

# Low serum magnesium levels and acute ischemic stroke

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## Significance of the Study

Magnesium is a key cation in plasma. Controversial results have been reported about the relation between magnesium levels and cerebral stroke. This study supports that low serum magnesium level may be associated with increased mortality in patients with cerebral infarct. Presence of hypomagnesemia in the ICU patients may be a preliminary finding for other organ damage such as brain.

## ABSTRACT

**Objective:** Magnesium is a key cation in plasma. It regulates ion channels and has activity in more than 300 enzymatic reactions. The aim of this study was to investigate the relationship between mortality and serum magnesium levels in acute cerebral infarct.

**Methods:** A total of 102 patients with acute cerebral infarct were retrospectively analyzed in this study.

**Results:** 102 patients (n: 102) with acute ischemic stroke who were admitted to the study were followed up in our hospital Neurology Intensive Care Unit (NICU). 67 of the patients were alive, transferred to our service, then discharged. The number of patients who died was 35. The mean serum magnesium levels value of the patients who died ( $1,8 \pm 0,4$ ) was significantly lower than the living patients ( $2,1 \pm 0,2$ ) ( $p < 0.001$ ). There was statistically significant difference between the serum calcium levels values of the dead patients ( $8,5 \pm 0,7$ ) and the living patients ( $8,8 \pm 0,5$ ) ( $p < 0.007$ ).

**Conclusions:** Low serum magnesium level may be associated with mortality in acute cerebral infarct. Therefore, the magnesium levels should be controlled in such patients.

**Keywords:** Acute cerebral infarct, mortality, hypomagnesemia

## INTRODUCTION

Magnesium is a key cation in plasma and necessary for the regulation of muscle activity, blood pressure, insulin metabolism and synthesis of proteins [1]. It regulates ion channels and has activity in more than 300 enzymatic reactions. Magnesium is also necessary for neuromuscular transmission. Extracellular magnesium levels contribute only a small fraction of the body's total magnesium but have a good correlation with intracellular magnesium [2]. Studies related to magnesium and cerebral infarct have not adequately investigated the relationship between the cerebral infarct severity and prognosis. Moreover, studies about magnesium in ischemic stroke are limited. In this study, we aimed to investigate the association between serum magnesium levels and cerebral infarct mortality.

## MATERIALS AND METHODS

This retrospective study was carried out in the neurology intensive care unit (NICU) of the Adana City Training and Research Hospital in Turkey, from July 2017 to June 2018. The institutional review board of the hospital approved this experiment. All procedures were followed in accordance with the ethical standards of the Responsible Committee on Human Experimentation, and with the Helsinki Declaration of 1975, as revised in 2008. Patients who stayed at least 24 hours in NICU were included, while patients with hemorrhagic stroke, acute or chronic renal failure, malabsorption, acute or chronic diarrhoea, malignancies, sepsis, a history of alcohol intake or smoking, taking medicines affect magnesium level and who were pregnant or lactating were excluded from the study. A total 102 patients with acute cerebral infarct were included in this study. They were divided into two groups according to survival (dead and survived). Finally, there were 35 (34.3%) and 67 (65.7%) patients who were survived and died, respectively. Serum magnesium, calcium, glucose, albumin, creatinine and complete blood counts of the patients were recorded from their hospital files. Magnesium levels had analysed using the colorimetric method, with the Roche C-501 (Japan). Serum glucose, calcium, albumin and creatinine levels had analysed on the Beckman Coulter Synchron LX 20 (Massachusetts, USA), using commercially available kits. Complete blood counts had measured by using fluorescence flow cytometry on the Sysmex XE 2100i (Japan) before the study in our institute. Glasgow coma scores of all the patients were noted. Groups were compared according to the serum magnesium, calcium, albumin, creatinine levels and Glasgow coma scores. MedCalc 15.8 software program (MedCalcBelgium) was used. Data were reported as mean  $\pm$  standard deviation. The Student's t-test was used to compare normal quantitative independent data and the Mann-Whitney U-test was used to compare independent quantitative data without normal distribution. Chi-square test was used to compare qualitative data. A correlation coefficient was used to analyse the degree of association between the two variables. An odds ratio was used to analyse the degree of association between the serum magnesium levels and acute cerebral infarct. Data were assessed at 95% confidence interval and  $p < 0.05$  values were considered significant.

## RESULTS

The data of 102 patients with acute cerebral infarct who were admitted to the NICU for a period (one year) were examined retrospectively. There were 67 ( 65.7%) patients who survived while there were 35 ( 34.3 % ) patients who died. Thirty-five (52.2%) and 15 patients (42.9%) of the groups were female, retrospectively ( $p=0.370$ ). The mean age of survivors was  $72.6 \pm 12.0$  and the mean age of deaths was  $73.6 \pm 12.4$  years. There was no statistically significant difference ( $p=0.698$ ). There was no statistically significant difference between the groups in terms of blood glucose ( $192.1 \pm 116.4$  vs.  $161.7 \pm 69.6$ ) ( $p=0.131$ ), albumin ( $3.1 \pm 0.73$  vs.  $3.3 \pm 0.5$ ) ( $p=0.158$ ), hemoglobin ( $11.6 \pm 1.9$  vs.  $12.3 \pm 2.1$ ) ( $p=0.135$ ), white blood cell count ( $13.1 \pm 5.4$  vs.  $10.9 \pm 3.3$ ) ( $p=0.053$ ). The mean platelets value of the patients who died ( $209.5 \pm 78.8$ ) was significantly lower than the living patients ( $265.0 \pm 90.8$ ) ( $p < 0.0028$ ). The mean creatinine levels of the patients who died ( $1.54 \pm 1.28$ ) was significantly higher than the living patients ( $1.03 \pm 0.58$ ) ( $p < 0.0028$ ). The mean magnesium value of the patients who died ( $1.8 \pm 0.4$ ) was significantly lower than the living patients ( $2.1 \pm 2.2$ ) ( $p < 0.001$ ). Frequencies of hypomagnesemia were 7 (10.4%) and 23 (65.7%), in survived and dead patients, respectively. Mean Glasgow coma score (GCS) was  $5.4 \pm 1.1$  in died patients while it was  $9.3 \pm 0.9$  in survived patients ( $p < 0.001$ ) (table 1). A significant correlation was persisted between magnesium and GCS ( $r=0.314$ ,  $p=0.0013$ , figure 1). There was a strong association between the serum magnesium levels and acute cerebral infarct (OR 20.1, CI 95% 5.3-76.4,  $p < 0.001$ ).

## DISCUSSION

In this study, we investigated serum magnesium levels and frequency of hypomagnesemia in patients with cerebral infarct in NICU. Moreover, we evaluated the association of magnesium and mortality of acute cerebral infarct. We have found low levels of magnesium, high frequency of hypomagnesemia in dead patients. Additionally, we have found a strong correlation between magnesium level and GCS. The relationship between ischemic stroke and magnesium has been extensively reviewed in many publications. Controversial results have been shown about the relationship between magnesium and stroke. When low serum magnesium level is considered to be associated with cerebral infarction and coronary heart disease. Induced hypoxic excitotoxicity consequent cell death resulting in aberrant cells. Magnesium has made two components of its role in influencing vascular function and the ability to protect against excitotoxicity mediated by NMDA receptors. Studies examining stroke and magnesium levels have produced mixed results [3,4]. Ohira, and colleagues concluded that their study did not find a relationship between serum ionized magnesium levels and stroke risk based on ischemic stroke cases [5]. Adebamowo and colleagues concluded that plasma magnesium levels were not associated with the risk of ischemic stroke in women, magnesium levels did not differ between ischemic stroke cases and controls [6]. Zhang et al reported low serum magnesium concentrations were significantly related to increased risk of stroke mortality and very low serum magnesium may be clinically useful for predicting mortality and other long-term health outcomes in the general population. Even if it is a community-based study and not a part of intensive care unit, that supported our hypothesis [7].

Rosique-Esteban et al. observed that higher Mg intake is associated with a protection against stroke. If hypomagnesemia prevention is protective against ischemic stroke, it supports our thesis [8].

You et al. reported admission low magnesium level is associated with in-hospital mortality in acute ischemic stroke patients. During hospitalization, only 92 patients (3.7%) died but neurology intensive care unit not specified. There were evaluated 35 ( 34.3 % ) died patients in our study in NICU. Similarly, this study with more number of patients supported the increased mortality in the presence of hypomagnesemia [9].

Bayir et al. reported a decrease in CSF magnesium levels in ischemic stroke patients and a positive correlation between low CSF magnesium levels and mortality after 7 days. Although we could not perform CSF examination in our study, it also supports increased mortality with hypomagnesemia [10].

The results of studies evaluating the relationship between magnesium and stroke prognosis are quite contradictory. The number of patients in the study and the laboratory technical differences may explain the contradictory results. In our study, there was significant relationship between magnesium levels and mortality in acute ischemic stroke. On the other hand, we found that magnesium was lower in dying patients and significant in determining the risk of death ( $p < 0.001$ ). Hypomagnesemia may increase mortality of patients with cerebral infarct in neurology intensive care unit. However, due to the inadequacy of patient numbers, mortality relation with magnesium levels should be investigated with further studies. When working on strengthening intensive care scoring systems with laboratory parameters, the magnesium levels need to be further examined. Presence of hypomagnesemia in the ICU patients may be a preliminary finding for other organ damage as brain.

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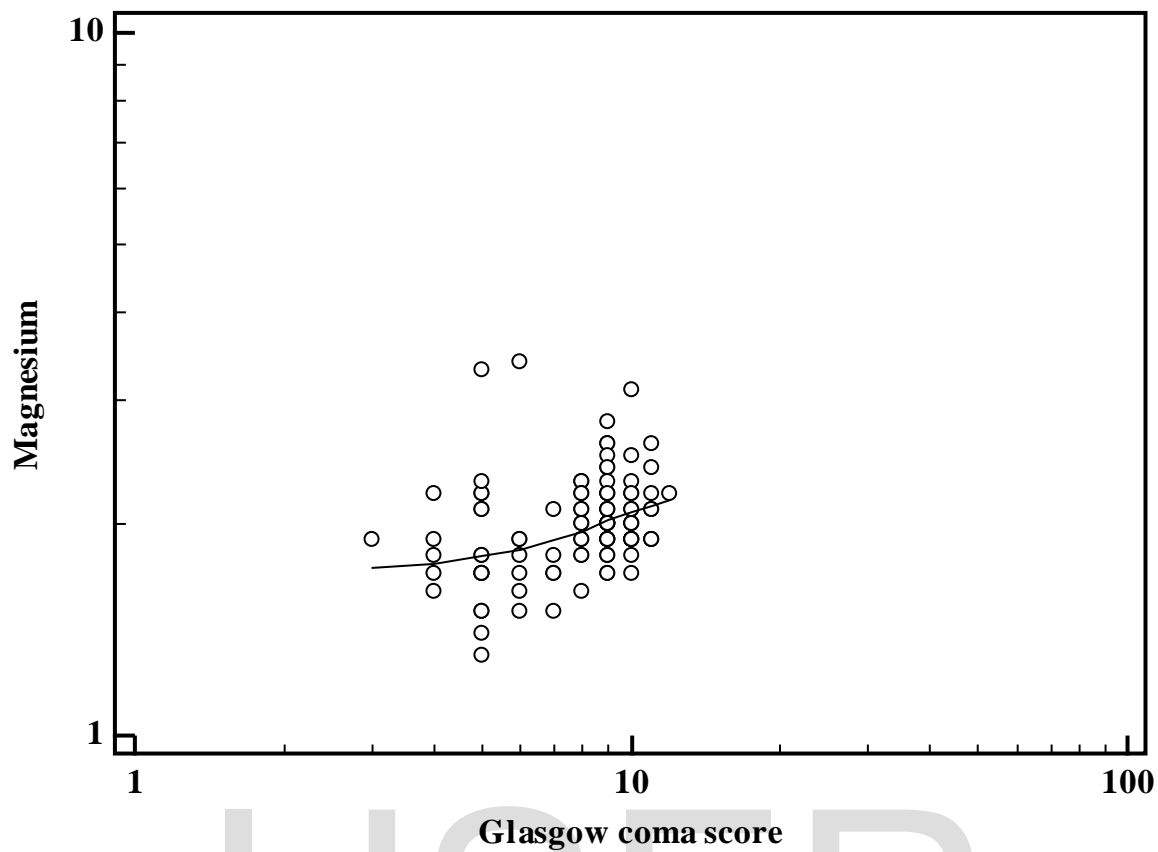


Figure 1: A scatter diagram shows the correlation between magnesium and Glasgow coma score

	Survived N=67	Ex N=35	p
Age (years)	72.6 ± 12.0	73.6 ± 12.4	0.370
Female N (%)	35 (52.2%)	15 (42.9%)	0.698
Magnesium (mg/dL)	2.1 ± 2.2	1.8 ± 0.4	<0.001
Frequency of hypomagnesemia N (%)	7 (10.4%)	23 (65.7%)	<0.001
Creatinine (mg/dL)	1.03 ± 0.58	1.54 ± 1.28	<0.0028
Glasgow coma score	9.3±0.9	5.4±1.1	<0.001

Table 1 shows clinical and demographical properties of the groups

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