

## Review

# Association of Magnesium and Incidence of Depression in Adults

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### Abstract

Depression affects more than 300 million individuals worldwide. The biggest source of nonfatal illness burden is depression. Individuals suffering from mental illness may have difficulty coping with their daily lives, including family and job. Depression may be linked to a disruption in magnesium metabolism. Resources may be motivated to prevent and promote healthy lifestyle behaviours based on evidence of a good influence on depressed symptoms of depression through dietary adjustments. Magnesium is necessary for energy production, dysrhythmia prevention, blood pressure regulation, insulin resistance prevention, and bone homeostasis. Oral magnesium supplementation may help to avoid depression and could be used as a supplement to other treatments. The purpose of this research is to review the available information about the association of magnesium with the incidence of depression among adults. According to existing literature there is an inverse relation between magnesium and depression. Magnesium supplementation may potentially be beneficial in the treatment of depression. Because of its impact on NMDA receptors, changes in magnesium levels in the body may play a significant role in the development of depression. However, further research is needed to generate evidence for association of magnesium with depression.

**Keywords:** Magnesium, depression, association, role, incidence

## Introduction

Depression and other mental health diseases are on the rise worldwide and continue to pose a hazard to public health, with depression and anxiety disorders posing the greatest threat. Depression affects more than 300 million individuals worldwide. The biggest source of nonfatal illness burden is depression. Furthermore, lifestyle choices have been linked to mental health in studies. Depression and other mental illnesses can afflict everyone, and the distinction between mental health and sickness is difficult to draw. Individuals suffering from mental illness may have difficulty coping with their daily lives, including family and job. Resources may be motivated to prevent and promote healthy lifestyle behaviours based on evidence of a good influence on depressed symptoms of depression through dietary adjustments (1). Depression is a widespread ailment that affects 3.8 percent of the world's population, with 5.0 percent of adults and 5.7 percent of persons over 60 years old suffering from depression. Around 280 million people worldwide suffer from depression (2).

Magnesium supplementation has been shown to alleviate depressive symptoms in people suffering from mild to severe depression (3). Magnesium is the fourth most prevalent mineral and second most abundant cation in the cell, and is essential for anaerobic and aerobic energy production, glycolysis, mitochondrial oxidative phosphorylation, potassium, and calcium management. Magnesium is required for energy production, the prevention of heart arrhythmias, blood pressure regulation, insulin resistance prevention, and bone homeostasis. Magnesium shortage has been linked to diabetes, cardiovascular illness, and chronic pain, among other things (4-6). Magnesium appears to be helpful in the treatment of depression, however evidence is limited and contradictory. Depression may be linked to a disruption in magnesium metabolism. Oral magnesium supplementation may help to avoid depression and could be used as a supplement to other treatments (7). The purpose of this research is to review the available information about the association of magnesium with the incidence of depression among adults.

## Methodology

This study is based on a comprehensive literature search conducted on January 17, 2021, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any

possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the association of magnesium with the incidence of depression among adults. There were no restrictions on date, language, participant age, or type of publication.

## Discussion

Psychiatric problems are thought to afflict more than one billion individuals globally, with current statistics claiming that mental illness accounts for one-third of years lived with disability (YLDs) and 13% of disability-adjusted life years (DALYs). In recent years, both pharmacologic and non-pharmacologic treatments have been accessible for the treatment of psychiatric diseases.(8, 9) Sadness, loss of interest or pleasure, feelings of guilt or low self-worth, interrupted sleep or food, feelings of weariness, and impaired concentration are all symptoms of depression. Depression affects over 264 million people globally and is expected to overtake diabetes as the largest cause of disease burden by 2030, according to disability-adjusted-life-year estimates (10, 11).

Magnesium (Mg) is a mineral that is included in most people's daily diets, although studies have shown that a considerable portion of the population has low Mg levels. Mg plays a variety of physiologic and protective roles in energy control and cellular balance, including neuronal homeostasis. It contains anti-inflammatory and antioxidant characteristics, as well as interactions with serotonin, a major neurotransmitter involved in depression pathogenesis. With both cross-sectional and longitudinal designs, epidemiologic investigations have revealed that low Mg status is associated with an increased frequency of depression. Mg has antidepressant effect equivalent to imipramine, and it can be a useful addition to antidepressants in treatment-resistant depression, according to promising research (12).

Because of the high-dose intervention in short-term intervals, findings from clinical studies on the effect of Mg supplementation on depression and anxiety are not generalizable to the general population. There is a scarcity of observational research relating Mg consumption and psychiatric illnesses. A study conducted on a total of 3172 Iranian adults (with an age range of 18–55 years) revealed that dietary magnesium consumption was found

to have a substantial inverse relationship with depression in both normal-weight males and overweight women. Several processes could explain the inverse relationship between magnesium consumption and sadness and anxiety. Mg, being an essential trace element, could have a function in a variety of processes. It serves as a cofactor in the production and release of a variety of enzymes, neurotransmitters, and hormones that are necessary for appropriate brain function. Mg has a crucial function in neuronal stability, such as membrane stability. The membrane of the neuron is involved in the release of neurotransmitters that alter intracellular communications. As a result, Mg plays an indirect role in intracellular communication. Furthermore, because there is a link between inflammatory markers and psychiatric illnesses, Mg's inhibitory effects on inflammatory marker secretion could be another factor explaining the inverse relationship between Mg consumption and mental disorders (13).

Depression is a widespread and often incapacitating illness. Magnesium supplementation has been associated to a reduction in depressed symptoms, however no consensus has been reached on the relationship between magnesium and depression. Even though both pharmacologic and behavioural therapy are beneficial for many individuals, they have significant drawbacks. Magnesium supplementation has been associated to benefits in major depression, premenstrual symptoms, postpartum depression, and chronic fatigue syndrome symptoms. Low magnesium levels have been linked to an increase in depressed symptoms across a variety of age groups and ethnic groups. A cross-sectional, population-based study conducted on 8894 US adults from 2007-2010 depicted that low magnesium intake was related with depression in participants younger than 65 years old (RR, 1.22; 95 percent CI, 1.06-1.40;  $P=0.007$ ), while it appeared to be protective in seniors (RR, 0.75; 95 percent CI, 0.56-0.98;  $P=0.032$ ). A significant association between very low magnesium consumption and depression, particularly in young individuals. The discovery of a possible protective benefit of decreased magnesium consumption in older persons is surprising and requires additional research (14).

Oral magnesium treatment, possibly through dietary supplements, may appeal to many patients more than other currently accessible options. In several trials, magnesium supplementation improves depression symptoms and increases serum magnesium levels. In Iranian and Canadian populations, a link between serum magnesium levels and depression has been discovered.

A recent meta-analysis of observational studies indicated a 1.3-fold greater risk of depression in patients with hypomagnesaemia, but following a sensitivity analysis, the results were marginally inconsequential. Previous meta-analyses had yielded mixed results. Magnesium is recognized as a short-fall nutrient in the 2015–2020 Dietary Guidelines for Americans, and while increasing consumption of high-magnesium foods is recommended, supplementation may not produce the same results. Serum magnesium levels could be a cost-effective way to identify people who could benefit from magnesium supplementation. Alternatively, serum magnesium might be used as a marker for treatment-resistant depression, or it could be used to identify changed magnesium metabolisms in a subgroup of patients who respond to treatment differently than expected (15).

Efficacy, cost, availability, side effects, and patient acceptability are all factors that limit current depression therapy options. Even though various studies have looked into the relationship between magnesium and depression, its importance in symptom management is uncertain. Between June 2015 and May 2016, 126 people diagnosed with and now experiencing mild-to-moderate symptoms took part in an open-label, blocked, randomized, cross-over trial at outpatient primary care clinics. Magnesium chloride consumption for six weeks resulted in a clinically significant net improvement of -6.0 points (CI -7.9, -4.2;  $P<0.001$ ) in PHQ-9 scores and a net improvement of -4.5 points (CI -6.6, -2.4;  $P<0.001$ ) in GAD-7 scores. Adherence was 83 percent on average based on pill count. The supplements were well accepted, with 61% of individuals saying they would take magnesium again. No difference in result was seen regarding age, gender, baseline depression severity, baseline magnesium level, and use of antidepressant medication. Within two weeks, the effects were visible. Magnesium can help adults with mild to moderate depression. It works swiftly and is highly tolerated, so there's no need to worry about toxicity (3).

Magnesium is one of the most important minerals in the human body, as it is linked to brain biochemistry and neuronal membrane fluidity. Magnesium insufficiency has been linked to several neuromuscular and mental symptoms, including several types of depression. Because ambiguous results were achieved depending on the investigation, plasma/serum magnesium levels do not appear to be adequate indicators of depressive disorders. In medical practice, there has been the advent of a novel approach to magnesium compounds. Apart from being

used as nutritional supplements, they are also thought to be beneficial in the treatment of migraines, alcoholism, asthma, heart disease, arrhythmias, renal calcium stones, premenstrual tension syndrome, and other conditions. Magnesium formulations are widely used in homeopathy as a treatment for a variety of mental health issues. The mechanisms of magnesium's antidepressant impact are still unknown. Magnesium is thought to affect several systems linked to the onset of depression. Nearly a century ago, the earliest evidence of the therapeutic effects of magnesium sulphate given hypodermically to individuals with agitated depression was published. Numerous pre-clinical and clinical investigations corroborated the first findings and proved magnesium supplementation's beneficial safety profile. As a result, magnesium supplements appear to be a helpful addition to the pharmaceutical arsenal for the treatment of depression (16).

Magnesium is the second most abundant intracellular cation, and it functions as a cofactor in approximately 300 enzyme reactions. It inhibits calcium entry into neurons by acting as a calcium antagonist and a voltage-dependent blocker of the N-methyl-D-aspartate channel. Other mechanisms, such as an inverse relationship with serious depression, provide biological credibility to magnesium's neuroprotective qualities. Magnesium supplementation has been linked to fewer depressed symptoms. However, there is a scarcity of epidemiological evidence on this topic. A study conducted on 12,939 Spanish university graduates revealed that there was no link found between total magnesium consumption and the occurrence of depression. The lack of a link between magnesium consumption and depression incidence in this study could be due to a variety of factors. First and foremost, magnesium is likely to have only a slight negative relationship with the risk of depression; perhaps a large cohort sample is required for generation of evidence. Another reason could be that magnesium absorption is influenced not just by magnesium intake but also by its bioavailability. Vitamins B-6 and D, for example, help the body absorb magnesium. It's reasonable to assume that overall magnesium and vitamin intake had a stronger impact on lowering depression risk (17).

Findings from a meta-analysis revealed that there is a significant inverse relationship between moderate Mg intake and depression risk, whereas no such relationship exists between dietary Ca intake and depression risk. In studies done in Asia and studies adjusted for energy consumption, dietary Mg intake was similarly associated

with a lower risk of depression. Because the bulk of the included studies were conducted in Asia, the pooled results of Asian research indicated the strongest correlation. Because energy consumption could be a confounding factor in the study of dietary Mg intake and depression, the strongest link was found in studies that adjusted for energy intake. Dietary Mg intake and depression risk were also found to have a nonlinear association. When dietary Mg intake was above 76 mg/day and below 360 mg/day, the link became significant, and the risk reductions were greatest at 320 mg/day. In fact, in China, 320 milligrams per day is about the recommended dietary limit (18).

Magnesium is a key cation in the central nervous system that is involved in a number of functions, including transmission and intracellular signalling. Several research investigations have shown that it is useful in the treatment of neurological and mental diseases. Magnesium levels also appear to be lowered during a range of mental diseases, especially depression. Multiple studies have been undertaken specifically for psychiatric illnesses to examine magnesium serum levels in cohorts of persons with depression and other mental illnesses. Magnesium has also been investigated as an adjuvant therapy for psychiatric conditions, such as anxiety and mood disorders, in the form of enriched diets and high-dose supplementation. However, studies on magnesium levels and supplementation in psychiatric illnesses commonly provide inconsistent results, which may be related to methodological heterogeneity, which includes, among other things, measuring techniques and supplementation modalities. Despite a large body of evidence showing lower plasma levels, particularly in depressed patients, there is no evidence that magnesium, either alone or in combination with other treatments, is beneficial in treating various mental illnesses. As a result, larger, more consistent studies are required to demonstrate the role of magnesium in psychiatric disorders (19).

Depression is a huge public health concern around the world. The cause of depression is unknown; however, certain minerals, such as magnesium, have been shown to improve depressed symptoms and reduce the likelihood of developing depression. After multivariable adjustments, participants in the middle tertile of dietary magnesium consumption had a statistically substantially lower risk of receiving a hospital discharge diagnosis of depression compared to those in the lowest tertile (HR 0.49, CI 0.25-0.95,  $P=0.035$ ) in the prospective scenario. When the combined middle and highest tertiles of magnesium

consumption were compared to the lowest tertile, an inverse relationship between magnesium intake and the incidence of depression was discovered (HR 0.53, CI 0.29-0.95, P=0.033). Magnesium intake may have link with depression. More research is needed to see if adequate magnesium consumption has any implications for the prevention or treatment of depression (20).

Magnesium is recognized to have a vital role in the physiological function of the brain, and magnesium insufficiency has been linked to a number of neuromuscular and mental symptoms, including various types of depression. The study group's overall mean value of serum Magnesium is  $1.72 \pm 0.33$  mg/dl, which is lower than the population's value of  $2.1 \pm 0.26$  mg/dl. There is also no discernible difference in serum Mg levels between male and female depression patients of various ages and genders. The findings show a link between hypomagnesemia and depression, indicating that magnesium could be used to track the effectiveness of depression treatments. Magnesium deficit results in less NMDA channel blockage, resulting in a hyperexcitable state. Magnesium's anti-depressant properties have also been linked to its effects on the serotonergic, noradrenergic, and dopamine systems (21).

## Conclusion

Magnesium supplementation may potentially be beneficial in the treatment of depression. Because of its impact on NMDA receptors, changes in magnesium levels in the body may play a significant role in the development of depression. However, further research is needed to generate evidence for association of magnesium with depression.

## Disclosure:

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None.

### *Ethical Consideration:*

Non applicable.

### *Data Availability:*

All the data is included within the article.

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