

Magnesium and Memory: Unraveling the Physiological Tapestry of Alzheimer's Disease

ABSTRACT:

Background: Alzheimer disease is the leading cause of Dementia throughout the world. There are multiple researches are undergoing globally to understand the etiology of this disabling disease. Magnesium is another suspicious factor that might produce this disease.

Objectives: The study was aimed to evaluate possible association between serum magnesium and Alzheimer disease.

Methodology: This case control study was conducted in the emergency Department in collaboration of Medical OPD of Lique University Hospital Hyderabad from January 2023 to December 2023. 300 participants were divided into control, 200 participants and 100 in the test group. Serum Magnesium was evaluated into both control and test group. Graph Pad Prism 9 was used to detect *P* value. Significance of variable was considered below 0.05.

Result: Those who were suffering from Alzheimer disease shows more Hypomagnesaemia (*p*-value= 0.001) than normal patients. The low serum Magnesium level was found 3.1 times greater (Odds ratio= 5.5, likelihood ratio= 1.9) in Alzheimer patients

Conclusion: there is a specific association between Hypomagnesaemia and Alzheimer disease.

Key Words Alzheimer disease, Serum Magnesium, Dementia

INTRODUCTION:

Alzheimer disease (AD) is a neurological disorder in which there is impairment in cognition and language comprehension.¹ Worldwide prevalence of Alzheimer diseases is nearly about 24 million and the risk of incidence get double after 65 years of age.² It is an estimate that 50 million peoples are suffering from this disease globally and it will rise to 150 million by the year 2050.³ Globally a huge amount is spent on the treatment of dementia. in 2015 55 million dollars and in 2030 2 trillion dollars will be be the cost of treatment⁴

Alzheimer is a defect in the cognition of brain caused by the patchy deposition of amyloid proteins in the neurons of hippocampus and cerebellar cortex which obstructs neuronal communication leading to neuronal death.⁵ The most common symptoms of Alzheimer's disease is impairment of short term memory and later on problem solving capacity, language integration behavior change occur²

It is found that a specific protein as p-STAT3-Tyr705 and were found increased in the signaling pathway called JAK2/STAT.⁶ Once the brain parenchyma is damaged, the glial cells receive signals of the damage, which triggers the tau protein, causing it to undergo hyper phosphorylation and oligomerization inside the axon. Additional axon damage results from this alteration in the tau protein's typical shape, leading to cognitive impairment⁷

Magnesium is a crucial part of cells glucose transport system which maintains cell integrity.⁸ The transport system across the cell membrane is dependent upon ATPASE enzyme system which need magnesium ion for its proper functioning.⁹ The concentration level of magnesium in CSF is much greater than concentration level in plasma.¹⁰ Multiple researches proves that

hypomagnesaemia causes neuronal damage which leads to cognitive dysfunction.¹¹ Magnesium plays an important role in integrity of cardiovascular system while Alzheimer is basically caused by the disintegration of vascular system of neurons.¹² The required amount of Magnesium in blood maintains structural and physiological integrity of synapse by which it enhances and improves the ability of hippocampus to restore memory.¹³

The normal range of magnesium in a healthy adult is between 0.70 mM to 1.05 mM. The synapses in hippocampus are quite sensitive to the fluctuations in magnesium concentration. Therefore an increase in half of magnesium concentration will double the density of synapse.¹⁴ Hypomagnesaemia is a potential risk factor for dementia, hypertension, cerebrovascular accidents, and thrombotic plaques.¹⁵

After extensive clinical experimentation on rodents it has been discovered that those pharmaceutical drugs which increase the concentration of magnesium in brain like (MgT), helps in regaining the ability to retain memory by increasing NMDA receptor signaling pathway and preventing degradation of synapses.¹⁶

The data which is gathered after performing several autopsies of Alzheimer patients brain indicates a lower gradient of magnesium as compared to a healthy individual.¹⁷ NMDA receptors in brain are responsible for maintaining synaptic transmission plasticity and neuronal modulation. While the excessive stimulation of these receptors causes excitotoxicity which leads to cell death. Magnesium prevents the over excitability of these receptors therefore hypomagnesaemia leads to increase incidence of Alzheimer.¹⁸

The current study was conducted to investigate a possible link between hypomagnesaemia and Alzheimer disease and want to see that, is this relation is also applicable in population of Hyderabad Sindh.

Methodology:

The current study was a case control study which was undergone in the Department of emergency medicine of Liate university hospital Hyderabad from January 2023 to December 2023 after approval from Ethical Review Committee of department of Physiology and MLT of Sindh university Jamshoro Sindh Pakistan with MR . no 127 and permission of the study was also taken from the in charge of Department Of Emergency Medicine Of Liate University Hospital, Hyderabad, Sindh, Pakistan. The study comprised of 300 patients who came into the department. The participants were divided into two groups, a control group of 200 participants who were not suffering from dementia and 100 participants in the study group suffering from dementia. The age group of patients was 60 and above 60 years. All those patients who were taking laxative, diuretics, alcohol and any other disease which can affect serum magnesium level were excluded.

Before the conduction of study participants were clearly explained about the purpose of study. A written consent was taken from all the participants. Three milliliter of blood was drawn from a visible vein using the aseptic technique, and the blood was then transfused into a test tube that had a red rubber top. It was forwarded to the research lab right away. The serum magnesium level was estimated using a Roche C311 auto analyzer.

Rosanoff A, West C et al. study establishes reference points for hypo- and hypermagneseemia as well as standard values for normal serum magnesium levels. The serum magnesium level is 0.73-

1.06mmol/1.8-2.6mg/dL in male and 0.77-1.03 mmol/1.9-1.03mg/dl. Serum level below 2.07 mg/dL was taken as hypo magnesia and more than 2.5mg/dL was taken as hyper magnesia.

The Alzheimer disease was diagnosed by the criteria laid down by the National Institute on Aging-Alzheimer's Association (NIA-AA) which included neuroimaging, Biomarker of cerebrospinal fluid and assessment of cognition.

Statistical analysis was conducted through Graph Pad Prism 9.the significance between variable was evaluated by P value less than 0.05. Descriptive statistics and Chi-square tests were applied to evaluate the Data.

RESULTS:

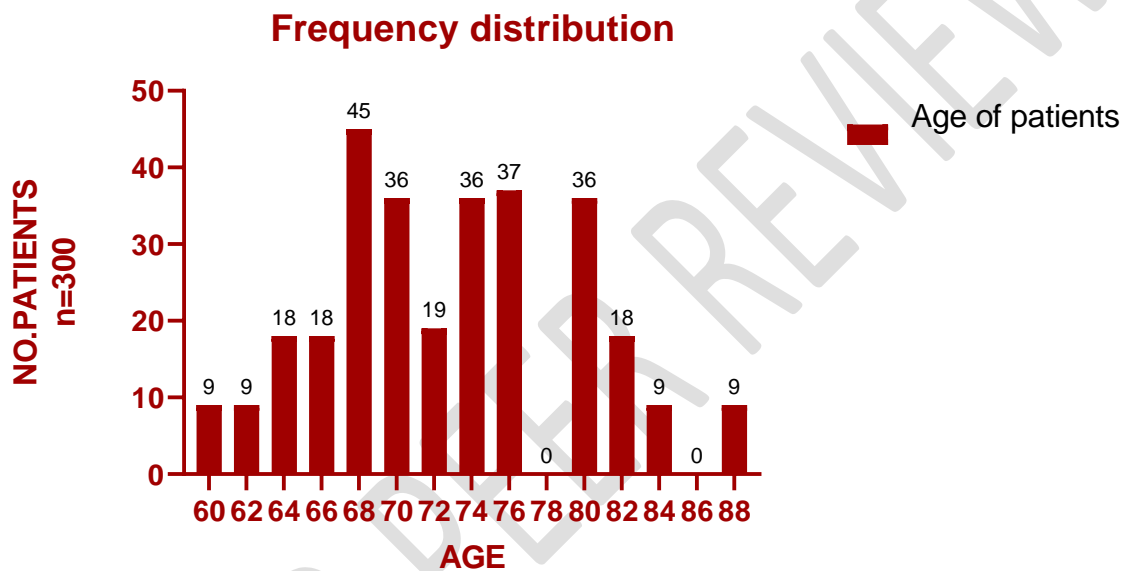
Table 1: Frequency of Age of participants

Gender	Total number	Average
Male	230	77%
Female	70	23%
Total	300	100%

Table 1 describes Age frequency of participants. According to table there were a total of 300 individuals, 77% are male, 23% are female, and the total percentage adds up to 100%.

Table 2:Descriptive statistics of Age of participants

Number of patients	Mean	Median	75 Percentile	CI	Minimum	Maximum
300	72.26±6.55 years	72y	76	71.5-73.01	60 y	87y

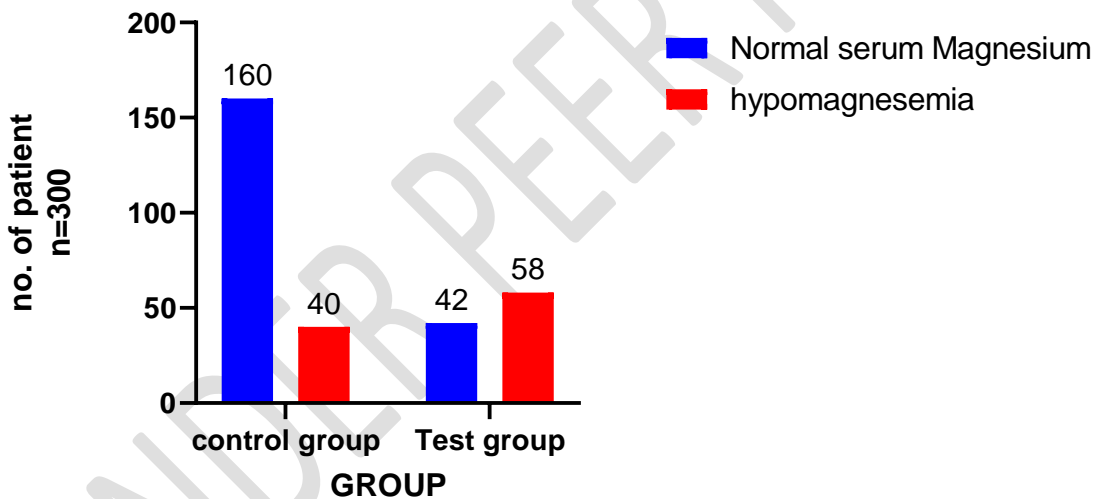


Graph 1 Bar graph showing descriptive statistics of age.

Table The Mean age was 72±6.55, Median 72, 75 Percentile was 76, CI was 71.5-73.01, Minimum age was 60 years and Maximum was 87 years.

Table.3: Serum Magnesium level in Normal versus Alzheimer patients .

Type of Patients	Normal Serum Magnesium	Hypomagnesaemia	Total	P value	R/R	Odds Ratio	likelihood Ratio	Sensit/Speciv
Normal n=200	160 53.33%	40 13.33%	200 66.66%	0.001	1.90	5.52	1.94	0.79/0.59
Alzheimer Disease N=100	42 14%	58 19,33%	100 33.33%					
Total N=300	202 67.33%	98 32.66%	300 100%					



Graph 2. Distinction between levels of serum magnesium among normal individuals

Table.3 and Graph. 2; delineates a noteworthy distinction between levels of serum magnesium among normal individuals (n=200) and those diagnosed with Alzheimer's disease (N=100), showing that hypomagnesaemia is more prevalent in alzhemeirs patients, that also statistically supported by (odds ratio =5.5) showing that low serum magnesium levels is 5.5 times more prevalent in alzhemeirs patient in comparison to normal individual

DISCUSSION:

Several studies throughout the world have investigated the relationship between serum magnesium level and the etiology of Alzheimer diseases. A consensus seems to be emerging globally regarding a potential impact of low serum Magnesium level on the cognition ability.

The current study concluded that low serum Magnesium level was observed in Alzheimer disease, 19% participants showed relevance between low serum magnesium and Alzheimer disease. The *P* value was 0.001 showing significance between the two variables. Serum magnesium prevent the over excitation of NMDA receptors. The deficiency of magnesium initiate a cascade of inflammation in the neurons due to release of inflammatory mediators e.g. interleukin 4 and tumor necrosis factor leading to neurodegeneration. Amyloid β -protein is the basic cause of Alzheimer disease, the excess of which is inhibited by serum magnesium.¹⁹

This relation of hypomagnesaemia in causing cognitive impairment in Alzheimer's patient is also supported by study results conducted by Lei Dy et al with *P* value of 0.001.²⁰ Further more Maier JAM also showed that correcting the magnesium levels in Alzheimer's patients will prevent cognitive impairment in Alzheimer's patients.²¹ In a recent study conducted by Kateba Al et al in 2020 stated that low serum Magnesium level by inhibiting GSK-3 β I protect the synaptic function and plasticity. Showing that low serum level of Magnesium leads to Neurodegeneration and synaptic disintegration. In another study conducted by Jasper et al in 2021 concluded that magnesium deficiency leads to neuronal damage and genesis of Alzheimer disease.²²

There are other factors besides altered levels of magnesium that plays pivotal role in developing cognitive impairment that include family history supported by study results of Gao et al that patients with family history of dementia are more likely to have cognitive impairment than patient with normal family history ($p=0.0009$).²³

The study raises the need for further evaluation of a possible link between serum Magnesium and Alzheimer disease

Conclusion:

The study concludes that there is a strong relationship between low serum Magnesium and Alzheimer diseases showing that low serum magnesium level is more prevalent in Alzheimer's patient (19.33%) in compare to normal individual (13.33%), further supported statistically by odd ratio =5.5 , i.e. Alzheimer's patient are 5.5 time more likely to have low serum magnesium level than normal individual.

ETHICAL APPROVAL AND CONSENT:

The current study was conducted according to Helsinki accord. A written consent was taken from all the participants.

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