Qeios

Peer Review

Review of: "Calcium-Magnesium Balance—Clinical Implications for Global Human Health"

Hayriye Esra Ataoğlu[1]

1. Internal medicine, Haseki Training and Research Hospital, İstanbul, Turkey

Open Peer Review Report for "Calcium-Magnesium Balance—Clinical Implications for Global Human Health"

Overall Evaluation:

This review presents a timely and thought-provoking synthesis on the calcium-to-magnesium (Ca:Mg) ratio and its potential impact on human health. The authors succeed in drawing attention to an often-overlooked nutritional parameter, and they provide compelling arguments linking Ca:Mg imbalance to several chronic disease pathways.

The manuscript is generally well-organized, clearly written, and informative. It has cross-disciplinary relevance across nutrition, endocrinology, cardiometabolic health, and public health. However, some key scientific and conceptual issues should be addressed to enhance the manuscript's impact and interpretative clarity.

Strengths:

The review highlights a clinically relevant but underexplored topic.

It integrates insights from diverse domains: physiology, epidemiology, micronutrient metabolism, and inflammation.

The authors emphasize the interaction of Ca:Mg ratio with vitamin D metabolism and systemic inflammation, which is a novel and promising line of thought.

The clarity of figures and summary tables aids reader comprehension.

doi.org/10.32388/HQVO4F

Points for Consideration:

Causality vs. Association:

In several places—particularly the Abstract and Introduction—the manuscript implies causal relationships (e.g., "Obesity is both a cause and consequence of Ca:Mg imbalance"). Given the primarily observational evidence base, it would be more appropriate to use cautious phrasing such as "associated with," "linked to," or "may influence."

Physiological Justification of Ratio Focus:

While both calcium and magnesium are essential, the manuscript heavily emphasizes the importance of maintaining a specific Ca:Mg ratio. However, some may argue—as another reviewer noted—that deficiencies can exist independently and that the ratio alone may not be the most informative measure. The authors should provide a stronger physiological rationale or acknowledge this counterpoint.

Evidence Base for Cut-Offs:

The paper suggests certain thresholds for a "balanced" Ca:Mg intake ratio. It would strengthen the argument to clearly cite the clinical or epidemiologic studies these cut-off values are based on, especially for practical application.

Intracellular vs. Extracellular Concentrations:

The review largely references serum or dietary levels. Yet magnesium, in particular, is predominantly intracellular. The authors should briefly comment on the limitations of using serum values as proxies for total body magnesium status.

Vitamin D Interaction – Mechanistic Detail:

The section on vitamin D's interaction with calcium and magnesium would benefit from a more detailed explanation of how these micronutrients affect vitamin D activation (hydroxylation steps), receptor sensitivity, or downstream signaling.

Inflammation and Post-COVID Link:

The link between Ca:Mg ratio and post-COVID conditions is intriguing but speculative. Consider tempering the language or clearly framing it as a hypothesis in need of further validation.

Minor Suggestions:

Ensure all bold claims (e.g., "imbalanced Ca:Mg ratio causes neurodegeneration") are supported by citations.

A comparison table showing intake recommendations (e.g., WHO, EFSA, USDA) for calcium and magnesium across regions would add value.

Language is generally clear, though a professional edit could further improve fluency and flow.

Conclusion:

This is a promising and informative review that will be of interest to a broad readership. With minor revisions and a more cautious interpretation of causality, it can contribute significantly to nutritional science and public health discussions.

Declarations

Potential competing interests: No potential competing interests to declare.