

MIGRAINE PRODROMAL SYMPTOMS AND THEIR CLINICAL MANIFESTATIONS, AN OBSERVATIONAL MULTICENTER STUDY

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Background. Migraine prodromal symptoms typically emerge 2–48 hours before headache onset and include cognitive, affective, and homeostatic disturbances. Although widely described in the literature, their reported prevalence varies considerably, likely due to methodological differences in symptom assessment. This multicenter observational study aimed to evaluate the prevalence, characteristics, timing, and distribution of prodromal symptoms across migraine subtypes in routine outpatient clinical practice.

Methods. Consecutive adult patients diagnosed with migraine without aura, migraine with aura, or chronic migraine according to ICHD-3 criteria were enrolled at multiple Italian headache centers between January and June 2025. Patients reporting prodromal symptoms constituted the study group, while those not reporting prodromal symptoms served as controls for prevalence analysis. An interviewer-administered questionnaire assessed symptom type, timing, duration, and recurrence. Descriptive statistics were performed; group differences were evaluated using t-tests and chi-square tests, with significance set at $p<0.05$.

Results. Among 3,711 migraine patients (mean age 41.3 ± 13.4 years; 86.0% female), 122 (3.3%) reported prodromal symptoms. Prevalence differed significantly across migraine subtypes ($\chi^2=7.67$, $p=0.02$): 3.5% in migraine without aura, 5.3% in migraine with aura, and 2.2% in chronic migraine. The most frequent prodromal manifestations were yawning/asthenia (37.7%), difficulty concentrating (33.6%), anxiety (26.2%), hunger (21.3%), and depressive symptoms (18.9%). Mean prodromal onset occurred 9.9 ± 11.4 hours before headache onset, with a mean duration of 6.3 ± 8.9 hours. Female patients reported significantly longer prodromal duration than males (6.9 ± 9.3 vs 1.1 ± 1.9 hours; $p<0.001$). Prodromal symptoms recurred in approximately 30% of attacks within the same patient and remained clinically consistent over time.

Conclusions. In this large outpatient cohort, migraine prodromal symptoms were infrequently reported, particularly in chronic migraine, suggesting substantial underrecognition in routine clinical practice. Prodromal manifestations were more common in episodic migraine and were mainly characterized by non-specific cognitive, affective, and homeostatic symptoms. Their variable recurrence and duration highlight the heterogeneity of the migraine prodrome and support the need for improved recognition to facilitate earlier therapeutic intervention.