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Lipid profile alterations associated with migraine: a systematic review

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Introduction
Patients with migraine present higher cardiovascular risk, relationship well established in the literature. However, findings regarding lipid profile alterations and their clinical implications require further understanding.

Objective
To investigate lipid profile alterations and their clinical implications in patients with migraine.

Methods
This systematic review was conducted using the PICO strategy and according to the PRISMA guidelines. A search was conducted for studies published in the last 5 years in English, Portuguese, and Spanish in PubMed, Scopus, and Embase databases using the MeSH terms Dyslipidemias and Migraine Disorders combined with the Boolean operator "AND". 585 studies were identified and underwent double independent screening. Inclusion criteria were studies assessing at least one lipid profile component in patients with migraine; observational studies and randomized clinical trials. Exclusion criteria were studies that did not specifically evaluate patients with migraine, resulting in 8 articles for data extraction.

Results
Its emphasized increased low-density lipoprotein cholesterol (LDL), Triglycerides (TG), and total cholesterol levels in adults ($p=0.0001$), and adolescents ($p<0.01$) with migraine, suggesting oxidative stress from an unfavorable lipid profile may sensitize the trigeminovascular system, increasing susceptibility to migraine, especially in aura-associated cases that presents greater lipid discrepancy ($p<0.0001$). High-density lipoprotein cholesterol (HDL) levels were reduced ($p=0.001$), suggesting diminished HDL antioxidant activity; however, in one cross-sectional study its levels were higher in migraine patients versus controls ($p<0.001$), supporting another hypothesis: increased HDL, due to its antioxidant properties, could alter neurodegenerative processes or pain perception as a negative feedback to the higher oxidative stress in migraine. Increased TG levels were associated with medication overuse ($p=0.037$), correlating with longer migraine duration, higher attack frequency and visual analog scale scores ($p<0.001$; $p=0.040$; $p=0.020$), suggesting worse prognosis and supporting that a dyslipidemic environment may reduce nociceptive thresholds and facilitate central sensitization. TG reduction was causally associated with lower migraine risk ($p=0.002$), as was LDL reduction ($p=0.0016$). Statin use was associated with lower migraine risk ($p<0.001$), while migraine itself was associated with left ventricular hypertrophy ($p<0.05$), frequent in patients with recurrent attacks ($p<0.05$); and females ($p<0.001$). Ocular studies showed greater ocular pain and retinal vascular tortuosity ($p<0.05$), suggesting vascular dysfunction and vasodilation by lipid alterations in migraine.

Conclusion
Migraine is associated with higher levels of LDL, TG and total cholesterol, with potential clinical impact. The underlying mechanisms remain hypothetical, and more longitudinal studies are needed to confirm causality.

Keywords:
Migraine
Pathophysiology
Dyslipidemias
Clinical features

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