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Research Article

Association Between Migraine and Non-Alcoholic Fatty Liver Disease (NAFLD): A Hospital-Based Observational Study

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Abstract: Background: Migraine is a complex neurovascular disorder characterized by recurrent disabling headaches, while non-alcoholic fatty liver disease (NAFLD) represents a hepatic manifestation of metabolic dysfunction. Emerging evidence suggests shared metabolic, inflammatory, and oxidative pathways linking these two conditions, yet their interrelationship remains poorly elucidated in the Indian population. **Objectives:** To evaluate the association between migraine and NAFLD, to analyze the pattern and severity of headache in NAFLD patients with migraine, and to assess correlations between migraine characteristics and biochemical markers of NAFLD. **Methods:** A hospital-based, open-label observational study was conducted in the Departments of General Medicine and Radiodiagnosis, Jawaharlal Nehru Medical College, Aligarh. Ninety-four clinically diagnosed migraine patients were enrolled after informed consent and ethical clearance. Each participant underwent anthropometric evaluation, liver function testing, lipid profiling, and ultrasonographic screening for NAFLD. Statistical analysis was performed using SPSS version 16.0, applying Chi-square and unpaired t-tests, with significance set at $p<0.05$. **Results:** Among 94 patients, 84% were female and 30.9% experienced migraine with aura. The majority were aged below 30 years. Alanine aminotransferase (ALT) levels were significantly higher in patients with aura (38.62±19.41 U/L) compared to those without (31.25±14.06 U/L; $p = 0.04$). Alkaline phosphatase also showed a significant difference ($p = 0.01$). No significant variations were observed in anthropometric, blood pressure, or lipid parameters. However, patients with aura had markedly higher attack frequency (9.17±3.04 vs 5.58±2.45 months; $p = 0.001$), greater attack severity (6.12±0.99 vs 3.87±1.39; $p = 0.001$), and longer attack duration (30.66±22.23 h vs 12.03±12.24 h; $p = 0.001$). The presence of hepatic grade (GRD) correlated significantly with aura occurrence ($p = 0.0001$). **Conclusion:** The study demonstrates a significant association between migraine—particularly migraine with aura—and biochemical markers of NAFLD, indicating a possible role of hepatic metabolic dysregulation and oxidative stress in migraine pathophysiology. Early identification of NAFLD in migraine patients could help mitigate long-term vascular and metabolic complications.

Keywords: Migraine, Non-Alcoholic Fatty Liver Disease, NAFLD, Aura, Oxidative Stress, Liver Enzymes, Metabolic Syndrome

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INTRODUCTION

Migraine is a disabling primary headache disorder that represents one of the most common and burdensome neurological conditions worldwide. It is defined by the International Classification of Headache Disorders (ICHD-3) as recurrent attacks of moderate to severe headache lasting 4–72 hours, typically associated with nausea, vomiting, photophobia, and phonophobia [1]. It affects over 17% of women and 5–8% of men globally [1]. Recent global burden data indicate that migraine prevalence may exceed 20% in some populations, ranking it among the leading causes of years lived with disability [2]. The chronic migraine subtype, characterized by headache on ≥15 days per month, affects 2–5% of the population and contributes disproportionately to personal and socioeconomic burden [3].

Pathophysiology of Migraine

The etiopathogenesis of migraine is multifactorial, involving genetic, neurovascular, and metabolic components. Genome-wide association studies have identified more than a dozen migraine-associated variants involving genes linked to glutamatergic neurotransmission, synaptic signaling, vascular tone regulation, and pain modulation [4]. Pathophysiologically, migraine is thought to arise from complex interactions between the trigeminovascular system, cortical spreading depression, and central pain processing centers [5,6]. During an attack, vasoactive neuropeptides such as calcitonin gene-related peptide (CGRP), substance P, and neurokinin A are released from trigeminal afferents, leading to neurogenic inflammation, dural vasodilation, and activation of nociceptive pathways [5]. Cortical spreading

depression (CSD) is believed to underlie the aura phenomenon and may itself trigger trigeminovascular activation [6]. Subsequent sensitization of second-order neurons within the trigeminal nucleus caudalis and brainstem nuclei contributes to headache perpetuation and central hypersensitivity. Additionally, hypothalamic activation and autonomic dysregulation have been implicated in prodromal and autonomic symptoms such as yawning, flushing, and diaphoresis.

Biochemical and Metabolic Dimensions

Recent advances have emphasized the role of oxidative stress, mitochondrial dysfunction, and impaired energy metabolism in migraine pathophysiology. Patients with migraine demonstrate altered levels of neuropeptides, amino acids, and inflammatory mediators, reflecting systemic metabolic dysregulation [7]. Metabolomic profiling studies have identified perturbations in lipid, glucose, and amino acid metabolism during migraine attacks, reinforcing the view that migraine is not purely a neuronal disorder but a systemic one involving vascular and hepatic pathways [8]. Oxidative imbalance characterized by depletion of endogenous antioxidants such as albumin, uric acid, and bilirubin has been reported in migraineurs, suggesting a compromised defense against reactive oxygen species. These biochemical derangements may contribute to endothelial dysfunction and vascular inflammation, thus linking migraine to broader metabolic disturbances.

Non-Alcoholic Fatty Liver Disease (NAFLD)

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most prevalent cause of chronic liver disease worldwide, with an estimated global prevalence of 24–30% [7-9]. It is defined as excessive hepatic fat accumulation in the absence of significant alcohol intake or other secondary causes of steatosis [10]. NAFLD encompasses a spectrum ranging from simple hepatic steatosis (NAFL) to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma [11]. Its pathophysiology is multifactorial, historically explained by the "two-hit hypothesis" wherein insulin resistance acts as the first insult and oxidative stress as the second [12]. However, current evidence favors the "multiple-hit" model involving inter-organ crosstalk among the adipose tissue, gut, pancreas, and liver, mediated by lipotoxicity, inflammatory cytokines, adipokines, and gut dysbiosis [13-14]. Insulin resistance promotes hepatic de novo lipogenesis and accumulation of free fatty acids in hepatocytes, which leads to mitochondrial dysfunction, lipid peroxidation, and chronic inflammation [15].

The disease is closely associated with components of metabolic syndrome (MetS)—central obesity, dyslipidemia, type 2 diabetes mellitus, and hypertension [16]. Up to 80% of patients with NASH are obese, 72% have dyslipidemia, and 44% have diabetes [17]. Genetic predispositions such as PNPLA3 I148M polymorphism and environmental factors, including high-fat diets and sedentary lifestyles, further increase susceptibility [18]. Interestingly, even "lean" NAFLD, prevalent among Asian populations, reflects metabolic dysregulation independent of obesity.

Biochemically, NAFLD is often detected incidentally through mildly elevated transaminases—particularly alanine aminotransferase (ALT)—although liver enzymes can be normal in more than 70% of cases [19]. Elevated γ-glutamyl transferase (GGT), alkaline phosphatase (ALP), and lipid profile abnormalities (high triglycerides and LDL-C) are frequently noted [20]. These alterations mirror systemic metabolic stress and endothelial dysfunction that may also influence extra-hepatic disorders, including cardiovascular disease, kidney disease, and possibly migraine [21-22].

Common Pathways Linking Migraine and NAFLD

Both migraine and NAFLD share overlapping pathophysiological mechanisms—namely insulin resistance, oxidative stress, inflammation, and endothelial dysfunction. Migraineurs, particularly those with aura, often demonstrate metabolic comorbidities such as dyslipidemia, obesity, and insulin resistance [23]. Similarly, NAFLD represents a hepatic component of systemic metabolic derangement [15]. Oxidative stress, central to NAFLD progression, may promote vascular dysfunction and neuroinflammation, both key processes in migraine pathogenesis.

Celikbilek *et al.* [24] investigated this link in 90 migraine patients and found significantly higher body mass index (BMI), waist circumference, serum insulin, triglycerides, and ALT in migraineurs with NAFLD compared to those without. The presence of aura and longer attack duration were notably more frequent in the NAFLD group. Although headache intensity did not correlate directly with hepatic steatosis grade, the findings suggested a metabolic overlap between the two diseases. Martami *et al.* [25] also reported a marginally significant association between migraine and NAFLD (OR 2.03, 95% CI 0.98–4.21; $p = 0.055$) in a cohort of obese patients. These studies underscore that hepatic steatosis and migraine may coexist within a common metabolic-inflammatory milieu.

Inflammatory mediators such as interleukins, tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP) are elevated in both conditions. In migraine, systemic inflammation and vascular endothelial dysfunction may sensitize trigeminal nociceptors, whereas in NAFLD, the same mediators drive hepatic fibrogenesis [21]. Reduced serum antioxidants—albumin, bilirubin, and uric acid—reported in migraine patients further suggest impaired

redox balance similar to that seen in NAFLD. Additionally, alterations in lipid metabolism, including increased triglycerides and LDL-C, have been documented in both disorders.

Clinical Implications

Understanding the link between migraine and NAFLD carries potential diagnostic and therapeutic significance. Identification of NAFLD in migraineurs may serve as a clinical marker of underlying metabolic dysfunction and cardiovascular risk. Conversely, management of hepatic steatosis through lifestyle modification and insulin sensitization could reduce migraine frequency and severity by improving systemic inflammatory status. Despite growing recognition of these shared pathways, limited data exist from Indian populations where both migraine and NAFLD are prevalent and often underdiagnosed.

Rationale and Need for the Study

While metabolic syndrome has been extensively studied in relation to both conditions, direct evidence connecting migraine and NAFLD remains scarce. Most available studies are cross-sectional and Western-based, lacking exploration of biochemical correlations such as liver enzyme derangements, lipid patterns, or fibrosis indices in migraine patients. Furthermore, variations in dietary habits, genetic background, and BMI distribution among Indian patients may influence disease manifestation. Therefore, evaluating the coexistence of NAFLD in migraine patients and its biochemical correlates is crucial to understanding whether hepatic metabolic disturbances contribute to migraine pathophysiology or vice versa.

Study Objectives

The present hospital-based observational study was designed to:

- Establish a correlation between migraine and NAFLD
- Study the pattern of headache, including aura and severity, in patients with NAFLD presenting with migraine
- Examine associations between migraine characteristics and biochemical markers of NAFLD, particularly liver function parameters and lipid profiles

This study aims to contribute to existing literature by elucidating possible metabolic and hepatic influences on migraine presentation within an Indian clinical setting. The findings may enhance clinical screening strategies, promote early detection of NAFLD in migraineurs, and open new avenues for integrated management of these intersecting disorders.

MATERIALS AND METHODS

- **Study Design:** A hospital-based, open-labelled, observational cross-sectional study was conducted to assess the association between migraine and non-alcoholic fatty liver disease (NAFLD)
- **Study Setting:** The study was carried out in the Departments of General Medicine and Radiodiagnosis, Jawaharlal Nehru Medical College (JNMC), Aligarh Muslim University (AMU), Aligarh, Uttar Pradesh, India
- **Study Duration:** The research was conducted over a defined period after obtaining institutional ethical clearance, with data collection spanning patients attending the Medicine Outpatient Department (OPD), Medicine Ward, and Radiodiagnosis Department
- **Ethical Considerations:** Prior approval was obtained from the Institutional Ethics Committee (IEC) of JNMC, AMU. All participants provided written informed consent before enrolment in accordance with the Declaration of Helsinki
- **Study Population:** The study included patients aged ≥18 years presenting with clinically diagnosed migraine (with or without aura) who were evaluated for NAFLD
- **Sample Size:** A total of 94 patients were included in the study. The sample size was calculated using the standard formula:
- n=Z2pqd2n = \frac{Z^2 pq}{d^2}n=d2Z2pq
- where Z = confidence interval, p = 0.05, q = 1−p, and d = allowable error

Inclusion Criteria

- Patients diagnosed with migraine according to the International Classification of Headache Disorders (ICHD-3) criteria
- Age ≥18 years of either sex
- Willingness to participate and provide written informed consent

Exclusion Criteria

- Patients with cirrhosis of the liver or chronic liver disease other than NAFLD
- History of significant alcohol intake (>20 g/day)
- Pregnancy and breastfeeding women
- Patients with hypothyroidism, chronic kidney disease, or those on hepatotoxic drugs
- Known cases of secondary or other primary headache disorders
- Patients unwilling to give consent

Clinical Evaluation

Each participant underwent a detailed history and physical examination focusing on:

- Headache pattern (duration, frequency, aura, relieving factors)
- Presence of hypertension, diabetes, dyslipidemia, or metabolic features
- Weight, height, BMI, waist circumference, and blood pressure
- Signs of hepatic or dyslipidemic stigmata

Symptomatology Assessment

History of associated symptoms such as epigastric pain, visual disturbances, palpitations, dyspnea, fatigue, and weight changes was documented using a structured proforma. Lifestyle factors including dietary lipid intake, drug use, and addiction were recorded.

Investigations

All patients underwent baseline and disease-specific investigations, including:

- Complete blood count (Hb, TLC, DLC, platelets)
- Liver function tests (AST, ALT, ALP, total, direct, and indirect bilirubin)
- Serum albumin, globulin, GGTP, blood urea, and serum creatinine
- Lipid profile (total cholesterol, HDL, LDL, VLDL, triglycerides)
- Fasting plasma glucose and other relevant biochemical markers

Radiological Assessment

Abdominal ultrasonography was performed in all cases to detect hepatic steatosis. The diagnosis of NAFLD was based on characteristic ultrasonographic findings in the absence of alcohol use or other causes of liver disease. Liver biopsy was performed wherever feasible to confirm the diagnosis and grade of steatosis.

Derived Indices and Scores

- AST/ALT ratio, APRI (AST-to-Platelet Ratio Index), and NAFLD Fibrosis Score were calculated for non-invasive assessment of hepatic involvement
- FibroScan was performed in selected cases to measure liver stiffness and quantify fibrosis

Data Analysis

Data were entered in Microsoft Excel and analyzed using SPSS version 16.0 (Chicago, IL, USA). Results were presented as mean±standard deviation (SD) for continuous variables and as frequencies or percentages for categorical variables.

- **Chi-square Test:** Was applied for categorical comparisons
- **Unpaired t-Test:** Was used for continuous variable comparison
- p-value <0.05 was considered statistically significant

Outcome Measures

The primary outcome was to determine the association between migraine (with or without aura) and the presence or severity of NAFLD**.** Secondary outcomes included correlations between migraine characteristics (frequency, duration, severity) and biochemical markers (ALT, ALP, lipid profile, and fibrosis indices).

RESULTS

The present observational study was conducted in the Department of General Medicine and the Department of Radiodiagnosis at Jawaharlal Nehru Medical College, Aligarh, with the objective of establishing a correlation between migraine and non-alcoholic fatty liver disease (NAFLD). A total of 94 patients diagnosed with migraine were included in the analysis.

Among these, 30.9% (29 patients) experienced migraine with aura, whereas 69.1% (65 patients) had migraine without aura. Thus, nearly one-third of the study population exhibited aura phenomena preceding or accompanying migraine attacks.

Age and Gender Distribution

The age of the participants ranged from less than 25 years to above 35 years**.** The largest proportion—44.7% (42 patients)—belonged to the <25-year age group**,** followed by 35.1% (33 patients) in the 25–30-year range, 9.6% (9 patients) in the 31–35-year range, and 10.6% (10 patients) older than 35 years. The prevalence of aura was highest among individuals aged **>**35 years (40%) and lowest among those aged 31–35 years (22.2%). Statistical analysis using the chi-square test indicated no significant association between age category and the presence of aura (p = 0.82).

With regard to sex distribution**,** 84% (79) were female and 16% (15) were male, resulting in a female-to-male ratio of roughly 5: 1. The prevalence of aura was 31.6% among females and 26.7% among males**,** again showing no statistically significant difference (p = 0.70). Hence, while migraine was markedly more common in women, the likelihood of aura occurrence did not differ substantially by gender (Table 1 and Figure 1).

Anthropometric Parameters

The mean height among aura-positive subjects was 158.00±8.76 cm, almost identical to 157.97±8.53 cm among those without aura (p = 0.98*).* The mean weight was 54.33±10.10 kg versus 53.70±6.08 kg, also nonsignificant (p = 0.71*).* Corresponding BMI values were 21.73±2.95 kg/m^2 and 21.77±2.71 kg/m^2, respectively (p = 0.95*).* Waist circumference averaged 86.08±7.25 cm in the aura group and 85.65±6.08 cm in the non-aura group (p = 0.77*).* Thus, no anthropometric parameter showed significant variation according to aura status (Table 2).

Table 1: Distribution of Migraine Patients According to Age and Sex (n = 94)

Age Group (years)	No. of Patients	Percentage	With Aura n (%)	Without Aura n (%)
< 25	42	44.7	13 (30.9)	29 (69.1)
25–30	33	35.1	10 (30.3)	23 (69.7)
31–35	9	9.6	2 (22.2)	7 (77.8)
> 35	10	10.6	4 (40.0)	6 (60.0)
Total	94	100.0	29 (30.9)	65 (69.1)
Mean Age: 27.8±6.4 years	p = 0.82 (NS)			
Sex	Frequency (n)	Percentage	With Aura n (%)	p-value
Male	15	16.0	4 (26.7)	0.70 (NS)
Female	79	84.0	25 (31.6)	

Table 2: Comparison of Anthropometric and Blood Pressure Parameters in Migraine with and Without Aura

Parameter	With Aura (Mean±SD)	Without Aura (Mean±SD)	p-value
Height (cm)	158.00±8.76	157.97±8.53	0.98 (NS)
Weight (kg)	54.33±10.10	53.70±6.08	0.71 (NS)
BMI (kg/m^2)	21.73±2.95	21.77±2.71	0.95 (NS)
Waist (cm)	86.08±7.25	85.65±6.08	0.77 (NS)
SBP (mmHg)	118.50±10.43	117.64±9.24	0.70 (NS)
DBP (mmHg)	75.42±7.13	76.58±8.74	0.55 (NS)

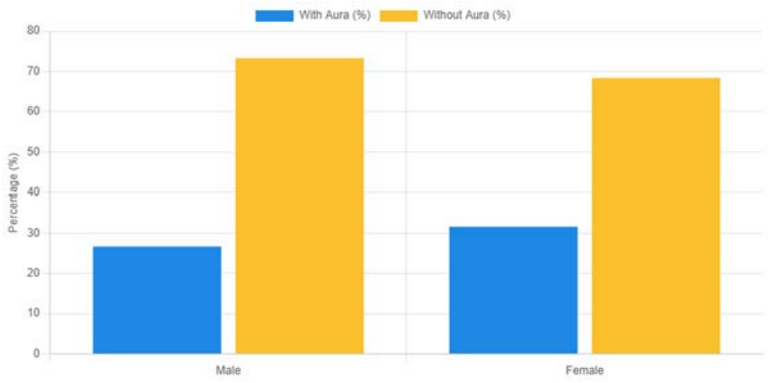


Figure 1: Distribution of Migraine Types Gender (n =94)

Table 3: Comparison of Liver Function Tests Between Migraine with and Without Aura

Parameter	With Aura (Mean±SD)	Without Aura (Mean±SD)	p-value
AST (U/L)	115.17±73.33	155.30±102.16	0.08 (NS)
ALT (U/L)	38.62±19.41	31.25±14.06	0.04 (S)
ALP (U/L)	126.18±45.60	213.14±56.12	0.01 (S)
Total Bilirubin (mg/dL)	0.54±0.15	0.60±0.15	0.13 (NS)
Direct Bilirubin (mg/dL)	0.39±0.10	0.42±0.13	0.26 (NS)
Indirect Bilirubin (mg/dL)	0.22±0.10	0.23±0.15	0.69 (NS)

S – Significant, NS – Not Significant

Liver Function Tests

Among liver enzymes, alanine aminotransferase (ALT) levels were significantly elevated in patients with aura (38.62±19.41 U/L) compared with those without aura (31.25±14.06 U/L), with p = 0.04. Similarly, alkaline phosphatase (ALP) values showed a highly significant difference, being 126.18±45.60 U/L in aura patients versus 213.14±56.12 U/L in non-aura subjects (p = 0.01*).*

Other liver parameters, however, did not differ notably between the two groups. Mean aspartate aminotransferase (AST) values were 115.17±73.33 U/L in the aura group and 155.30±102.16 U/L in the non-aura group (p = 0.08*).* Total bilirubin levels averaged 0.54±0.15 mg/dL and 0.60±0.15 mg/dL**,** respectively (p = 0.13*).* Direct bilirubin was 0.39±0.10 mg/dL versus 0.42±0.13 mg/dL (p = 0.26*), and indirect bilirubin was 0.22±0.10 mg/dL versus 0.23±0.15 mg/dL (p = 0.69*).* Hence, the significant parameters among liver enzymes were ALT and ALP, suggesting hepatic metabolic differences between aura and non-aura migraineurs (Table 3).

Lipid Profile Analysis

Lipid levels demonstrated no statistically significant variation between groups. The total cholesterol concentration was 186.12±51.29 mg/dL in patients with aura and 204.72±45.53 mg/dL in those without (p = 0.09*).* Mean triglyceride levels were 111.67±40.29 mg/dL versus 105.88±29.68 mg/dL (p = 0.45*).* High-density lipoprotein (HDL) values averaged 33.88±20.28 mg/dL and 33.51±21.54 mg/dL (p = 0.94*).* Low-density lipoprotein (LDL) concentrations were 107.38±15.91 mg/dL versus 108.29±18.95 mg/dL (p = 0.83*).**** Very-low-density lipoprotein (VLDL) values were 24.88±8.66 mg/dL and 24.00±8.44 mg/dL (p = 0.66*).* These findings imply that lipid abnormalities were not significantly associated with aura occurrence.

Other Biochemical Parameters

Comparison of general biochemical indices also failed to reveal significant inter-group differences. Mean white blood cell count (WBC) was 5.56±1.09 × 10^9/L in the aura group and 5.49±1.27 × 10^9/L in the non-aura group (p = 0.83*). * Platelet count was 246.38±79.07 × 10^3/µL versus 250.36±71.96 × 10^3/µL (p = 0.82*).* Hemoglobin levels were virtually identical—12.13±1.57 g/dL and 12.14±1.61 g/dL (p = 0.98*).* Serum creatinine values were 0.47±0.19 mg/dL and 0.51±0.19 mg/dL (p = 0.41*).* Fasting plasma glucose averaged 85.12±7.44 mg/dL and 82.67±6.84 mg/dL, also nonsignificant (p = 0.14*).* Hence, no notable deviation in hematological or renal indices was observed between migraine subgroups.

Ultrasound and FibroScan Findings

Ultrasonographic evaluation confirmed hepatic steatosis in a subset of participants. Grade of fatty liver (GRD) was GRADE ONE (I) present in 12.8% (12 patients) of the total cohort. Among these, 75% exhibited migraine with aura, compared with 24.4% among those without hepatic grade. This association was statistically highly significant (p = 0.0001), implying a strong correlation between the presence of NAFLD and migraine with aura.

Liver stiffness measured by FibroScan showed a mean value of 4.70±0.61 kPa in the aura group and 4.58±0.55 kPa in the non-aura group. The difference was not statistically significant (p = 0.38), suggesting comparable fibrosis levels between groups.

Disease Duration and Headache Characteristics

The mean duration of migraine illness was 1.54±1.17 years among aura patients and 1.79±1.54 years in those without aura. The difference was not significant (p = 0.46*). *

In contrast, parameters related to the attack profile showed marked variation. The mean attack frequency was significantly higher in the aura group (9.17±3.04 attacks per month) compared to the non-aura group (5.58±2.45 attacks per month), with a p-value of 0.001.

The mean attack severity score (on a visual analog scale) was 6.12±0.99 in aura patients and 3.87±1.39 in non-aura patients, indicating a highly significant difference (p = 0.001*). *

Similarly, the mean attack duration was prolonged in aura patients (30.66±22.23 hours) relative to those without aura (12.03±12.24 hours), and this difference too was highly significant (p = 0.001).

Table 4: Comparison of Headache Characteristics Between Migraine with and Without Aura

Headache Feature	With Aura (Mean±SD)	Without Aura (Mean±SD)	p-value
Attack Frequency (per month)	9.17±3.04	5.58±2.45	0.001 (S)
Attack Severity (VAS Score)	6.12±0.99	3.87±1.39	0.001 (S)
Attack Duration (hours)	30.66±22.23	12.03±12.24	0.001 (S)
Duration of Illness (years)	1.54±1.17	1.79±1.54	0.46 (NS)

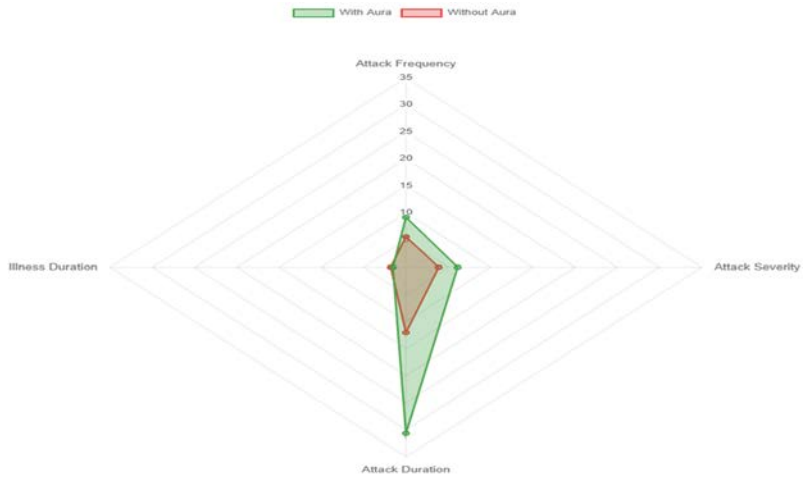


Figure 2: Comparison of Headache Characteristics (Mean±SD)

Together, these findings demonstrate that migraine with aura was associated with more frequent, severe, and longer-lasting headache episodes compared with migraine without aura (Table 4 and Figure 2).

Summary of Numerical Findings

In summary:

- 94 migraine patients were studied
- 29 (30.9%) had aura; 65 (69.1%) did not
- Females: 84%; Males: 16%
- **Age distribution:** <25 years = 44.7%; 25–30 years = 35.1%; 31–35 years = 9.6%; >35 years = 10.6%

Significant iochemical Findings:

- **ALT:** 38.62±19.41 vs 31.25±14.06 (p = 0.04)
- **ALP:** 126.18±45.60 vs 213.14±56.12 (p = 0.01)
- GRD presence strongly associated with aura (p = 0.0001)
- **Non-significant variables:** anthropometry, BP, lipid profile, WBC, platelets, Hb, creatinine, glucose, and FibroScan values.

Attack parameters (Significant)

- **Frequency:** 9.17±3.04 vs 5.58±2.45 (p = 0.001)
- **Severity:** 6.12±0.99 vs 3.87±1.39 (p = 0.001)
- **Duration:** 30.66±22.23 h vs 12.03±12.24 h (p = 0.001)

Interpretation

Overall, the analysis reveals that while general anthropometric and lipid measures were similar across migraine types**,** hepatic enzyme elevations (ALT and ALP) and presence of fatty liver on imaging (GRD) showed significant association with migraine with aura**.** Furthermore, aura-positive patients suffered from more frequent, longer, and more severe

Table 5: Association of NAFLD (Ultrasound Grade) With Migraine Type

Ultrasound Finding	With Aura n (%)	Without Aura n (%)	Total n (%)	p-value
Fatty Liver Grade I Present (GRD+)	9 (75.0)	3 (25.0)	12 (12.8)	0.0001 (HS)
No Fatty Liver (GRD–)	20 (24.4)	62 (75.6)	82 (87.2)	
Total	29 (30.9)	65 (69.1)	94 (100)	

HS – Highly Significant

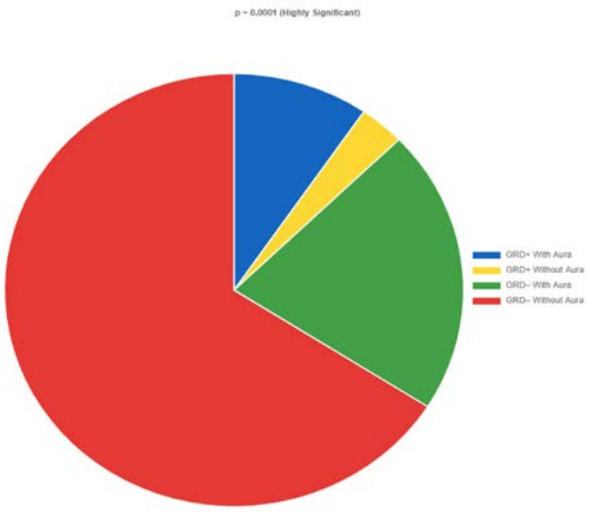


Figure 3: Association of NAFLD (Fatty Liver Grade I) With Migraine Type

headache attacks. These results imply a potential hepatic-metabolic contribution to migraine severity and suggest that NAFLD may play a role in modulating disease expression among migraineurs (Table 5 and Figure 3).

DISCUSSION

Migraine is a highly prevalent, recurrent neurological disorder characterized by disabling headache episodes often accompanied by sensory and autonomic symptoms [1-2]. It affects approximately 15% of the global population, ranking among the top causes of years lived with disability [2-3]. Although the disorder is primarily neurovascular in origin, a growing body of research suggests a significant metabolic and inflammatory component underlying its pathophysiology [4–6]. Non-alcoholic fatty liver disease (NAFLD), the hepatic manifestation of metabolic syndrome, shares similar risk factors and pathophysiological pathways, including insulin resistance, oxidative stress, and endothelial dysfunction [24-25,16,21]. The present hospital-based observational study sought to explore the possible association between migraine and NAFLD, analyze headache patterns in affected individuals, and determine whether biochemical markers of liver dysfunction correlate with migraine characteristics such as aura, severity, and frequency.

Demographic Profile

In this study, 94 patients with migraine were evaluated, out of which 30.9% experienced migraine with aura and 69.1% had migraine without aura. The predominance of females (84%) over males (16%) aligns with existing epidemiological data, which consistently demonstrate that migraine affects women two to three times more frequently than men [27-28]. The hormonal influence of estrogen fluctuations is thought to explain the higher susceptibility and increased attack frequency among women [29,23]. Although the proportion of female participants was substantially higher, the presence of aura did not significantly differ between sexes ($p = 0.70$), suggesting that gender-related hormonal variation influences migraine occurrence but not necessarily the aura subtype.

Age-wise, the majority of patients (44.7%) were younger than 25 years, followed by 35.1% between 25 and 30 years. The prevalence of aura was highest among those above 35 years (40%) and lowest among 31–35 years (22.2%). Similar trends have been reported by Martami *et al.* [25], who found that migraine with aura was more common in older participants within a cohort of overweight and obese subjects. The current findings indicate that younger adults constitute the dominant demographic affected by migraine, consistent with global observations that the disorder peaks between 20 and 40 years of age [27].

Anthropometric and Hemodynamic Observations

In this study, no statistically significant differences were observed in anthropometric parameters such as height, weight, BMI, and waist circumference between patients with and without aura ($p>0.05$). Similarly, systolic and diastolic blood pressures were comparable across both groups ($p = 0.70$ and 0.55, respectively). These findings indicate that while metabolic factors may contribute to migraine risk, general body composition indices alone are not sufficient discriminators of migraine subtypes.

Contrastingly, Celikbilek *et al.* [24] observed significantly higher BMI and waist circumference among migraine patients with NAFLD, suggesting a possible role of central obesity in linking migraine with hepatic steatosis. The lack of such association in the present study may be due to a younger study population and lower prevalence of obesity (mean BMI 21.7 kg/m^2).

Moreover, while hypertension is often considered part of the metabolic syndrome complex linked to NAFLD [16,21], it was not a distinguishing feature between migraine types in this cohort. The normotensive status of most patients indicates that vascular factors in migraine might arise from transient neurovascular dysregulation rather than persistent systemic hypertension.

Liver Enzyme Alterations and Biochemical Correlates

The most notable biochemical differences in this study were observed in liver function tests (LFTs). Alanine aminotransferase (ALT) levels were significantly higher among migraine patients with aura (38.62±19.41 U/L) compared to those without aura (31.25±14.06 U/L, $p = 0.04$). Alkaline phosphatase (ALP) was also significantly different ($p = 0.01$). However, other liver enzymes, including aspartate aminotransferase (AST) and bilirubin fractions, did not differ significantly between groups.

The significance of ALT elevation suggests subclinical hepatocellular injury or metabolic hepatic stress in migraineurs with aura. Previous studies on NAFLD have documented that ALT is often the earliest and most sensitive marker of hepatic steatosis [19-20]. Mansour-Ghanaei *et al.* [11] similarly reported significant elevation in hepatic enzymes (AST, ALT, GGT) in NAFLD patients compared to controls, with a direct relationship to disease grade on ultrasonography. In our study, the correlation of elevated ALT and ALP with migraine aura suggests that hepatic metabolic derangements might influence the neural or vascular mechanisms underlying aura phenomena.

Notably, Yang *et al.* [13] reported that serum albumin (ALB), total bilirubin (TBIL), and uric acid (UA) were significantly lower in migraine patients than in healthy controls, indicating a compromised antioxidant defense. The present study reinforces this oxidative link, as hepatic enzyme abnormalities reflect oxidative stress and metabolic imbalance—factors implicated in migraine pathophysiology.

Hence, hepatic biochemical changes seen in migraine with aura could be a peripheral manifestation of systemic oxidative and inflammatory stress. This supports the "metabolic hypothesis" of migraine, wherein abnormal mitochondrial energy metabolism and oxidative imbalance increase cortical excitability and susceptibility to cortical spreading depression (CSD), the electrophysiological substrate of aura [5-6].

Lipid and Metabolic Findings

In this study, the lipid profile, including total cholesterol, triglycerides, HDL, LDL, and VLDL, showed no significant difference between migraine with and without aura. These findings are consistent with Warkade *et al.* [10], who reported variable dyslipidemia among NAFLD patients but no strong correlation with migraine frequency or subtype.

However, several prior studies suggest that dyslipidemia may play a contributory role in migraine pathogenesis. Celikbilek *et al.* [24] demonstrated higher triglyceride levels and insulin resistance indices (HOMA-IR) in migraine patients with NAFLD compared to those without. Alshehri *et al.* [17] reported elevated total cholesterol and LDL levels with reduced HDL among Saudi female migraineurs, supporting the role of lipid disturbances in neuronal excitability and vascular dysfunction. The absence of lipid variations in the present study might reflect the smaller sample size or younger age group with fewer comorbidities.

The pathophysiological link between lipid metabolism and migraine likely involves endothelial dysfunction and inflammation. Low HDL and high LDL can increase vascular permeability and oxidative stress, predisposing to migraine attacks [20-21]. Furthermore, oxidative stress-induced peroxidation of lipids could activate trigeminovascular pathways, promoting neurogenic inflammation. Thus, while no statistical significance was observed in our data, biochemical trends consistent with metabolic stress remain plausible.

NAFLD and Migraine Association

A central finding of this study is the strong relationship between NAFLD grade and migraine with aura. Fatty liver (graded on ultrasonography) was present in 12.8% of patients, and within this subset, 75% had migraine with aura

compared to only 24.4% without hepatic grade (p = 0.0001). This highly significant association suggests that hepatic steatosis is more prevalent among aura-positive migraineurs.

These results are consistent with those of Celikbilek *et al.* [18], who found that the incidence of migraine with aura and the duration of disease and attacks were significantly higher in patients with NAFLD. Although their study did not establish a direct correlation between hepatic steatosis grade and headache intensity, it highlighted that metabolic and hepatic abnormalities are more pronounced in migraineurs with aura. Similarly, Martami *et al.* [25] identified a marginal association between migraine and NAFLD (OR 2.03, p = 0.055) and found higher odds for gastrointestinal comorbidities like dyspepsia and irritable bowel syndrome, suggesting systemic metabolic dysregulation in primary headaches.

The present study's findings reinforce that NAFLD may not merely coexist with migraine but could modulate its severity and clinical expression. The liver, being a central metabolic organ, influences systemic energy homeostasis, insulin sensitivity, and inflammatory balance—all of which impact cerebrovascular tone and neuronal excitability [15]. The presence of NAFLD, thus, may create a pro-inflammatory milieu that lowers the threshold for migraine initiation.

FibroScan and Non-Invasive Fibrosis Scores

Although the mean liver stiffness measured by FibroScan was slightly higher among patients with aura (4.70±0.61 kPa) than without aura (4.58±0.55 kPa), this difference was not statistically significant (p = 0.38). These values correspond to minimal hepatic fibrosis. The lack of significant variation suggests that in migraine patients, hepatic dysfunction remains largely at the steatosis stage rather than progressing to fibrosis. Non-invasive fibrosis scores like APRI and NAFLD Fibrosis Score further corroborated mild disease severity.

Previous large-scale studies, such as those by Ando and Jou [27] and Singh *et al.* [30], note that progression from steatosis to fibrosis occurs slowly, often over decades. The relatively young mean age (<30 years) of participants in our study explains the absence of advanced fibrosis. Nonetheless, the co-presence of even early hepatic fat infiltration with migraine could represent a common subclinical manifestation of systemic metabolic stress.

Headache Characteristics and Disease Severity

The study revealed that migraine with aura was associated with a significantly greater attack frequency, severity, and duration compared to migraine without aura. Specifically, aura-positive patients experienced an average of 9.17±3.04 attacks per month versus 5.58±2.45 attacks (p = 0.001), with mean severity scores of 6.12±0.99 versus 3.87±1.39 (p = 0.001), and mean duration of 30.66±22.23 hours versus 12.03±12.24 hours (p = 0.001). These findings suggest that aura is not only a distinguishing clinical feature but also a marker of greater disease burden [31-35].

The enhanced attack severity may reflect greater cortical excitability and more profound neurovascular dysregulation among aura patients. Similar findings were reported by Zanigni *et al.* [19], who observed longer attack durations and higher aura frequency in migraineurs with NAFLD. These parallels imply that hepatic metabolic dysfunction may amplify cortical spreading depression susceptibility or impair vascular autoregulation, thereby intensifying migraine episodes [36-40].

Moreover, the association between elevated liver enzymes and more severe migraine attacks supports the involvement of systemic inflammation. ALT and ALP elevations may represent hepatic oxidative stress secondary to systemic inflammatory signaling [21]. This shared oxidative environment could potentiate neuronal hyperexcitability, enhancing migraine intensity and duration. Thus, the hepatic metabolic axis might serve as a key modulator of migraine chronicity [41-44].

Pathophysiological Interlinks Between Migraine and NAFLD

Several overlapping mechanisms may explain the observed association between migraine and NAFLD:

- **Insulin Resistance:** Both disorders exhibit insulin signaling impairment. Hyperinsulinemia and reduced insulin sensitivity enhance sympathetic activity, vascular tone fluctuations, and pro-inflammatory cytokine release, all of which facilitate migraine onset [16-17]
- **Oxidative Stress:** NAFLD progression is driven by lipid peroxidation and mitochondrial dysfunction [13-14]. Migraine likewise involves reactive oxygen species (ROS)-induced vascular and neuronal injury
- **Endothelial Dysfunction:** Chronic inflammation in NAFLD impairs endothelial nitric oxide synthesis, reducing vasodilatory capacity. A similar mechanism contributes to cortical vasoconstriction in migraine aura [5]
- **Inflammatory Cytokines:** Elevated TNF-α, IL-6, and C-reactive protein are common to both diseases, mediating neurogenic inflammation and hepatic injury
- **Altered Lipid Metabolism:** Dyslipidemia seen in NAFLD contributes to altered membrane fluidity and neuronal excitability, factors linked with migraine frequency

- **Reduced Antioxidant Reserve:** As observed by Yang *et al.* [13], lower serum albumin, bilirubin, and uric acid levels in migraine reflect impaired antioxidant capacity, a hallmark also found in NAFLD

These shared pathophysiological cascades support the concept of a "neuro-hepatic metabolic axis", whereby hepatic metabolic dysfunction can influence cerebral excitability and vascular reactivity.

Comparison with Other Studies

The prevalence of NAFLD in our migraine cohort (12.8%) falls within the global range of 6–33% for the general population [8], but its higher representation among aura patients aligns with studies by Celikbilek *et al.* [24] and Martami *et al.* [25]. The significant correlation between liver enzymes and migraine severity parallels observations by Alshehri *et al.* [17], who reported biochemical alterations in migraine patients suggestive of hepatic metabolic involvement.

Unlike the study by Warkade *et al.* [10], which found strong associations between triglyceride levels and NAFLD, our cohort did not exhibit significant lipid abnormalities. This may relate to regional dietary differences or smaller sample size. Nonetheless, the overall pattern supports that hepatic metabolic stress, rather than overt dyslipidemia, correlates more closely with migraine activity.

Clinical Implications

The findings underscore the need for metabolic and hepatic evaluation in patients with frequent or severe migraine, particularly those with aura. Routine screening for NAFLD through liver enzyme assays and ultrasonography could identify at-risk individuals early. Addressing modifiable factors such as diet, physical inactivity, and obesity could yield dual benefits—improving hepatic health and reducing migraine burden.

Furthermore, the study provides a rationale for exploring hepatoprotective and antioxidant therapies as adjuncts in migraine management. Agents such as vitamin E, coenzyme Q10, or lifestyle interventions that enhance hepatic lipid metabolism might improve both hepatic and neurological outcomes.

Limitations

The study's limitations include its single-center design, small sample size, and cross-sectional nature, which preclude causal inference. Liver biopsy, the diagnostic gold standard, was feasible in only a limited number of cases. Moreover, advanced imaging (MRI-PDFF or elastography) for fat quantification was not routinely available. Longitudinal studies with larger cohorts and controlled confounders such as diet, medication, and hormonal status are warranted to validate these findings.

CONCLUSION

The present study establishes a statistically significant association between migraine—particularly migraine with aura—and biochemical and radiological markers of NAFLD. Elevated liver enzymes (ALT, ALP) and ultrasonographic evidence of hepatic steatosis correlated with increased headache frequency, severity, and duration. These results suggest that hepatic metabolic dysregulation and oxidative stress may contribute to migraine pathophysiology.

Given the rising prevalence of NAFLD in younger adults, especially in South Asian populations, clinicians should consider routine hepatic screening in migraineurs. Early identification and management of metabolic abnormalities may not only prevent liver disease progression but also help in reducing migraine morbidity. Future research integrating neuroimaging, metabolomic, and hepatic profiling could elucidate the molecular basis of this emerging neuro-metabolic interaction.

Ethical Approval

Approved by Institutional Ethics Committee of JNMC, AMU (Reference No.: [insert IEC number])

Conflict of Interest

None declared

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REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS). "The International Classification of Headache Disorders, 3rd Edition." *Cephalalgia*, vol. 33, no. 9, 2013, pp. 629–808.
2. Stovner, L.J. *et al.* "The Global Burden of Headache: A Documentation of Headache Prevalence and Disability Worldwide." *Cephalalgia*, vol. 27, no. 3, 2007, pp. 193–210.

3. Valade, D. "Chronic Migraine: Epidemiology and Pathophysiology." *Revue Neurologique*, vol. 169, no. 5, 2013, pp. 355–363.
4. Ferrari, M.D. *et al.* "Migraine Pathophysiology: Lessons from Mouse Models and Human Genetics." *The Lancet Neurology*, vol. 14, no. 1, 2015, pp. 65–80.
5. Noseda, R. and Burstein, R. "Migraine Pathophysiology: Anatomy of the Trigeminovascular Pathway and Associated Neurological Symptoms, Cortical Spreading Depression, Sensitization and Modulation of Pain." *Pain*, vol. 154, suppl. 1, 2013, pp. S44–S53.
6. Burstein, R. *et al.* "Migraine: Multiple Processes, Complex Pathophysiology." *The Journal of Neuroscience*, vol. 35, no. 17, 2015, pp. 6619–6629.
7. Lonardo, A. *et al.* "Nonalcoholic Fatty Liver Disease: Evolving Paradigms." *Nature Reviews Gastroenterology & Hepatology*, vol. 15, no. 5, 2018, pp. 273–287.
8. Deng, M. *et al.* "Metabolomic Biomarkers in Migraine Pathogenesis." *Metabolomics*, vol. 17, no. 3, 2021, pp. 1–15.
9. Tekeşin, A. and Tunç, A. "Inflammatory and Hematological Markers in Migraine." *Neurological Research*, vol. 41, no. 9, 2019, pp. 787–793.
10. Warkade, H.R. *et al.* "Biochemical Parameters in NAFLD Patients." *International Journal of Research in Medical Sciences*, vol. 6, no. 10, 2018, pp. 3411–3415.
11. Mansour-Ghanaei, F. *et al.* "Biochemical Markers and Lipid Profile in NAFLD." *Clinical and Experimental Hepatology*, vol. 5, no. 3, 2019, pp. 234–240.
12. Harder, A.V.E. *et al.* "Metabolic Profiles in Migraine: A Serum NMR Study." *Brain and Behavior*, vol. 11, no. 7, 2021, e02214.
13. Yang, F. *et al.* "Serum Antioxidant Markers and Migraine: A Case-Control Study." *Frontiers in Neurology*, vol. 13, 2022, 852418.
14. Burch, R.C. *et al.* "Epidemiology and Impact of Migraine." *Current Neurology and Neuroscience Reports*, vol. 15, no. 1, 2015, article 7.
15. Kurth, T. *et al.* "Migraine with Aura: Risk Factors and Comorbidities." *BMJ*, vol. 368, 2020, m292.
16. Villegas, R. *et al.* "Association between Metabolic Syndrome and NAFLD." *Diabetes Care*, vol. 34, no. 8, 2011, pp. 1730–1735.
17. Alshehri, A. *et al.* "Correlation between Migraine and Biochemical Parameters in Saudi Females." *Journal of Clinical Medicine Research*, vol. 11, no. 6, 2019, pp. 401–407.
18. Lonardo, A. *et al.* "Genetics and Metabolic Syndrome in NAFLD." *Journal of Gastroenterology and Hepatology*, vol. 30, no. 3, 2015, pp. 436–445.
19. Obika, M. and Noguchi, H. "Diagnosis and Evaluation of Nonalcoholic Fatty Liver Disease." *Hepatology Research*, vol. 42, no. 8, 2012, pp. 744–752.
20. Siddiqui, M.S. *et al.* "NAFLD and Cardiovascular Disease Risk." *Clinical Gastroenterology and Hepatology*, vol. 13, no. 4, 2015, pp. 681–688.
21. Targher, G., Byrne, C.D. and Tilg, H. "NAFLD and Cardiovascular Disease: Risk and Mechanisms." *Nature Reviews Gastroenterology & Hepatology*, vol. 15, no. 8, 2018, pp. 425–440.
22. Mantovani, A. *et al.* "Nonalcoholic Fatty Liver Disease and Risk of Cardiovascular Disease." *Metabolism*, vol. 65, no. 8, 2016, pp. 1136–1150.
23. Day, C.P. and James, O.F.W. "Steatohepatitis: A Two-Hit Hypothesis." *Gastroenterology*, vol. 114, no. 4, 1998, pp. 842–845.
24. Celikbilek, A. *et al.* "Relationship between Migraine and Nonalcoholic Fatty Liver Disease." *European Journal of Neurology*, vol. 21, no. 9, 2014, pp. 1124–1130.
25. Martami, F. *et al.* "Primary Headaches and Gastrointestinal Disorders: An Association with NAFLD." *Neurological Sciences*, vol. 39, no. 11, 2018, pp. 1889–1897.
26. Chalasani, N. *et al.* "The Diagnosis and Management of Non-Alcoholic Fatty Liver Disease: Practice Guideline by the AASLD, ACG and AGA." *Hepatology*, vol. 55, no. 6, 2012, pp. 2005–2023.
27. Ando, Y. and Jou, J.H. "Nonalcoholic Fatty Liver Disease: New Insights and Clinical Management." *Clinical and Molecular Hepatology*, vol. 27, no. 3, 2021, pp. 354–364.
28. Marchesini, G. *et al.* "Nonalcoholic Fatty Liver Disease: Epidemiology and Natural History." *Journal of Hepatology*, vol. 64, no. 3, 2016, pp. 668–673.
29. Younossi, Z.M. *et al.* "Global Epidemiology of NAFLD." *Hepatology*, vol. 68, no. 1, 2018, pp. 349–360.
30. Yazar, T. *et al.* "Role of Oxidative Stress in Migraine Pathophysiology." *The Journal of Headache and Pain*, vol. 21, no. 1, 2020, pp. 1–9.
31. Wang, X.J. *et al.* "Pathogenesis and Diagnosis of Nonalcoholic Fatty Liver Disease." *World Journal of Gastroenterology*, vol. 22, no. 37, 2016, pp. 7953–7963.
32. Tan, C.E. *et al.* "Can We Apply the IDF Definition of Metabolic Syndrome to Asians?" *Diabetes Care*, vol. 27, no. 5, 2004, pp. 1182–1186.
33. Pokharel, D.R. *et al.* "Metabolic Syndrome in Asian Populations." *International Journal of Diabetes in Developing Countries*, vol. 34, no. 4, 2014, pp. 209–214.
34. Zanigni, S. *et al.* "Migraine with Aura and Metabolic Disturbances." *Headache*, vol. 54, no. 8, 2014, pp. 1345–1355.
35. Global Burden of Disease (GBD) Study 2019. *The Lancet*, vol. 394, no. 10204, 2019, pp. 121–163.
36. Headache Classification Committee of the International Headache Society (IHS). "The International Classification of Headache Disorders (ICHD-3 Beta)." *Cephalalgia*, vol. 38, no. 1, 2018, pp. 1–211.
37. Frederiksen, S.D. *et al.* "Biomarker Discovery in Migraine." *Cephalalgia*, vol. 40, no. 8, 2020, pp. 813–825.
38. Tietjen, G.E. *et al.* "Vasoactive Peptides and Oxidative Stress in Migraine." *Headache*, vol. 58, no. 1, 2018, pp. 56–69.
39. Buzzetti, E. *et al.* "Multiple-Hit Pathogenesis of NAFLD." *Metabolism*, vol. 65, no. 8, 2016, pp. 1038–1048.
40. Eslam, M. *et al.* "MAFLD: A New Definition for Metabolic-Associated Fatty Liver Disease." *Journal of Hepatology*, vol. 73, no. 1, 2020, pp. 202–209.

41. Gozke, E. *et al.* "Migraine, Tension Headache and Metabolic Syndrome." *Headache*, vol. 53, no. 1, 2013, pp. 116–123.
42. Sheng, J. *et al.* "Oxidative Stress and Vascular Dysfunction in Migraine." *Free Radical Biology and Medicine*, vol. 153, 2020, pp. 141–149.
43. Erdener, S.E. *et al.* "Neurovascular Mechanisms in Migraine: Oxidative and Metabolic Pathways." *Frontiers in Physiology*, vol. 12, 2021, 640896.
44. Xie, N. *et al.* "Serum Antioxidants and Oxidative Stress Markers in Migraine Patients." *Headache*, vol. 60, no. 5, 2020, pp. 945–955.