



A COMPARATIVE STUDY OF SERUM CALCIUM AND SERUM MAGNESIUM LEVEL IN DEPRESSION

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ABSTRACT

BACKGROUND: OBJECTIVE OF THE STUDY The objective of the study was to assess and compare serum calcium and magnesium level in Depression patients and healthy controls and to find out correlation of serum Mg^{++} and Ca^{++} levels with Depression. Depression is reported to be the most common mood disorder which can be manifest as a single episode or as recurrent episodes. Globally, the proportion of the population affected with depression is estimated to be 4.4%. In one of the reports of the World Health Organization, depression and heart disease will be the most common diseases on Earth by 2020.

METHODOLOGY: The study is based on a sample of 200 subjects – 100 healthy normal individuals and 100 patients, from Department of Psychiatry, Mahatma Gandhi Memorial Medical College and M. Y. Hospital, Indore, who were diagnosed as having Depression as per the ICD-10 criteria. Estimation of the parameters of the study was done by using spectrophotometer (Spectra scan UV 2600). The result values of both the groups were compared by using SPSS 23 for windows were used for data analysis.

RESULTS: Analysis of data reveals the mean value of serum magnesium among subjects of the case group was lowered then compared to the subjects of the control group. The differences in mean values were found to be statistically significant. While in case of serum calcium, Case group has shown less serum calcium levels than control group, but it was not statistically significant.

CONCLUSION: The present study shows that alterations in the concentrations of magnesium and calcium may play a role in depressive illnesses and thus, may have a possible role in causing various mood disorders like MDD.

KEYWORDS :

INTRODUCTION

Depression is reported to be the most common mood disorder which can be manifest as a single episode or as recurrent episodes. Nearly half of all cases of depression remain undetected for years or inadequately controlled.

Globally approx. 322 million people were affected by depression in 2015.¹ In one of the reports of the World Health Organization, depression and heart disease will be the most common diseases on Earth by 2020.²

Depression Gives rise to notable disease burden globally and at national levels.

According to Global Health Estimates 2015, depression is accounting for 7.5% of global years lived with disability (YLDs) and 2.0% of global disability adjusted life years (DALYs) in 2015.^{3,4}

The average age of onset for recurrent unipolar major depressive episode falls between the ages of 30 and 35 years, whereas single-episode major depression usually begins some years later.

Pathophysiology of MDD is still a matter of research and not much is known about it. The glutamatergic mechanism of antidepressant treatments is now in the centre of research to overcome the limitations of monoamine-based approaches. It has been established in studies that both magnesium (Mg^{++}) and calcium (Ca^{++}) are most abundantly found cations in the body and are implicated in numerous cellular functions including regulation of various neurotransmitters. Variations in these cation's levels in blood, platelets, erythrocytes, cerebrospinal fluid have been noted in many mental illnesses.

PATHOPHYSIOLOGY

Magnesium (Mg^{++}) and calcium (Ca^{++}) play major role in numerous cellular functions including regulation of various neurotransmitters. Amino acids glutamate and aspartate in the NMDA receptors involved in most of the brain's regular functions such as gene expression, circuit development, synaptic plasticity, and cell survival.⁵ NMDA receptors comprising combination of two subunits NR1 and NR2, together forms a heteromeric complex, which forms a channel that Permits influx of Ca^{++} , which shows voltage-dependent blockade by Mg^{++} ions.⁶⁻¹⁰ Ca^{++} influx through the NMDA receptor determined by the amount and duration of the NMDA receptor activation.¹¹ At normal neuronal resting membrane potentials, NMDA receptors permit only the amount of Ca^{++} that is necessary for their function, but in the absence of voltage dependent magnesium ions regulation, abnormally functioning NMDA receptors increase influx of cellular Ca^{++} . Depolarization of membranes relieves the Mg^{++} block and causing Ca^{++} overloading, which implicated in neuronal swelling and cell death.^{12,13}

The excess Ca^{++} ions combines with the calmodulin and activate calmodulin- Ca^{++} dependent enzyme, the neuronal nitric oxide synthase (nNOS).¹⁴ Activated nNOS catalyses the oxidation of L-arginine resulting in the formation of L-citrulline and toxic reactive oxygen species nitric oxide (NO), which is a diffusible, free-radical messenger, involved in cell communication.^{8,15,16} Following its synthesis, NO may diffuse back to the presynaptic terminal to activate soluble guanylate cyclase and increase cyclic guanosine monophosphate (cGMP) level¹⁷ and subsequent activation of cGMP-dependent kinases in the responder cells. NO/Cgmp regulate gene expression by affecting neuronal differentiation and survival in the nervous system^{18,19} and have been linked in the regulation of Persistent adult mammalian hippocampus ne

urogenesis throughout life, including humans.

Shortage of magnesium ion and excess amount of calcium ion leads to brain cell synaptic dysfunctions, which leads to mood and behavioural disorders including depression.

MATERIALS AND METHODS

The study was conducted in department of psychiatry, Mahatma Gandhi Memorial Medical College, after clearance obtained from institutional ethic committee of M.G.M.M.C., Indore. The duration of the study was of about 1 year from the date of approval of study. The study was carried out with a case control cross sectional design so that samples were selected from two groups—case group and control group.

CASE GROUP

The case group consisted of 100 patients with MDD from among the indoor and outdoor patients of the Department of Psychiatry of M.G.M. Medical College, Indore.

CONTROL GROUP

The subjects of the control group were selected randomly from a group of 100 individuals. The group consisted of healthy individuals not having any psychiatric diseases from different sections of the society and willing to co-operate voluntarily in this study. However, while selecting subjects, focus had been on selecting only 'age and sex matched' individuals.

INCLUSION AND EXCLUSION CRITERIA

The subjects-both male and female, age should be between 18 to 65 years (both inclusive) and meet ICD -10 criteria for Depression included in study. Depression pt. having psychotic symptoms / Bipolar depression patients were excluded. Female patients during pregnancy and lactation were excluded. Also excluded were those who were alcohol/ drug abuse or dependence, those who had been taking medications for any medical reasons and also those with any clinically significant abnormality evident in routine serum biochemistry. Subjects not willing to give consent were excluded from study.

METHODS

After applying strict inclusion and exclusion criteria participants are included in study. Rational of study is explained to patient and relative as well as to healthy controls after taking informed consent. Diagnosis of depression is confirmed by treating Psychiatrist on clinical interview fulfilling the criteria of ICD-10. The severity of depressive symptoms was measured using the Hamilton Depression Rating Scale (HAM-D).

According to the study protocol, 5 ml of blood was obtained from each patient and healthy volunteer. Estimation of the parameters of the study—serum Mg++ and serum Ca++ was done by using spectrophotometer (Spectra scan UV 2600) at M.Y.hospital.

STATISTICAL ANALYSIS

After compilation of collected data, SPSS 23.0 for Windows was used for data analysis. Data are expressed as the mean ± SD. Result values of serum Mg++ and serum Ca++ of subjects of case group were compared with that of subjects of control group Mann-Whitney U test was used. For comparisons between three or more groups, the Kruskal-Wallis test was used and, when a significant difference was noted, the Mann-Whitney U-test was used to determine the significance of differences between groups. For the analysis of correlation coefficients, Spearman's rank correlation coefficients were used.

RESULTS AND OBSERVATIONS

Table -1 – socio-demographic variables of the subjects

	case	Control
Mean age of study sample	33.62	35.50

Sex distribution	men-39% Women- 61%	Men-52% women-48%
Religion	84% Hindu	93% Hindu
Education	92% educated	95% educated
Employment	41% employed	74% employed
Marital status	69%- married	66%- married
Socioeconomic status	73% middle class, 13% Lower class	58% middle class
Locality	73% urban 27% rural	63% urban 37% rural
Family type	76% nuclear	82% nuclear

Average age of subjects was 34.56 (± 12.28) years. Majority of the subjects were educated (n=170, 85%), married (n=135, 67.5%) and belonging to middle socio-economic status (n=66, 83.5%) and from nuclear family (n=144,72%). Most of the subjects belongs to urban locality(n= 136, 68%). Majority of patients were unemployed (41%).

TABLE – 2 Comparison of Mean Serum Calcium of two Groups

Parameter	Group	N	Mean	Std. Deviation	T Test	P Value
SERUM CALCIUM	Case	100	9.33	0.87	1.786	0.076 Non Sig
	Control	100	9.52	0.59		

The difference among the two groups was found to be statistically non-significant (P>0.05). For Control group, the mean Serum Calcium (9.52) is higher than that of the Case Group (9.33).

TABLE – 3 Comparison of Mean Serum Magnesium of two Groups

Parameter	Group	N	Mean	Std. Deviation	T Test	P Value
SERUM MAGNESIUM	Case	100	1.8	.39	2.43	0.016
	Control	100	2.00	.22		

The difference among the two groups was found to be statistically significant (P 0.05). For Control group, the mean Serum Magnesium (2.00) is higher than that of the Case Group (1.89).

Table-4: Comparison of serum calcium levels between socio-demographic groups in depression patients

Serum calcium	Variables		Depression patients n=100 Mean ± SD	t value	p value
Marital Status	Married		9.17 ± 0.80	-.43	.662
	Others		9.25 ± 1.14		
Religion	Hindu		9.20 ± 0.96	.198	.843
	Others		9.15 ± 0.65		
Family type	Nuclear		9.10 ± 0.92	-1.93	.056
	Joint		9.51 ± 0.87		
Locality	Urban		9.15 ± 0.99	.785	.434
	Rural		9.31 ± 0.70		

Table – 04 displays various socio-demographic parameters of serum calcium levels. None of the parameters for s. calcium was statistically significant. The mean S. Ca++ values were high in other married subtype, Hindu religion, joint family type, and rural locality.

Table-5: Comparison of serum magnesium levels between socio-demographic groups in depression patients

Serum magnesium	Variables		Depression patients n=100 Mean ± SD	t value	p value
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	Marital Status	Married	1.95 ± 0.37	0.75	0.455
		Others	1.89 ± 0.40		
	Religion	Hindu	1.90 ± 0.36	-2.18	0.031
		Muslim	2.12 ± 0.44		
	Family type	Nuclear	2.00 ± 0.40	3.08	0.003
		Joint	1.73 ± 0.20		
	Locality	Urban	1.97 ± 0.40	-1.36	.176
		Rural	1.85 ± 0.31		

Table 5 displays various socio-demographic parameters of S. magnesium levels. Parameters religion and family type for s. magnesium was statistically significant. The mean S. Mg++ values were high in married subtype, muslim religion, nuclear family type, and urban locality.

DISCUSSION

Several studies have assessed role of serum Mg++ and serum Ca++ in depression. However, data on these two cation's levels have been inconsistent, and both increase and decrease have been observed in depressed patients. Our study was a cross sectional hospital based study to compare serum Ca++ and serum Mg++ levels among depressive patients and their respective age and sex matched healthy controls.

The mean age of case group was 33.62 ± 10.90 years while that of control group was 35.43 ± 11.11 years. All the samples of our study were identified with major depression as per inclusion criteria and had a mean age of onset of 32.66 ± 10.27 Year. This result is consistent with previous studies stated similar mean age of onset of depression like Park et al.²⁰, Yang et al.²¹, Srivastava et al.²². Among the cases maximum 38% belonged to 26-35 year age group, among control maximum 40% belonged to 26-35 age group. The patients belonging to age group 56-65, reported depression less. These results are consistent with some previous findings by TJ Wade, J Cairney et al. 1997²³, Wade TJ et al in 2000²⁴ and Streiner DL et al. in 2006²⁵, who found that there was a linear decrement for depressive illness after the age of 55 years.

The female participants were outnumbered to male participants. Among all 200 participants, female participants were 109 (54.5%) and male participants were 91 (45.5%). Patten SB, Wang JL, Williams JV, et al. 2006²⁶ also reported similar results that major depression was more common in women than in men. Our results are consistent with Niladri Deb et al. 2015²⁷, where out of total number of subjects in control and case group, female participants were more than males.

The mean serum calcium for cases was 9.19 ± 0.92 mg/dl, while for control group was 9.52 ± 0.59 mg/dl. Case group has shown less serum calcium levels than control group, but it was not statistically significant. However, Banki CM et al in 1985²⁸, who had studied 16 psychiatric patients suffering from major depression, reported higher mean level of CSF calcium in depression. Another study by Niladri Deb, Deepika Lahon, Suresh Chakravarty in 2015²⁷ concluded that mean value of serum Ca++ among subjects of control group was higher than that of the subjects of the case group.

The mean value of serum Mg++ among subjects of control group (2.00 mg/dl) was higher than that of the subjects of the case (1.89 mg/dl). However, there was found statistically significant difference between the mean values of serum Mg++ among subjects of control and case groups. These findings are consistent with those obtained in the previous

studies.

Banki CM et al in 1985²⁸ found significantly lower CSF Mg++ in patients with depression.

Also Linder J. et al in 1989²⁹ noted, Depressive symptoms were positively correlated to morning and 24 hour serum Mg++ in remission and longstanding depression.

Joseph Levine et al. in 1999³⁰ examined CSF and serum Ca++ and Mg++ in acutely depressed patients diagnosed as having major depressive disorder. They concluded Serum and CSF Ca++/Mg++ ratios were found to be elevated in the depressed patients as compared with the controls. Also as per Hashizume N, Mori M, 1990³¹, who studied hypo-magnesemia in 165 patients, concluded that the most common clinical findings of hypomagnesemia were personality changes and depression.

Another study by Zièba A et al. in 2000³², reported the results of serum magnesium levels in a clinical study of 19 patients with unipolar depression and compared them to 16 normal controls. Unipolar depressed patients exhibit significantly lower serum magnesium levels than the controls.

Arragan-Rodríguez L et al., 2007³³ studied patients, aged 65 years or older, with depressive symptoms and compared them with a control group in a case/control study. They noted that Serum magnesium levels were significantly lower among depressive than control subjects. They concluded that hypomagnesemia is independently associated with depressive symptoms in older people with diabetes.

Niladri Deb, Deepika Lahon and Suresh Chakravarty in 2015²⁷, studied and estimated S. Mg++ level. They concluded that, the mean value of serum magnesium among subjects of control group was higher than that of the subjects of the case.

CONCLUSION

The present study has found that patients with depression had statistically significant low serum magnesium level than control. Serum calcium level in patients with depression was low as compared to control but this difference was statistically not significant. Thus, conclusively it can be said that alterations in the concentrations of Mg++ and Ca++ specially hypomagnesaemia may be independently play a role in depressive illnesses as concluded by Arragan-Rodríguez L et al. However, despite of taking all necessary precautions and using a very rigorous methodology there are some limitations to our study.

Sample size of our study was relatively small and we conducted single centred tertiary level institutional study so results of our study can't be generalized.

Extracellular concentration of calcium and magnesium may not reflect its intracellular level so measuring brain magnesium by using phosphorus NMR spectroscopy could be the apparent best predictor of magnesium deficiency.

Thus more advanced research methods are required to estimate accurate level of serum Ca++ and serum Mg++ level and establish importance of Magnesium and Calcium imbalance in depressed patients.

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CONFLICTS OF INTEREST

There are no conflicts of interest

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