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Original Research Article

Serum Levels of Magnesium and Calcium in Depression: A Cross Sectional Study

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Abstract

Introduction: Depression is a complex psychiatric disorder marked by persistent sadness, loss of interest, cognitive difficulties, and various physical symptoms that disrupt daily life and overall well-being. It is a major global health issue, affecting over 280 million people and ranking among the leading causes of disability and disease burden worldwide, according to the World Health Organization (WHO).

Aims and Objectives: The study aimed to evaluate serum magnesium and calcium levels in patients with depression and analyse their relationship with the severity of depressive symptoms. It sought to determine whether alterations in these mineral levels are associated with depression and to explore their possible role as biochemical indicators or contributing factors in the disorder's development and progression.

Materials and Methods: The study was conducted in the Department of Biochemistry at AJ Institute of Medical Sciences and Research Centre, Kuntikana, Mangalore, from March 2022 to February 2023. Blood samples for the study were collected from patients at the same institution during this period.

Results: A total of 84 patients diagnosed with depression were included in the study. Most participants (61.9%) were between 51 and 60 years of age, indicating that middle-aged individuals formed the predominant group in the study population.

Conclusion: This study analysed 84 patients with depression to assess the relationship between serum magnesium and calcium levels and the severity of their symptoms, finding that most participants experienced moderate to severe depression.

Keywords: Depression, Serum magnesium, Serum calcium, Biochemical markers, Mood disorders, Cross-sectional study.

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Introduction

Depression is a common, multifactorial psychiatric disorder characterized by persistent low mood, anhedonia, cognitive impairment, and a range of somatic symptoms that significantly impair daily functioning and quality of life. According to the World Health Organization (WHO), depression affects more than 280 million people worldwide, representing one of the leading causes of disability and disease burden globally. It contributes significantly to morbidity, diminished productivity, and increased suicide risk, making it a major public health concern [1]. Despite the availability of effective pharmacological and psychotherapeutic interventions, the underlying biological mechanisms contributing to the onset and progression of depression remain incompletely understood. In recent years, growing evidence has highlighted the role of trace elements and minerals in the pathophysiology of neuropsychiatric disorders. Among these, magnesium and calcium have received considerable attention due to their crucial roles in neurochemical transmission, synaptic plasticity, and regulation of mood-related neurotransmitters such as serotonin, dopamine, and norepinephrine [2,3]. These ions are essential for maintaining neuronal excitability, modulating the hypothalamic-pituitary-adrenal (HPA) axis, and influencing stress responses — all of which are

implicated in depressive disorders [4].Magnesium is the second most abundant intracellular cation and acts as a cofactor for over 300 enzymatic reactions, including those involved in energy metabolism and neurotransmitter synthesis. It plays a critical role in regulating N-methyl-D-aspartate (NMDA) receptor activity, thereby modulating glutamatergic neurotransmission and protecting against excitotoxicity [5]. Hypomagnesaemia has been associated with increased neuronal excitability, oxidative stress, and neuroinflammation, processes that are frequently observed in major depressive disorder [6]. Several clinical and experimental studies have reported lower serum magnesium levels in patients with depression compared to healthy controls, suggesting a potential link between magnesium deficiency and depressive symptomatology [7].Calcium, another vital divalent cation, is equally important for neuronal signalling, synaptic transmission, and intracellular communication. It acts as a secondary messenger in several signal transduction pathways and regulates the release of neurotransmitters from presynaptic terminals. Disturbances in calcium homeostasis can alter neuronal function, leading to mood disturbances and affective disorders [8]. Moreover, calcium dysregulation has been implicated in altered circadian rhythms, sleep disturbances, and stress responses—all recognized contributors to depressive illness [9]. Some studies have demonstrated that serum calcium levels may be altered in depression, although findings have been inconsistent, with reports of both elevated and reduced levels, suggesting complex homeostatic mechanisms and potential confounding factors such as diet, hormonal status, and medication use.The interplay between magnesium and calcium is particularly noteworthy, as these cations share similar transport and signalling pathways and often exert antagonistic effects within neural tissues. Magnesium acts as a natural calcium antagonist, controlling calcium influx into neurons and thereby preventing over activation of NMDA receptors and subsequent neuronal injury.

Thus, a disturbed magnesium-to-calcium ratio may be more relevant than individual ion concentrations in influencing depressive pathology [10].Despite numerous studies, the relationship between serum magnesium and calcium levels and depression remains inconclusive. Variations in study design, population characteristics, dietary habits, and methodological differences have contributed to inconsistent findings across the literature. Furthermore, most existing studies have been conducted in Western populations, with limited data available from developing countries such as India, where nutritional status and environmental factors may further influence trace element balance. Understanding these biochemical alterations may provide valuable insights into the neurobiological basis of depression and offer potential avenues for adjunctive treatment strategies, such as nutritional supplementation or dietary modification.

Hence, the present cross-sectional study aims to assess the serum levels of magnesium and calcium in patients diagnosed with depression and compare them with those of healthy controls. This study seeks to elucidate possible biochemical correlates of depression and contribute to the growing body of evidence on the role of micronutrients in mental health. Establishing such associations could help identify simple, cost-effective biomarkers and open new preventive or therapeutic strategies in the management of depressive disorders.

Materials and Methods

Study design: The study was carried out in AJ Institute of medical sciences and Research centre, Kuntikana, Mangalore, in the department of biochemistry during the period of March 2022 to February 2023. Blood sample were collected from AJ Institute of Medical Sciences and Research Centre, Kuntikana, Mangalore

Place of study: The study was carried out in AJ Institute of medical sciences and Research centre, Kuntikana, Mangalore, in the department of biochemistry.

Period of study: The study was carried out in AJ Institute of medical sciences and Research centre, Kuntikana, Mangalore, in the department of biochemistry during the period of March 2022 to February 2023.

Study Population: Clinically diagnosed Patients suffering from depression in the age group of 18-60 years.

Sample Size: 84 clinically diagnosed patients of depression will be considered for this study.

Type of study: Cross-sectional study

Inclusion Criteria

- Clinically diagnosed patients suffering from depression.
- Age group of 18-60 years.

Exclusion Criteria

- Clinically diagnosed patients of depression, undertaking medications, vitamin supplements, and/or mineral supplements.
- Patients of depression having CKD, heart disease, liver disease.
- Pregnancy

Study Variable

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version

27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5).

Numerical variables were summarized using means and standard deviations, while Data were entered into Excel and analyzed using SPSS and GraphPad Prism. Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Two-sample t-tests were used to compare independent groups, while paired t-tests accounted for correlations in paired data. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Result

Table 1: Demographic and Depression Severity Distribution in the Study Population

Variable	Category	Frequency (n)	Percentage (%)
Age Groups	40 – 50 years	32	38.10%
	51 – 60 years	52	61.90%
	Total	84	100.00%
Gender	Males	42	50.00%
	Females	42	50.00%
	Total	84	100.00%
Severity of Depression	Mild	9	10.70%
	Moderate	40	47.60%
	Severe	35	41.70%
	Total	84	100.00%

Table 2: Age Distribution of Participants by Gender

Group	Age in years
	Mean ± SD
All participants	52.48 ± 5.79
Males	52.93 ± 5.92
Females	52.02 ± 5.69

Table 3: Association between Age, Serum Calcium, and Serum Magnesium Quartiles with Severity of Depression

Variable	Category	Severity of Depression			Total (n, %)	p-value
		Mild n (%)	Moderate n (%)	Severe n (%)	84 (100%)	
Age Group and Severity of Depression	40–50 years	2 (22.2%)	20 (50.0%)	10 (28.6%)	32 (38.1%)	0.095
	51–60 years	7 (77.8%)	20 (50.0%)	25 (71.4%)	52 (61.9%)	
	Total	9 (100.0%)	40 (100.0%)	35 (100.0%)	84 (100.0%)	
Serum Calcium Quartiles and Severity of Depression	Q1 (≤ 4.20 mg/dL)	0 (0.0%)	11 (27.5%)	18 (51.4%)	29 (34.5%)	0.035
	Q2 (4.21–4.5 mg/dL)	2 (22.2%)	5 (12.5%)	7 (20.0%)	14 (16.7%)	
	Q3 (4.6–7.4 mg/dL)	3 (33.3%)	13 (32.5%)	4 (11.4%)	20 (23.8%)	
	Q4 (> 7.4 mg/dL)	4 (44.4%)	11 (27.5%)	6 (17.1%)	21 (25.0%)	
	Total	9 (100.0%)	40 (100.0%)	35 (100.0%)	84 (100.0%)	
Serum Magnesium Quartiles and Severity of Depression	Q1 (≤ 1.1 mg/dL)	0 (0.0%)	0 (0.0%)	30 (85.7%)	30 (35.7%)	< 0.001
	Q2 (1.11–1.30 mg/dL)	0 (0.0%)	15 (37.5%)	4 (11.4%)	19 (22.6%)	
	Q3 (1.31–1.40 mg/dL)	0 (0.0%)	14 (35.0%)	1 (2.9%)	15 (17.9%)	
	Q4 (> 1.40 mg/dL)	9 (100.0%)	11 (27.5%)	0 (0.0%)	20 (23.8%)	
	Total	9 (100.0%)	40 (100.0%)	35 (100.0%)	84 (100.0%)	

Table 4: Correlation between serum calcium and magnesium in all study participants

Correlation between	r value	p value
Serum calcium and serum magnesium	0.25	0.022

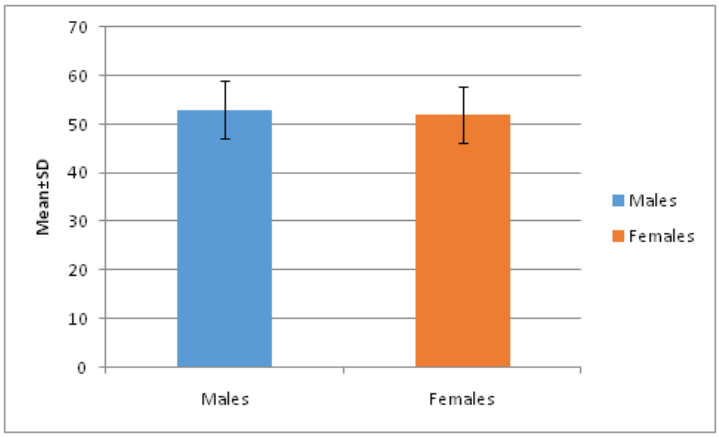

Figure 1: Age Distribution of Participants by Gender

A total of 84 participants diagnosed with depression were included in the present study. The age distribution of the study population is shown in Table 1. The majority of the participants (61.9%) were in the 51–60 years age group, while 38.1% were between 40–50 years. The mean age of all participants was 52.48 ± 5.79 years, with males having a mean age of 52.93 ± 5.92 years and females 52.02 ± 5.69 years (Table 2). The study sample consisted of 42 males (50.0%) and 42 females (50.0%), indicating equal gender distribution.

Based on the severity of depressive symptoms, as assessed using a standardized depression rating scale, 9 participants (10.7%) were classified as having mild depression, 40 participants (47.6%) as moderate, and 35 participants (41.7%) as severe. Thus, the majority of individuals in the study exhibited either moderate or severe depression.

The association between age, serum calcium, and serum magnesium quartiles with depression severity is presented in Table 3. Although a higher proportion of severe depression cases was observed in the older age group (51–60 years), the association between age and depression severity was not statistically significant ($p = 0.095$). In contrast, a significant relationship was observed between serum calcium quartiles and depression severity ($p = 0.035$). Participants with severe depression were predominantly found in the lowest calcium quartile (≤ 4.20 mg/dL), comprising 51.4% of those with severe symptoms, whereas those in the highest calcium quartile (> 7.4 mg/dL) showed a greater proportion of mild and moderate cases. This suggests an inverse association between serum calcium concentration and severity of depressive symptoms. A highly significant association was found between serum magnesium levels and depression severity ($p < 0.001$). All participants with mild depression (100%) had magnesium levels above 1.40 mg/dL (Q4), while the majority of severely depressed individuals (85.7%) were in the lowest magnesium quartile (≤ 1.1 mg/dL). None of the severely depressed patients had magnesium concentrations exceeding 1.4 mg/dL. These findings indicate that lower serum magnesium levels were strongly correlated with greater severity of depression.

The correlation analysis between serum calcium and serum magnesium levels among all participants revealed a positive correlation ($r = 0.25$, $p = 0.022$) (Table 4). This suggests that individuals with lower calcium levels also tended to have lower magnesium levels, indicating a possible synergistic role of these cations in the neurochemical pathways involved in mood regulation.

Overall, the results of this study demonstrate that both serum magnesium and calcium concentrations are significantly associated with depression severity. While the relationship with calcium was moderate, magnesium showed a much stronger and more consistent inverse relationship with depressive symptom intensity. These findings highlight the potential utility of monitoring serum magnesium and calcium as biochemical correlates of depression and suggest that correcting deficiencies may hold adjunctive therapeutic value.

Discussion

The present study's finding of a strong inverse association between serum magnesium and depression severity — with the majority of severely depressed patients clustered in the lowest magnesium quartile — is consistent with multiple clinical and experimental reports that implicate magnesium deficiency in affective disorders. Several authors have described lower serum or dietary magnesium in depressed cohorts and observed antidepressant-like effects of magnesium supplementation in animal and some human studies, supporting a biologically plausible role for magnesium via modulation of NMDA receptor activity, glutamatergic transmission, and HPA-axis regulation [11, 12, 13, 14]. For example, Eby&Eby reported rapid mood improvement with magnesium therapy in an open clinical series, which aligns with

our observation that higher magnesium (Q4) was associated with milder symptoms . Kirkland et al. summarized mechanistic and clinical data linking magnesium to neurological and mood disorders, further substantiating our biochemical correlations [15]. Tarleton et al.'s population-based analysis also found relationships between magnesium intake/status and depressive symptoms, supporting the public-health relevance of our results [16].

The relationship between serum calcium and depression observed here — an overrepresentation of severe cases in the lowest calcium quartile and a modest positive calcium–magnesium correlation (r = 0.25) — partly concurs with prior but less consistent literature. Calcium's role as an intracellular second messenger and regulator of neurotransmitter release makes a mechanistic link plausible, but earlier clinical studies have reported mixed findings [17, 18, 19]. Some reports note altered plasma calcium in affective disorders while others find no clear pattern; our results add to this heterogeneous body of evidence by suggesting an inverse association in this sample. The modest positive correlation between calcium and magnesium suggests co-variation of these cations in this population, echoing prior discussions that magnesium often functions as a natural calcium antagonist and that disturbances in their ratio — rather than absolute values alone — may be clinically important [20]. Differences between our findings and some prior reports may reflect methodological and population factors: many existing studies were performed in Western cohorts or animal models, used differing assays (total versus ionized levels), varied in controlling for dietary intake, medications, or comorbid medical conditions, and applied diverse depression-rating instruments.

Our study's cross-sectional design precludes causal inference — whether low magnesium/calcium predisposes to greater depression severity or results from illness-related changes (nutrition, inflammation, medication) cannot be determined — a limitation shared by several earlier investigations. Strengths of the current work include balanced gender representation and quartile-based analysis that clarified dose–response relationships; however, future studies should measure ionized calcium and intracellular magnesium, control prospectively for confounders (diet, renal function, vitamin D, thyroid status), and assess the effect of supplementation in randomized trials to test causality. Overall, our results are congruent with a growing literature that supports a role for magnesium in depression and suggest calcium may also be relevant, reinforcing the rationale for further mechanistic and interventional research.

Conclusion

This study evaluated the association between serum magnesium and calcium levels with depression severity in 84 patients. The majority of participants had moderate to severe depression. A strong inverse relationship was found between serum magnesium levels and depression severity, with lower magnesium levels significantly associated with more severe symptoms. Serum calcium levels also showed a moderate but significant inverse relationship with depression severity. Both cations were positively correlated with each other, suggesting a possible synergistic role in mood regulation. Age and gender did not show any significant association with depression severity. These findings highlight the importance of magnesium and calcium in the neurobiochemical mechanisms underlying depression. Regular monitoring of these minerals may help identify at-risk individuals. Correction of deficiencies could serve as an effective adjunct to standard antidepressant therapy. Further large-scale studies are needed to confirm these findings and explore therapeutic implications.

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