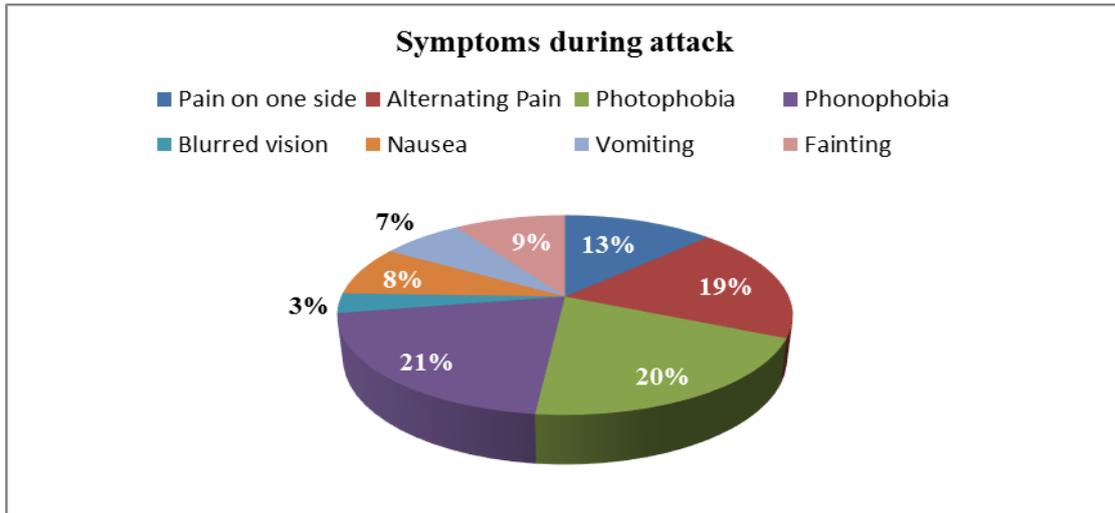


Fig 3. Symptoms during headache attack

The major Prodrome symptoms include generalized weakness 129 (63.23%), moodiness 73(35.78%), sensitivity to light 23(11.27%) and sound 19(9.31%) as described in fig 4.

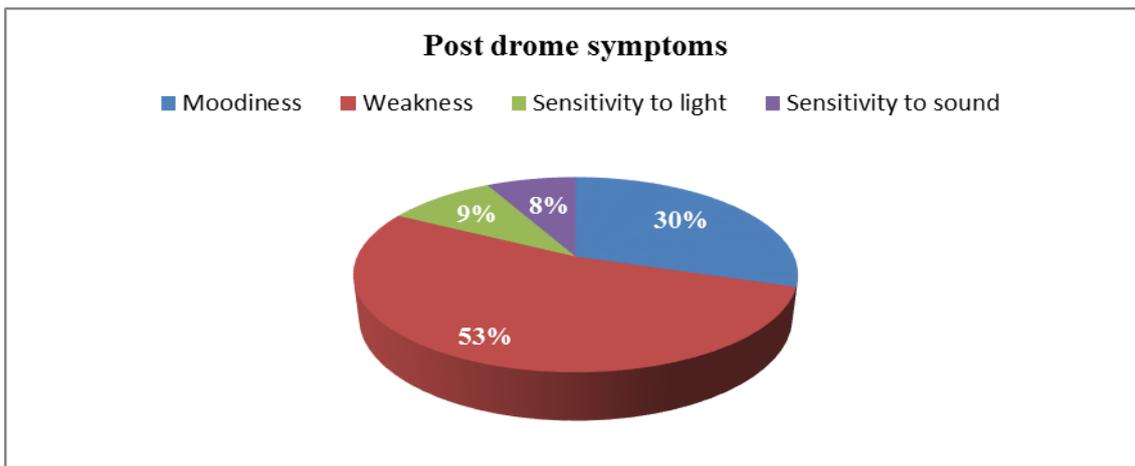


Fig 4. Symptoms after headache attack

Triggering factors of migraine in study population

A number of precipitating factors were observed in the patients (Table 8). Triggers were found in 198(97.01%) patients, which included emotional stress in 113 (55.39%), fasting in 68 (33.3%), physical exhaustion or traveling in 109(53.43%), menstruation in 57(27.94%), sleep deprivation in 64 (31.37%), food in 12(5.88%), smell in 64 (31.37%), excess noise in 16(7.84%), and change in weather in 106 (51.96%) patients. Majority of the patients had multiple triggers.

Table 8. Major triggers of migraine

Triggers	Frequency	Prevalence
Travel	109	53.43
Smell	64	31.37
Fasting	68	33.33
Weather changes	106	51.96
Sleep deprivation	64	31.37
Stress	113	55.39
Hormonal changes	57	27.94
Crowd/sound	16	7.84
Food	12	5.88
System usage	10	4.9

Co-morbidities of migraine

Smaller groups of patient population are presented with co-morbidities [Table 9]. Majority of patients in our study are presented with gastrointestinal co-morbidities 70(34.30%), hypothyroidism 24(11.76%), diabetes 11(5.39%), hypertension 19 (9.31%), cholesterol 29(9.8%), urinary infections 16(7.84%), neurologic diseases like epilepsy, stroke, psychological co-morbidities like depression, anxiety and the other observed co-morbidities are anemia, otitis, rhinitis, arthritis etc.

Table 9. Comorbidities of migraine

Co-morbidities	Frequency	Prevalence
Hypothyroidism	24	11.76
Hypertension	19	9.31
Diabetes	11	5.39
Cholesterol	20	9.8
Gastric problems	70	34.31
Neurological problems	7	3.43
Psychologic co-morbidities	37	18.14
Urinary problems	16	7.84
Other	25	12.25

Treatment of migraine

Pharmacologic treatment of migraine includes treatment of acute attacks and preventive therapy. The prescription pattern of migraine in our study population is expressed in table 10.1. Anti-hypertensives are mostly prescribed 272(57.14%) followed by anti-emetics 90(18.90%) and analgesics 69(14.49%). Glucocorticoid is prescribed only for a single participant.

Table 10.1 Prescription pattern of migraine

Therapy	Frequency	Prevalence
Anti-hypertensives	272	57.14
Psychotropic drugs	44	9.24
Analgesics	69	14.49
Anti-emetics	90	18.91
Glucocorticoids	1	0.36

The antihypertensives prescribed for migraine therapy include calcium channel blocker [Flunarizine] and non-selective beta blocker [Propranolol]. Flunarizine is prescribed as single drug for 5 (2.45%) participants and Flunarizine together with Propranolol for 28 (13.72%) participants as described in Table 10.2.

Table 10.2 Prescription of anti-hypertensives

Anti-hypertensives prescription pattern	Frequency
Calcium channel blocker -	5
Calcium channel blocker Beta-blocker	29

The anti-hypertensive drugs flunarizine and propranolol are prescribed along with psychotropic drugs, analgesics and anti-emetics, as in detailed description in Table 10.3. Anti-hypertensives with anti-emetics 68 (33.33%) and analgesics 46(22.55%) are prescribed more. The least prescribed double drug combination was with Glucocorticoids 1(0.49%).

Table 10.4 represents the drug prescription pattern other than those with anti-hypertensive drugs. Analgesics together with anti-depressants are prescribed more in this class 8 (3.92%).

Table 10.3 Prescription pattern of anti-hypertensives with other drugs

	+Drug	+Drug	+Drug	+Drug	Frequency
ANTI-HYPERTENSIVES [calcium channel blocker- flunarizine/ beta blocker- Propranolol]	Analgesics	-	-	-	46
	Anti-emetics	-	-	-	68
	Anti-epileptics	-	-	-	4
	Anti-depressants	-	-	-	5
	Glucocorticoids	-	-	-	1
	Anti-emetics	Anti-epileptics	-	-	3
	Analgesic	Anti-emetics	-	-	2
	Anti-depressants	Anti-emetics	-	-	5
	Anti-epileptics	Analgesics	-	-	5
	Analgesics	Anti-depressants	-	-	3
	Anti-depressants	Anti-epileptics	-	-	1
	Anti-epileptics	Analgesics	Anti-emetics	-	1
	Anti-epileptics	Anti-depressants	Analgesics	Anti-emetics	2

Table 10.4

Drug prescription pattern	+ Drug	Frequency
Analgesic	-	4
Analgesics	Anti-emetics	6
	Anti-depressants	8
	Anti-epileptics	2
	Anxiolytics	1
	-	1
Anti-epileptic	Anti-emetic	2

Quality of life

Transformed domain score of the WHOQOL-BREF provide the values comparable to WHOQOL-100 questionnaire. Table 11 shows the scores which represent the quality of life at each domain. The study shows that migraine populations have a least quality of living on physical health domain (57.82±13.936) and high quality of living in environmental health domain (68.08±14.254). Psychological health domain has the second least QOL (60.66±16.860) and social relationship domain have a score of 67.36±21.191.

Table 11. Quality of Life

TRANSFORMED DOMAIN SCORE					
DOMAIN	MINIMUM	MAXIMUM	MEDIAN	MEAN±SD	CRONBACH'S ALPHA
Overall QOL	1	5	4.00	3.62±0.769	0.560
Overall perception of health	1	5	3.00	3.22±0.913	0.560
Physical	13	94	56.00	57.82±13.936	0.767
Psychological	19	100	63.00	60.66±16.860	0.767
Social relation	0	100	75.00	67.36±21.191	0.767
Environmental	13	100	69.00	68.08±14.254	0.767

Migraine disability assessment

Migraine disability was assessed using 7 item MIDAS questionnaire and results are as shown in table 12. 55.88% of participants are experiencing severe disability, 35.78% experiencing a moderate disability, 7.3% having mild disability and only 0.9% is having little or no disability. The statistical analysis shows a mean value of 20.04 with a standard deviation of 7.948.

Table 12. Migraine Disability Assessment

MIDAS SCORE	FREQUENCY	PREVALENCE
Severe Disability	114	55.88
Moderate Disability	73	35.78
Mild Disability	15	7.3
Little or No Disability	2	0.9

Treatment outcome was evaluated and their statistics were described in Table 13. The study shows that after the treatment, patients have high improvement on their ability to do works and households. That means patients have lessened their disability due to migraine with a difference of 9.65 ± 5.241 .

Table 13. Treatment Outcome

	Minimum	Maximum	Mean	Standard deviation	P value
Baseline	2	45	21.98	8.739	<0.0001
Follow-up	1	27	12.27	5.945	<0.0006
Difference of baseline and follow-up	1	26	9.65	5.241	<0.0018

The study is significant since p-value <0.05.

DISCUSSION

Migraine is described by unilateral pulsating headache associated with nausea, vomiting, and photophobia. World Health Report 2001 by World Health Organization ranked headache among the top 20 causes of healthy life lost to disability. In India, given the population load, headache has been and continues to be underestimated in scope and scale, and remains under-recognized and undertreated everywhere. TTH and migraine ranked respectively as second and third most common diseases in the world (behind dental caries) in both males and females. The Global Burden of Disease Study which was updated in 2004 found that migraine account for 1.3% of years lost due to disability (YLD) ^[16].

Migraine is a common disorder with overall prevalence of 5–15%. The prevalence of migraine in females is higher (6–22%) compared to males (3–7%) ^[17]. Younger age and female sex are contributory factors as prevalence of both allergic rhinitis and migraine is

higher in these groups ^[18]. In a population-based study on obesity and migraine evaluating 30,215 participants whose mean age was 38.4 years including 65% females, revealed lack of association of BMI with the prevalence of migraine but was associated with the frequency of headache attacks. In the normal weight group, 4.4% had 10–15 headache days per month increasing to 5.8% in the overweight and 20.7% in the morbidly obese ^[19]. Increased waist circumference and body mass index (BMI) were more frequent in migraine patients compared to those without migraine.

A study conducted by Mayo Clinic showed that the common triggers for migraine are hormonal changes in women, foods like cheese, salty foods and processed foods, skipping meals or fasting, alcohol, especially wine, stress, changes in wake-sleep pattern, physical exertion, weather changes ^[20].

Rist et al. Al in their study confirmed the link of migraine with increased levels of cholesterol and extends these findings to triglycerides and demonstrates that this association is still apparent among the elderly and limited to patients with migraine with aura ^[21]. In our study, 29 out of the 204 patients have a higher cholesterol level as concluded in the study conducted by Rist et al. Grebe et al. retrospectively analyzed 64 files of headache outpatient clinic (Coimbra, Portugal), chosen randomly among patients suffering from migraine or tension headache. The authors found that the prevalence of hypertension was 35.9% (28.5% among migraine patients and 44.8% of patients with tension headache) ^[22]. Our study found an association of only 9.31% prevalence of hypertension among the Migraineurs. Only a very less prevalence of diabetes (5.39%) was observed in our study group which coincides with the study conducted by Cook NR et al. which illustrated lower prevalence of migraine in patients with diabetes ^[23]. The prevalence of probable anxiety and depression (score ≥ 11) in a migraine clinic study by Jarman et al. ^[24] was 20% and 8% as compared to our study with 18.14% prevalence of psychological co-morbidities, anxiety and depression contributing the most. The prevalence of headache in patients with hypothyroidism differs from 14 to 73 percent in different studies ^[25] as stated by Hagen K et al., our study shows a higher prevalence of hypothyroidism 24 (11.76%) as comorbidity compared to others.

The migraine sufferers had substantial and statistically significantly lower total QOL scores and physical health and psychological health domain scores than the healthy control group ^[26] which relates to our study representing lower QOL in the physical health domain and psychologic health domain. The study shows a major portion of participants have severe

disability which is consistent with the study conducted by Shaik MM et al. Their study report as the group with severe disability reported significantly higher MIDAS scores, which signified a high number of days with less than 50% of predictability at work, school, and home or in recreational gatherings^[27]. Sharma et al. conducted a study with 71 participants to assess the quality of life and psychiatric comorbidity in migraine patients, which satisfies to our results in the MIDAS. The study shows patients have high disability in their physical activities due to migraine^[28].

CONCLUSION

Our data suggest that migraine prevalence was observed higher in females compared to males. Many factors like emotional stress, travel and weather changes may trigger or worsen migraine and self-management of these triggers can probably reduce the prevalence or severity of migraine. The symptoms presented during each stage may vary on patients, though photophobia and phonophobia are mostly experienced during the attack stage of migraine in major study population. Apart from the normal body mass index group, pre-obese patients have more prevalent migraine. The study suggests a prevalence of O blood group among the study population. Though the study implicates acidity as the major comorbidity followed by anxiety and depression among the study group, a vast observational study can be recommended to seek out the association of gastrointestinal diseases with Migraine as detailed by several studies. A less no. of participants have hypothyroidism as co-morbidity. The major prescribing drugs for migraine are calcium channel blockers and non-selective beta blocker and their combinations. The study demonstrates a less quality of living in physiological health domain of Migraineurs followed by psychological health domain. They possess high quality of living in their environmental health status. Majority of the study population have severe disability due to migraine, that impacts on their households and work. Treatment outcome evaluation shows improvement in patient status. The disability due to migraine is lessened on the follow-up study. The mean difference of 9.65 is experienced between the baseline and follow-up.

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