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Migraine with or without metabolic syndrome: Is there any difference?

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Migraine; Metabolic Syndrome; Obesity; Headache

Abstract

Background: Migraine is a common neurological disorder that affects 12-15 percent of the general population. There are few studies in the literature comparing various characteristics of patients with migraine with and without metabolic syndrome with variable results. This study identifies distinct patterns in migraine frequency, severity, or triggers associated with patients with migraine with and without metabolic syndrome.

Methods: This was a cross-sectional study and patients fulfilling the International Classification of Headache Disorders-3rd edition (ICHD-3) for defining migraine were included in the study. National Cholesterol Education Program (NCEP)-Third Report was used to define metabolic syndrome. Headache severity [visual analog scale (VAS) scoring] and disability grading [Migraine Disability Assessment (MIDAS) scoring] were noted. We compared various clinical parameters in patients with migraine with and without metabolic syndrome.

Results: A total of 204 patients with migraine were recruited. We found that the majority of migraineurs were women (female to male ratio = 4.2:1), with a mean age of 28 years (12-58). A total of 25 patients with migraine (12.25%) had metabolic syndrome. In migraineurs with metabolic syndrome, the mean age at onset, female preponderance, and mean duration of illness were significantly higher than migraineurs without metabolic syndrome. Those with and without metabolic syndrome did not significantly differ from one another in terms of migraine triggers, frequency, severity of headache, or disability severity.

Conclusion: This study showed that metabolic syndrome was present in about 12% of patients with migraine. Individuals with metabolic syndrome had longer mean durations of illness and female preponderance and were older at initial presentation compared to migraineurs without metabolic syndrome.

Introduction

Migraine is a common disorder that affects 12-15 percent of the general population.[1,2] The Global Burden of Disease (GBD) study states that migraine is the second most common neurological condition globally and that it causes more disability than all other neurological conditions combined.[3]

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Migraine is usually characterized by a moderate or severe throbbing headache, unilateral pain, nausea or vomiting, light and sound sensitivity, and disability. Neurologic, gastrointestinal, and autonomic symptoms may also be present.[4,5] Abnormalities such as hypertension (HTN), insulin resistance, atherogenic dyslipidaemia, proinflammatory and prothrombotic states, and increased waist circumference (WC) or obesity are all part of the metabolic syndrome.[6] There are several criteria defined to diagnose metabolic syndrome, which makes it difficult to determine which definition is best for a particular patient population.[6] Among these, the National Cholesterol Education Program (NCEP)-Third Report is preferred to define metabolic syndrome [metabolic syndrome is present if three or more of the following five criteria are met: WC over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women), and fasting blood sugar (FBS) over 100 mg/dl].[7]

The association and causality of migraine with obesity and metabolic syndrome is not well understood.[8] There is a growing body of research linking metabolic syndrome to an increased risk and severity of migraines. Some mechanisms can be hypothesized to suggest a link between migraine and metabolic syndrome, including: 1) insulin resistance and brain metabolism: Insulin resistance can impair glucose metabolism in the brain, which may trigger migraines, 2) obesity and migraine frequency: Studies suggest that obesity, a core component of metabolic syndrome, is linked to more frequent and severe migraines, 3) HTN and vascular dysfunction**:** High blood pressure and impaired vascular function can contribute to migraine by affecting blood flow regulation in the brain, 4) the influence of socioeconomic, environmental, genetic and/or psychological factors, and 5) inflammation and oxidative stress: Metabolic syndrome increases inflammatory markers, including neuropeptides, pro-inflammatory mediators, which also play an important role in the pathophysiology of migraine.[9-19]

Studies on migraine and metabolic syndrome are scarce in India. In this study, we examine the clinical profile and intensity of headache in patients with migraine with and without metabolic syndrome, as well as the prevalence of metabolic syndrome in patients with migraine.

This study determines distinct patterns in migraine frequency, severity, or triggers associated with patients with and without metabolic syndrome.

Materials and Methods

Study design and participants: This cross-sectional study was carried out between July 2021 and December 2022 in the Department of Neurology, Indira Gandhi Institute of Medical Sciences, Patna, India. The study was approved by the institutional ethics committee (284/IEC/IGIMS/2021). Written informed consent for participation in the study was obtained from all patients.

Inclusion criteria: Patients fulfilling the following inclusion criteria were included: 1) age 12 years and above and 2) written informed consent. Diagnosis of migraine was based on the International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria for defining migraine.[20]

Exclusion criteria: Patients with drug-induced metabolic syndrome (antiepileptic, immunosuppressive, antipsychotic medications), medication overuse headache, and patients using oral contraceptives were excluded from the study.

Clinical Examination and Evaluation: Using the ICHD-3 criteria, two consultant neurologists and one senior resident from the neurology department diagnosed migraines. Information about each patient's examination and clinical history was recorded. A family history of migraines was acquired.

Migraine triggers for various exogenous (sun exposure, noise, odour, travel, weather change, hair wash, food items, etc.) and endogenous factors (fasting, sleep deprivation, menstruation, stress, etc.) were inquired using a questionnaire. Presence of cutaneous allodynia was noted. Using the Migraine Disability Assessment (MIDAS) examination, patients' levels of disability were graded as follows: grade 1 (no disability, score 0-5), grade 2 (mild disability, score 6-10), grade 3 (moderate disability, score 11-20), and grade 4 (severe disability, score 21+). A visual analog scale (VAS), with 0 representing no pain and 10 representing severe or intolerable pain, was used to assess the severity of the headache. NCEP-Third Report (metabolic syndrome is present if three or more of the following five criteria are met: WC over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting TG level over 150 mg/dl, fasting HDL cholesterol (HDL-C) level less than 40 mg/dl

(men) or 50 mg/dl (women), and FBS over 100 mg/dl) was used to define metabolic syndrome.[21] The following anthropometric measures were taken [height, weight, body mass index (BMI), WC]. Brain magnetic resonance imaging (MRI) and relevant blood investigations, i.e., total blood counts, haemoglobin (Hb), erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hsCRP), blood urea nitrogen (BUN), serum creatinine, liver function test, thyroid stimulating hormone (TSH), blood sugar, and lipid profile, were done. Patients with and without metabolic syndrome were compared in terms of frequency, duration, VAS score, and MIDAS score.

The collected data were analyzed statistically to examine the clinical, demographic, biochemical, and radiological characteristics of patients with migraine. Descriptive statistics were applied to summarize quantitative data, while frequencies and percentages were used to describe categorical (qualitative) data. To compare the distributions between two groups, the Mann-Whitney U test, a non-parametric method, was employed due to the non-normal distribution of data, as determined by the Shapiro-Wilk test. Associations between categorical variables were evaluated using chi-square and Fisher's exact tests, depending on the data characteristics, with effect sizes calculated to assess the strength of associations. Multivariate binary logistic regression analysis was done adjusting the covariates with a P-value of ≤ 0.10 in the univariate analysis. Statistical significance was defined as a P-value less than 0.05.

Results

Baseline characteristics of all migraineurs: The total patients with migraine included in the study were 204. The mean age of migraine onset among these 204 patients was 28.19 ± 11.53 years. The mean duration of illness in these patients was 4.51 ± 4.03 years. The study group comprised 39 men (19.1%) and 165 women (80.9%), resulting in a female to male ratio of 4.2:1. The majority of the patients had bilateral headache (82.4%). Headache was side-locked in 2.5% (n = 5) of patients, while 15.2% (n = 31) had headaches that shifted sides in different attacks. Headache was most commonly located frontally, followed by temporal, occipital, and parietal regions (Table 1). Throbbing and bursting quality of pain was seen in 32.4% and 36.8% of cases, respectively. On the VAS, the average headache intensity was 7.73 ± 1.30. 98% of patients reported at least one trigger for their migraine headaches. The most common trigger was traveling in 76.0% followed by hunger, stress, and sleep deprivation in 53.9%, 35.8%, and 33.8% of cases, respectively (Table 1). Phonophobia was the commonest associated symptom (80.8%) followed by nausea and photophobia, which were seen in 75.9% and 74.9% of cases, respectively.

Table 1. Frequency distribution of various parameters in patients with migraine

Headache characteristics	Total migraine (n = 204)	Headache characteristics	Total migraine (n = 204)
Mean age at onset (year) (mean ± SD)	28.19 ± 11.53	Piercing [n (%)]	7 (3.4)
Female/male ratio	4.2:1	Heaviness [n (%)]	12 (5.9)
Laterality [n (%)]		VAS score (mean ± SD)	7.73 ± 1.30 (range: 3-10)
Unilateral side locked	5 (2.5)	Triggers and symptoms [n (%)]	200 (98.0)
Unilateral side shifting	31 (15.2)	Travelling	155 (76.0)
Bilateral	168 (82.4)	Hunger	110 (53.9)
Location [n (%)]		Mental stress	73 (35.8)
Frontal	77 (37.7)	Odours	55 (27.0)
Temporal	51 (25.0)	Sleep deprivation	69 (33.8)
Parietal	32 (15.7)	Weather change	57 (27.9)
Occipital	35 (17.2)	Aura	11 (5.3)
Supraorbital	4 (2.0)	Phonophobia	165 (80.8)
Neck	5 (2.5)	Photophobia	152 (74.9)
Character of pain [n (%)]		Nausea	154 (75.9)
Throbbing	66 (32.4)	Vertigo	51 (25.1)
Bursting	75 (36.8)	Vomiting	73 (36.0)
Pricking	25 (12.3)	Pain/restriction of neck movements	108 (53.2)
Pulsating	19 (9.3)	Cutaneous allodynia	67 (33.0)

SD: Standard deviation; VAS: Visual analog scale

Eleven patients had auras, and all of them had visual auras. One patient had sensory aura in addition to visual aura. MIDAS grade 4 was seen in 44.6% (n = 91) of patients and 25 (12.25%) and 88 (43.13%) patients had grade 2 and 3, respectively. 179 (87.7%) had severe disability according to MIDAS score. The mean VAS score for severity of headache was 7.73 ± 1.30 (3-10).

Baseline characteristics of migraineurs with metabolic syndrome: Metabolic parameters were studied in all patients with migraine. 27.9% (n = 57) of patients were found to be hypertensive. 27.9% of patients had elevated systolic blood pressure (SBP) while diastolic blood pressure (DBP) was elevated in only 13.2% of patients. 36.3% (n = 74) of patients with migraine in our study had elevated BMI (obese). 9.3% (n = 19) of patients were found to be underweight. In 27.9% (n = 57) of the patients, the waist-hip ratio (WHR) was abnormal; in women, it was more abnormal than in men.

An abnormal lipid profile was seen in 71.6% (n = 146) of patients. Most of them had decreased HDL-C levels (51%, n = 104) followed by raised TG (25.5%, n = 52) and elevated total cholesterol (22.5%, n = 46). FBS was elevated in 61.8% (n = 126) of patients. 22.1% (n = 45) of patients with migraine were found to have elevated hsCRP levels.

Comparison of parameters between migraineurs with metabolic syndrome and those without metabolic syndrome: 12.2% (n = 25) of patients with migraine had metabolic syndrome. In a comparative study of patients with metabolic syndrome and those without metabolic syndrome, on univariate analysis, a significant difference was found in age of onset of illness (35.64 ± 8.68 years vs. 27.15 ± 11.46 years, P = 0.005) and duration of illness (6.14 ± 5.15 years vs. 4.28 ± 3.78 years, P = 0.03) (Figure 1A and 1B). A trend towards female preponderance was noted in patients with migraine with metabolic syndrome but statistical significance was not achieved (P = 0.054). There was no association observed in terms of frequency, associated symptoms, migraine triggers, VAS score, and MIDAS score (Table 2). On multivariate binary logistic regression, a significant association was found in age of onset of illness [confidence interval (CI) = 0.896-0.979, P = 0.004], duration of illness (CI = 0.795-0.975, P = 0.014), and female sex preponderance (CI = 0.120-0.920, P = 0.042) between patients with metabolic syndrome and those without metabolic syndrome (Table 3).

Discussion

In line with earlier research, metabolic syndrome was discovered in 12.25% of our study participants.[11,12,22] Obesity was present in 36.3% of migraineurs. Increased WC (57.8%), hypertriglyceridemia (25.5%), HTN (27.9%), low HDL (51%), and elevated FBS (61.8%) were the criteria used to diagnose metabolic syndrome.

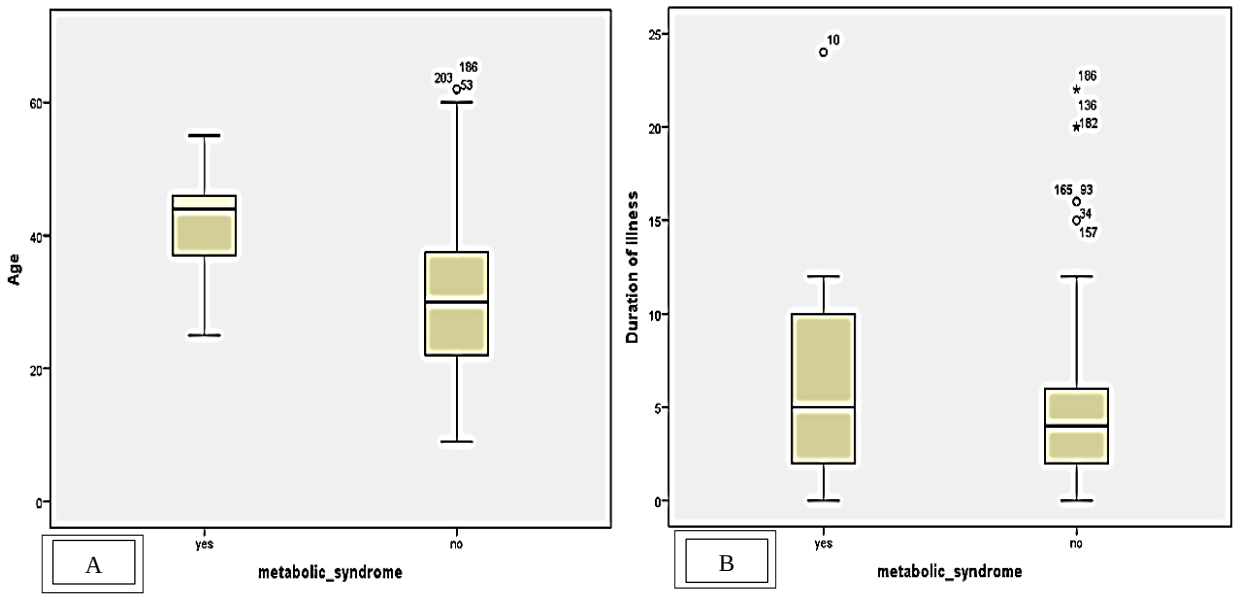

Figure 1. A) Box and whisker plot showing median (thick black line) and interquartile range (IQR) with whisker showing 95% confidence interval (CI) for correlation between age and metabolic syndrome in patients with migraine; B) Box and whisker plot showing median (thick black line) and IQR with whisker showing 95% CI for correlation between duration of illness and metabolic syndrome in patients with migraine

Table 2. Comparison of various parameters between with and without metabolic syndrome in patients with migraine

	Metabolic syndrome present (n = 25)	Metabolic syndrome absent (n = 179)	P
Mean age at onset (year) (mean ± SD)	35.64 ± 8.68	27.15 ± 11.46	0.001
Women	24	141	0.054
Aura	2	9	0.630
Mean duration of illness (year) (mean ± SD)	6.14 ± 5.15	4.28 ± 3.78	0.030
Frequency of headache (mean ± SD)	8.96 ± 7.68	11.79 ± 8.64	0.122
Duration of headache (hour) (mean ± SD)	15.92 ± 14.23	17.42 ± 14.24	0.622
VAS score (mean ± SD)	7.80 ± 1.15	7.72 ± 1.33	0.777
MIDAS score (mean ± SD)	3.28 ± 0.67	3.33 ± 0.68	0.735
Triggers			
Travelling	21	134	0.450
Hunger	9	101	0.080
Mental stress	8	67	0.660
Sleep deprivation	10	59	0.500
Weather change	9	48	0.350
Odours	4	51	0.200
Menstruation	3	16	0.420
Associated symptoms			
Photophobia	21	134	0.450
Phonophobia	16	148	0.060
Nausea	16	138	0.210
Neck pain	13	95	> 0.999
Allodynia	10	57	0.500
Headache laterality			
Unilateral side shifting	6	25	0.230
Bilateral	19	149	0.400
Headache location			
Parietal	5	27	0.560
Frontal	6	69	0.190
Occipital	4	31	> 0.999
Temporal	8	43	0.460
Headache character			
Throbbing	9	57	0.660
Bursting	6	69	0.190
Pulsating	3	16	0.710

VAS: Visual analog scale; MIDAS: Migraine Disability Assessment; SD: Standard deviation

Table 3. Multivariate logistic regression analysis of various parameters between with and without metabolic syndrome in patients with migraine

Parameters	OR	95% CI	P
Age of onset	0.937	0.896-0.979	0.004
Duration of illness	0.880	0.795-0.975	0.014
Female sex	0.104	0.012-0.920	0.042
Hunger	0.494	0.193-1.268	0.143
Headache frequency	1.050	0.990-1.114	0.107
Phonophobia	0.478	0.170-1.340	0.161

OR: Odds ratio; CI: Confidence interval

In our study, migraineurs with metabolic syndrome had significantly higher mean onset ages, mean illness durations, and female preponderance than migraineurs without metabolic syndrome. Age could be closely linked to different elements of metabolic syndrome, including obesity, high blood pressure, glucose intolerance, and elevated lipids, which might represent a correlation rather than a causal factor. There was no discernible difference between migraineurs with and without metabolic syndrome in terms of triggers, related symptoms, aura status, frequency, headache intensity, and disability rating.

The link between migraine and metabolic syndrome has been investigated in several previous research. According to a study by Bhoi et al., migraine was linked to metabolic syndrome in 31.9% of cases.[11] In migraineurs with metabolic syndrome, such as those in our study, the mean age at onset, female preponderance, and mean duration of illness were higher. There were no significant differences in triggers between migraineurs with and without metabolic

syndrome, except for head wash, which was more prevalent in the former group. There was no significant difference between patients with and without metabolic syndrome in terms of headache frequency and intensity.[11]

According to a study by Guldiken et al., metabolic syndrome was present in 19.5% of migraineurs.[22] The Nord-Trondelag Health Study (HUNT), an 11-year longitudinal study, reported a 14.6% incidence of metabolic syndrome in migraine with aura, and patients with migraine with metabolic syndrome were more likely to be woman as in our study. Among the components of the metabolic syndrome, migraine with aura was positively correlated with low HDL-C levels, abdominal obesity, and hyperglycemia.[23] Salmasi et al. conducted a case control study and discovered no difference in the frequency of metabolic syndrome between migraineurs and controls (17% and 15%, respectively).[12]

According to a study by Celikbilek et al., metabolic syndrome was present in 33% of migraineurs. Attack frequency was significantly lower in migraineurs with metabolic syndrome than those without metabolic syndrome but they did not differ in duration and severity of headache.[24]

According to a study by Maghbooli et al., 16.25% of patients with migraine had metabolic syndrome; frequency of migraine attacks had no effect on the frequency of metabolic syndrome. There was no significant difference observed in terms of headache duration between patients with and without metabolic syndrome.[25] Our study showed a significant difference in the duration of migraine illness between patients with and without metabolic syndrome, which may be due to increased mean age of patients with metabolic syndrome than those without metabolic syndrome; therefore, it may be a correlation rather than a causal factor.

The identification of metabolic syndrome in 12.25% of migraineurs in our study carries significant implications for clinical practice and patient management. The relatively high prevalence of individual metabolic syndrome components – especially increased WC (57.8%), elevated FBS (61.8%), and low HDL (51%) – suggests that routine metabolic screening in patients presenting with migraine, particularly in middle-aged and older adults or those with a longer history of migraine is necessary. Early detection of metabolic abnormalities helps in timely interventions that may mitigate long-term cardiovascular risks. Some migraine medications, especially certain preventive agents (e.g., beta-blockers, antiepileptics), can affect weight, blood pressure, or glucose metabolism. Awareness of coexisting metabolic syndrome can help in medication choice, i.e., agents that are metabolically neutral or beneficial (e.g., topiramate for weight reduction, candesartan for blood pressure control and migraine prevention). Lifestyle factors that influence both metabolic syndrome and migraine – such as Mediterranean diet, regular aerobic exercise, and behavioral interventions (e.g., stress management and sleep hygiene) – should be done in patient counseling. The consistent findings across multiple studies highlight the need for guideline revisions to reflect the importance of metabolic screening in migraine management.

Although the current study focuses on a population from Eastern India, the prevalence of metabolic syndrome (12.25%) among migraineurs and certain metabolic abnormalities, including low HDL levels (51%), elevated FBS (61.8%), and an increased WC (57.8%), are consistent with trends found in other studies conducted worldwide.[12,22,23,25] This consistency across diverse geographic and ethnic populations suggests that the association between migraine and metabolic dysfunction may represent a shared biological or pathophysiological mechanism.

Limitations: The cross-sectional design of our study inherently restricts the capacity to draw causal conclusions. The relatively small sample size may affect the generalizability of the results. The lack of a control group, small sample size, and unequal number of patients with and without metabolic syndrome in our study were among its limitations. Disproportionately large number of women may limit the applicability of results to men. The study included patients with migraine from different regions of Eastern India, including both urban and rural population comprising diverse socioeconomic classes. Case-control studies with larger cohorts may provide more robust data to assess whether such associations/causal bases exist in patients with migraine with metabolic syndrome. Further research should be explored to see whether targeted interventions for metabolic syndrome can alter the clinical course of migraine and reduce its burden.

Conclusion

Migraine was associated with metabolic syndrome in 12.25% of patients. The patients with migraine

with metabolic syndrome were associated with longer duration of migraine and female preponderance and presented at an older age. The severity, frequency, and duration of headache episodes did not significantly differ between patients with and without metabolic syndrome. Metabolic syndrome in patients with migraine might not have an impact on the frequency, intensity, or length of migraine attacks. Clinicians or physicians may treat migraines in patients with or without metabolic syndrome using similar approaches, focusing on medications and lifestyle modifications that can improve both metabolic syndrome and migraine.

Conflict of Interests

The authors declare no conflict of interest in this study.

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