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Clinical, behavioral, and metabolic determinants of migraine chronification: a systematic review

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Introduction
Migraine is a highly prevalent and potentially progressive neurological disorder, whose chronification—defined as the transition from episodic to chronic forms—poses a major clinical challenge. Multiple risk factors, particularly modifiable ones such as high attack frequency, inadequate management, and comorbid conditions, play a central role in this process and are critical targets for preventive strategies.

Objective
To evaluate clinical, behavioral, and metabolic risk factors associated with migraine chronification, with emphasis on modifiable determinants and their impact on disease progression.

Methods
This systematic review included studies retrieved from PubMed and LILACS databases using the descriptors "Risk Factors," "migraine," and "chronification" combined with the Boolean operator AND, yielding 84 records. The research question was structured using the PICO framework: in patients with episodic migraine (P), does exposure to modifiable risk factors and triggers (I), compared with non-exposure (C), increase the risk of migraine chronification, defined by higher attack frequency and disability (O). Studies published between 2021 and 2026, with full-text availability and in English, were considered eligible. After applying inclusion and exclusion criteria, 17 studies were selected for full analysis.

Results
Migraine chronification was predominantly associated with modifiable factors. Medication overuse emerged as a major determinant, increasing the risk of progression by up to threefold (OR≈3.0). Higher baseline attack frequency and disability were also strongly linked to chronification (OR≈2.08 for high disability). Psychiatric comorbidities, including depression (OR≈1.33–1.42) and anxiety (OR≈1.24), showed increasing prevalence with rising attack frequency. Additional contributors included allodynia, greater interictal burden, multiple pain-related comorbidities (OR≈1.24–1.30), and increased body adiposity, which was associated with up to a 2.8-fold higher risk. Behavioral factors such as stress, insomnia, smoking, and physical inactivity were also related to increased attack frequency. Conversely, preventive therapies demonstrated a protective effect (OR≈0.69–0.82), underscoring the relevance of prevalent and modifiable epidemiological factors in disease progression.

Conclusion
Migraine chronification is strongly associated with modifiable risk factors, particularly medication overuse, high attack frequency, and psychiatric comorbidities, highlighting the importance of early identification. Targeted strategies focusing on optimized treatment and lifestyle modifications are essential to prevent disease progression and mitigate its clinical burden.

Keywords:
Migraine disorders
Disease progression
Risk factors

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