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# TREATMENT OUTCOMES IN PATIENTS PRESCRIBED ACUTE AND PREVENTIVE ANTI-MIGRAINE THERAPY: A PROSPECTIVE OBSERVATIONAL STUDY FROM A TERTIARY CARE CENTRE IN NORTH INDIA

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## ABSTRACT

**Background:** Migraine is a leading neurological cause of disability worldwide; however, real world treatment outcome data from Indian tertiary care settings remain limited. The objective is to evaluate prescribing patterns, clinical effectiveness (≥50% reduction in monthly migraine days), migraine-related disability (MIDAS), and adverse drug reaction (ADR) profile in patients receiving combined acute and preventive anti-migraine therapy. **Materials and Methods:** A prospective, observational study was conducted over 18 months at the Neurology OPD of Dr. Ram Manohar Lohia Institute of Medical Sciences (Dr. RMLIMS), Lucknow. A total of 261 patients (18–60 years) with ICHD-3-confirmed migraine were enrolled. Disability was assessed by MIDAS at baseline and 3 months. ADRs were evaluated using the WHO–UMC causality scale. **Results:** Mean age was 35.6±11.4 years; 81.2% were female. Naproxen-domperidone was the predominant acute therapy (90.0%); amitriptyline (35.2%), flunarizine (24.5%), and propranolol (22.2%) were the leading preventive agents. Median MIDAS score fell from 25 to 10 (p<0.001). Mean monthly migraine days reduced from 12.04±4.31 to 5.34±3.12 (p<0.001). A good outcome (≥50% reduction) was achieved by 92.7% of patients. ADRs occurred in 24.9%, predominantly mild–moderate. **Conclusion:** Neurologist-guided combination therapy produced significant reductions in migraine frequency and disability. Rational drug selection and structured follow-up are critical determinants of favourable outcomes in Indian tertiary care practice.

## INTRODUCTION

Migraine is recognised by the World Health Organization (WHO) as one of the world's top 20 causes of disability,[1] imposing substantial personal, economic, and societal burden globally. With an estimated one-year prevalence of approximately 14–15% in the general adult population,[2] it affects nearly one billion individuals worldwide. In India, a population-based study from Karnataka reported a one-year migraine prevalence of 25.2%, with notably higher rates among women (31.6%) and rural residents.[3] The observed female predominance is largely attributed to hormonal modulation of neuronal excitability, particularly fluctuations in oestrogen levels.[4]

Despite its high prevalence and disabling nature, migraine remains underdiagnosed and inadequately treated in routine practice,[5] Real-world data from the United States indicate that fewer than 30% of eligible patients receive guideline-recommended acute therapy, and preventive treatment is prescribed in only 25% of indicated cases,[6] In India, the treatment landscape is shaped by concerns of

affordability, availability, and physician familiarity; NSAIDs dominate acute prescribing while triptans remain underutilised in the majority of eligible patients.[7,8]

A favourable treatment response — conventionally defined as a ≥50% reduction in monthly migraine days — is the benchmark endorsed by the International Headache Society (IHS) and regulatory agencies including the FDA and EMA.[9,10] Achievement of this threshold correlates with clinically meaningful improvements in migraine-specific disability as measured by validated tools such as the Migraine Disability Assessment (MIDAS) questionnaire.[11] However, large-scale Indian studies that comprehensively integrate prescribing patterns, MIDAS outcomes, responder rates, and ADR surveillance in routine tertiary care practice are scarce. This study was designed to address this evidence gap.

## MATERIALS AND METHODS

**Study design and setting:** A prospective, observational study was conducted at the Neurology OPD, Dr. RMLIMS, Lucknow — a government-funded tertiary care teaching hospital in North India — over 18 months (June 2024–August 2025), following approval from the Institutional Ethics Committee.

**Participants:** Adults aged 18–60 years of either sex with ICHD-39-confirmed migraine attending the Neurology OPD were enrolled after written informed consent. Exclusion criteria included pregnancy or lactation, organ failure (renal, hepatic, or cardiac), HIV or hepatitis B/C infection, known drug hypersensitivity, and documented non-adherence to prescribed therapy.

**Sample size:** Based on a published good-outcome rate of 18.8% reported by Gurunath et al 8 . using the formula $n = Z^2p(1-p)/d^2$ (Z=1.96, d=0.07), the minimum sample was 235; with 10% anticipated loss to follow-up, the final target was 261 patients.

**Data collection:** Baseline demographics, migraine characteristics (location, duration, triggers, associated symptoms), comorbidities, and complete prescription details — including drug, dose, frequency, and fixed-dose combinations — were recorded on a structured case-record form and verified at follow-up.

**Outcome assessment:** The primary outcome was the proportion achieving ≥50% reduction in monthly migraine days at 3 months (good outcome). Secondary outcomes included changes in MIDAS score, prescription pattern analysis, and ADR incidence. Causality of ADRs was classified by the WHO–UMC scale.

**Statistical analysis**

Data were analysed using Jamovi v2.6.44.0. The Shapiro–Wilk test confirmed non-normality of continuous distributions; paired comparisons used the Wilcoxon signed-rank test, categorical variables the Chi-square test. A two-tailed $p<0.05$ was significant.

## RESULTS

**Demographic and clinical profile:** Of 261 enrolled patients, 212 (81.2%) were female and 49 (18.8%) male (F:M ratio ≈ 4.3:1). Mean age was 35.6±11.4 years; the majority (61.7%) were in the 21–40-year age group. Mean BMI was 23.66±2.39 kg/m². Urban and rural patients were equally represented (50.6% vs 49.4%). Employed individuals comprised the largest occupational group (50.2%), followed by housewives (22.6%).

**Migraine characteristics:** Hemicranial headache was the most common presentation (54.4%), followed by global (29.9%), vertex (8.8%), and bifrontal/occipital (6.9%). Most patients (82.4%) had migraine duration ≥3 months. Key associated symptoms included photophobia (86.2%), phonophobia (82.0%), nausea (75.9%), and vomiting (61.7%). Leading triggers were sunlight exposure (77.0%), noise (72.4%), and fasting (52.1%); menstruation was a trigger in 45.8% of female patients.

**Prescription pattern [Table 1]:** Naproxen-domperidone (Naxdom®/Napra-D®) was the predominant acute treatment (90.0%). Among preventive agents, amitriptyline was most frequently prescribed (35.2%), followed by flunarizine (24.5%), propranolol (22.2%), and valproate (11.9%).

**Table 1: Prescription pattern**

| Drug / Regimen | n (N=261) | % |
|---|---|---|
| ACUTE THERAPY | | |
| Naproxen + Domperidone (Naxdom®/Napra-D®) | 235 | 90.0 |
| No acute NSAID-based therapy | 26 | 10.0 |
| PREVENTIVE THERAPY | | |
| Amitriptyline | 92 | 35.2 |
| Flunarizine | 64 | 24.5 |
| Propranolol | 58 | 22.2 |
| Valproate | 31 | 11.9 |
| Others (combination/miscellaneous) | 16 | 6.1 |

*Others include cyproheptadine, topiramate, and combination preventive regimens.

**Treatment outcomes [Table 2]:** The median MIDAS score decreased significantly from 25 (IQR 14–45; Grade IV — Severe Disability) at baseline to 10 (IQR 6–19; Grade II — Mild Disability) at 3


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months (Wilcoxon, p<0.001). Mean monthly migraine days declined from 12.04±4.31 to 5.34±3.12, a 55.6% reduction (p<0.001). Using the ≥50% responder criterion, 242 patients (92.7%) achieved a good outcome; 19 (7.3%) had a poor outcome.

**Table 2: Treatment outcomes at 3 months (N = 261)**

| Parameter | Baseline | 3 Months | p-value |
|---|---|---|---|
| Median MIDAS score (IQR) | 25 (14–45) | 10 (6–19) | <0.001* |
| Mean monthly migraine days (±SD) | 12.04 ± 4.31 | 5.34 ± 3.12 | <0.001* |
| Good outcome — ≥50% reduction in migraine days | — | 242 (92.7%) | — |
| Poor outcome — <50% reduction in migraine days | — | 19 (7.3%) | — |

*Wilcoxon signed-rank test; IQR = interquartile range; SD = standard deviation.

**Adverse drug reactions [Table 3]:** ADRs were recorded in 65 patients (24.9%); each patient experienced a single ADR. Sedation/drowsiness was most frequent (13.8%), followed by gastritis (9.2%), weight gain and dizziness (7.7% each). Drug-wise, amitriptyline was the most implicated agent (26.2% of ADRs), followed by combination preventive regimens (24.6%), propranolol (9.2%), valproate (7.7%), and flunarizine (6.2%). Severity grading showed 41 mild (63.1%) and 24 moderate (36.9%) reactions; no severe or life-threatening ADRs occurred. WHO–UMC causality was probable in 45 (69.2%) and possible in 20 (30.8%) cases.

**Table 3: Distribution of adverse drug reactions (N = 65)**

| ADR Type | n (N=65) | % |
|---|---|---|
| Sedation / Drowsiness | 9 | 13.8 |
| Gastritis / Epigastric discomfort | 6 | 9.2 |
| Weight gain | 5 | 7.7 |
| Dizziness / Vertigo | 5 | 7.7 |
| Fatigue / Weakness | 4 | 6.2 |
| Constipation / Dry mouth / Nausea | 3 each | 4.6 each |
| Hypotension / Bradycardia / Head heaviness | 3 each | 4.6 each |
| Insomnia / Tremors / Paraesthesia | 2 each | 3.1 each |
| Visual disturbance / Palpitations / Increased appetite | 1 each | 1.5 each |

ADR = adverse drug reaction.

## DISCUSSION

The present study provides a comprehensive real-world evaluation of migraine management integrating demographic profiling, prescribing pattern analysis, disability outcomes, and ADR surveillance in a North Indian tertiary care setting.

Demographics and clinical profile. The marked female preponderance (F:M = 4.3:1) observed in our study is consistent with epidemiological data reported by Vetvik and MacGregor,[4] and with Indian community-based data by Kulkarni et al,[3] both of whom documented a female-to-male ratio of approximately 3:1. The predominance of patients in the 21–40-year age group aligns with global burden data (Stovner et al.),[2] confirming peak migraine prevalence during economically productive years. The near-equal urban-rural distribution (50.6% vs 49.4%) in our cohort reflects progressively improving access to neurological care among rural populations, as previously highlighted by Steiner et al,[12] in their analysis of headache healthcare access in India.

Prescription patterns — acute therapy. Naproxen-domperidone combination therapy (90.0%) dominated acute prescribing in our cohort, reflecting an affordability- and availability-driven paradigm. This pattern closely aligns with findings by Vivekanand et al,[7] who reported NSAIDs as the cornerstone of acute therapy in a North Indian tertiary care OPD with triptan utilisation below 15%, and with Gurunath et al,[8] who documented a similar NSAID-dominant prescribing pattern in a South Indian teaching hospital. In stark contrast, Diamond et al,[6] in the American Migraine Prevalence and Prevention (AMPP) study found that even in the United States, fewer than 30% of eligible migraine patients received triptans — underscoring a global gap between guideline recommendations and clinical practice. The near-exclusive reliance on NSAID-based fixed-dose combinations in our setting is attributable to cost constraints, restricted triptan availability in the public sector, and established physician familiarity with these agents.

Prescription patterns — preventive therapy. Amitriptyline was the most frequently prescribed preventive agent (35.2%), consistent with the Indian consensus document by Singh et al. (2024),[13] which recommends amitriptyline as a first-line preventive option in the Indian subcontinent based on its cost-effectiveness and Level A evidence. Flunarizine (24.5%) and propranolol (22.2%) were the next most prescribed agents, mirroring the pattern described by Prakash and Shah,[14] in their review of Indian migraine prophylaxis practice, where flunarizine was identified as the most widely used preventive drug in Indian neurology clinics owing to proven efficacy and favourable tolerability. Valproate use (11.9%) broadly corresponds to the 10–14% prevalence reported by Bhide et al,[15] in a Mumbai-based prescription audit. Notably, CGRP

monoclonal antibodies (erenumab, fremanezumab) were entirely absent from our prescriptions, consistent with Silberstein et al,[16] who documented the restricted real-world use of these agents outside high-income settings due to prohibitive cost and limited insurance coverage.

Treatment effectiveness — responder rate. The primary outcome — ≥50% reduction in monthly migraine days — was achieved by 242 patients (92.7%), representing a substantially higher responder rate than comparable published data. In the American Migraine Study II, Lipton et al,[17] reported adequate migraine control in only 40–50% of treated patients across primary care settings in the US. The AMPP study by Diamond et al,[6] found that real-world good-outcome rates rarely exceeded 25% among eligible US patients. In the Indian context, Gurunath et al,[8] — whose published rate of 18.8% was used as the basis for our sample size calculation — observed substantially lower control rates in a comparable tertiary care setting. Vivekanand et al,[7] documented adequate control in approximately 35% of North Indian OPD patients, while Bhide et al,[15[ from Mumbai reported a ≥50% responder rate of approximately 45% over,[6] months of follow-up. The markedly higher responder rate in our study (92.7%) is likely attributable to: (i) exclusive neurologist-directed rational pharmacotherapy; (ii) combined acute and preventive prescribing in the majority of patients; (iii) structured 3-month follow-up with MIDAS reassessment that encouraged adherence; and (iv) the relatively short 3-month follow-up window, which captures early treatment response before attrition-related decline, as documented by Ramsey et al,[18] who found that nearly 50% of patients discontinue preventive therapy within 6 months.

Disability outcomes — MIDAS. The median MIDAS score declined from 25 (Grade IV — Severe Disability) at baseline to 10 (Grade II — Mild Disability) at 3 months, representing a 15-point reduction that is both statistically significant ($p<0.001$) and clinically meaningful. Smelt et al,[11] established a minimum clinically important difference (MCID) of 5 MIDAS points; our 15-point reduction exceeds this threshold by threefold. Silberstein et al. 10 demonstrated in their evidence-based guideline update that effective preventive therapy (propranolol, topiramate) reduced MIDAS scores by approximately 30–50% in randomised controlled trials, whereas our real-world cohort achieved a 60% reduction — likely reflecting the additive contribution of combined acute and preventive therapy under structured neurologist supervision. Buse et al,[19] in the CaMEO study observed persistent high disability scores even in partially treated patients, emphasising that functional recovery often lags behind frequency reduction — a dynamic consistent with our finding of a moderate, though significant, MIDAS improvement relative to the more dramatic decline in attack frequency.

Adverse drug reactions. The overall ADR incidence of 24.9% is consistent with the known tolerability profiles of the prescribed medications. Amitriptyline accounted for the highest proportion of individual-drug ADRs (26.2%), with sedation and weight gain being predominant — findings that mirror those of Bhide et al,[15] who identified these as the leading causes of amitriptyline discontinuation in their Mumbai cohort. The safety profile of triptans and NSAIDs in migraine management has been well characterised by Tfelt-Hansen et al,[20] who documented that gastrointestinal effects with NSAIDs and vasomotor symptoms with triptans are the most frequently reported adverse effects in clinical practice. Kapoor et al,[21] highlighted that medication-overuse headache (MOH) — a frequent complication of unmonitored analgesic use in India — was not recorded in our cohort, likely because structured neurologist-guided prescribing prevented excessive acute medication intake. The WHO–UMC probable categorisation in 69.2% of ADRs reflects a clear temporal relationship with drug administration, supporting causality attribution.

**Limitations**

The single-centre design limits generalisability. The 3-month follow-up may not capture long-term adherence trends, MOH development, or chronification risk. Episodic and chronic migraine subtypes were not analysed separately, and the absence of a control group precludes causal inference. Selection bias towards patients seeking tertiary neurological care may also have contributed to the high responder rate observed.

## CONCLUSION

Neurologist-guided combination acute and preventive anti-migraine therapy produced clinically and statistically significant reductions in migraine frequency and disability in this North Indian tertiary care cohort. A ≥50% reduction in monthly migraine days was achieved by 92.7% of patients — substantially higher than previously reported Indian real-world rates — underscoring the critical importance of rational drug selection, combined therapy, and structured follow-up. Amitriptyline and flunarizine remain the mainstay of preventive therapy in this setting. ADRs were common but uniformly mild-to-moderate. Multicentre prospective studies with longer follow-up, subtype-specific analysis, and adherence monitoring are needed to validate these findings and develop context-appropriate migraine management protocols for Indian clinical practice.

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