Letter to the Editor

Magnesium - The Silent Partner or the Next Vitamin D? Shifting Paradigm in Mineral Metabolism in Health and Disease

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Magnesium is a critical yet greatly overlooked micronutrient, acting as a cofactor in over 300 enzymatic reactions [1-4]. Its role is integral in nucleic acid synthesis, energy metabolism, and antioxidant defenses, serving as a cofactor for key enzymes including superoxide dismutase and glutathione peroxidase [1, 2, 5]. It also regulates extracellular calcium, acts as a messenger in intracellular signaling and modulates circadian clock genes [6]. Despite its significance, standard serum magnesium testing is unreliable; patients may have normal serum levels of 0.75-0.95 mmol/L yet present with evidence of chronic, underlying deficiency [1,4,5,7]. Evidence suggests that up to 42% of young adults exhibit undetected insufficiency and nearly half of the US population fails to meet the RDA of 300-400 mg/day [1, 4, 6]. This can be met through magnesium rich foods like leafy green vegetables, legumes, whole grains, nuts and fortified products [8]. Inclusion of such foods in routine diet will meet overall magnesium requirements safely and effectively, with supplementation used only when dietary intake is inadequate and under medical supervision.

There are a multitude of causes for deficiency ranging from insufficient nutritional intake, increased excretion, malabsorption disorders, renal elimination, common medications along with aging and stress [1, 5, 6].

Studies have shown that daily doses reduce depression scores and anxiety [2, 3, 9]. This effect may stem from magnesium's role in converting tryptophan to serotonin [2, 4]. Its benefits extend into sleep medicine, 500 mg/day of magnesium improves insomnia severity index, sleep efficiency, shortens latency and restores cortisol, and

melatonin [4,10]. Beyond neuropsychiatric benefits, Type 1 diabetics supplemented with 300 mg/day showed reduced neuropathy progression relative to the control. Furthermore, Magnesium has reduced the frequency, intensity, and duration of migraines by 41% versus 15.8 % with placebo [1, 4, 6].

In relation to cardiovascular health, it improves blood pressure, decreases carotid intima thickness, with cohort data highlighting 77% reduction in sudden cardiac death in individuals with the highest percentile of magnesium intake [1, 4, 7, 11]. Supplementation has also been beneficial in inhibiting thrombus formation in patients with coronary artery disease [12].

Current evidence is limited with studies employing small sample sizes or short supplementation periods making it difficult to draw conclusions. Moreover, positive outcomes weren't consistent across the study population as some studies showed that Magnesium has no effect on anxiety of premenstrual or postpartum women while benefiting others. Additionally, while Magnesium can be beneficial, excessive intake can cause toxicity, emphasising the need for supplementation under medical supervision.

Table 1 summarizes evidence from PubMed and Google Scholar, keywords used included "magnesium supplementation" "magnesium deficiency" "neurological function" "sleep quality", prioritizing RCTs, systematic reviews, and large-scale studies, while incorporating smaller studies where relevant. Studies from 2018 onwards were included. Human studies were emphasized to ensure clinical applicability.

The rise of Vitamin D from being an overlooked micronutrient to becoming a part of routine evaluation illustrates how easily key nutrients can be overlooked. Magnesium seems to be following a similar pattern, with research steadily emphasising its role in neurological and cardiovascular health. Its benefits are recognised but underutilised, highlighting the need for well-designed studies to guide its application in patient care.

Table 1: Summary of selected studies on Magnesium and related health outcomes.

Author	Study type	Population	Sample size	Intervention	Outcome
Mohammed S. Razzaque1, 2018	Commentary	N/A	N/A	N/A	Magnesium deficiency is linked to clinical complications like muscle spasms, fibromyalgia, arrhythmias, and migraines.
Violeta Cepeda2, 2025	Systematic Review	General population, rats and mice with or without pathology	Systematic Reviews- 28 Meta-Analysis-6	Oral Mg intake	Magnesium supplementation, alone or with zinc, Vitamin C, Vitamin E, or selenium, reduces blood pressure in diabetes and cardiovascular disease, and, when combined with zinc, alleviates anxiety and depression symptoms.
Mahdi Moabedi3, 2023	Systematic Review	Adults with depression (20-60 years old)	7 RCTs (n=325)	Oral Magnesium supplementation	Depression scores have shown marked reduction when treated with Magnesium relative to placebo.
Gerry K. Schwalfenberg4, 2017	Review	Various studies on Mg supplementation	N/A	N/A	It reduces migraine frequency and severity, slows peripheral neuropathy progression, improves depression and anxiety, prevents arteriosclerosis changes, and relieves symptoms in mitral valve prolapse.
Veer Patel5, 2024	Review	Various studies on Magnesium supplementation	N/A	N/A	Evidence suggests association between magnesium intake and cognitive function in healthy individuals.

Ligia J. Dominguez6 ,2025	Review	Acute and Chronic Migraines	12 RCT for Acute Migraines and 8 RCT for Chronic Migraines	IV Magnesium supplementation in Acute and Oral in chronic migraines patients.	Evidence supports the benefits of both intravenous and oral magnesium administration acute migraine episodes as well as migraine prophylaxis.
Remi Fritzen7, 2023	Review	Various studies on Magnesium deficiency.	N/A	N/A	Magnesium deficiency increases risk of cardiovascular. Evidence, including NHANES data, shows magnesium is protective, with supplementation linked to lower risk of hypertension, atrial fibrillation, and heart failure, and improved blood pressure.
Ligia J. Dominguez 8, 2020	Review	Hypertensives	18 Studies	Magnesium supplementation	Evidence shows a close relationship between magnesium deficit and high blood pressure.
Alexander Rawji 9, 2024	Systematic Review	Adults with anxiety and sleep disorders.	15 studies	Oral Magnesium supplementation	A majority of included trials demonstrated at least modest positive results in regards to sleep quality and anxiety, with higher doses of magnesium being more effective.
Micheal J. Breus 10, 2024	Research Article	Adults with poor sleep quality	N = 31 adults, M age = 46.01	Participants were randomized to Magnesium Condition or Placebo Condition.	Magnesium supplementation had significant improvements compared to the placebo for sleep quality, mood, and activity outcomes
Lianbin Xu 11,2023	Systematic Review	1,325 T2D Individuals	24 RCTs	Oral Magnesium supplementation	Magnesium supplementation lowers glycated hemoglobin, systolic and diastolic blood pressure.
James J DiNicolantonio12, 2018	Review	General population	N/A	N/A	Subclinical magnesium deficiency linked to cardiovascular disease.

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