# Low Serum Phosphorus Levels and Acute Ischemic Stroke

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## Abstract

**Objective:** The aim of this study was to investigate the relationship between the mortality and serum phosphorus levels in patients with acute ischemic stroke.

Methods: The data of 86 patients admitted to the study were analysed retrospectively.

**Results:** A total of 86 patients (n:86) with acute ischemic stroke who were followed up in our hospital Neurology Intensive Care Unit (NICU). Fifty of 86 patients were survived and transferred to our service, then discharged. The number of patients who died was 36. The mean level of serum phosphorus of patients who died (2.77 ± 0.39) was significantly lower than that of the living patients (3.14 ± 0.20) (p<0.001).

**Conclusions:** This study supports that low serum phosphorus level is associated with mortality in patients with acute ischemic stroke.

**Keywords:** Acute ischemic stroke; Mortality; Serum phosphorus level

## Introduction

Phosphorus plays an important role in delivery of oxygen to tissues by regulating the level of 2,3-DPG and ATP in erythrocytes. It is part of an important urinary buffer system permitting excretion of fixed acids. It is critical in the defence against infectious organisms. Phosphorus could have an important role in the brain where oxidation of glucose through the Krebs cycle is necessary for synthesis of ATP [1]. Studies related to phosphorus and ischemic stroke mortality in NICU has not adequate. The association between serum levels of phosphate and stroke has been investigated in studies, with controversial results [2-4]. There are many studies on phosphorus and cardiovascular diseases in the literature; hypophosphatemia can induce heart failure even in healthy subjects [5]. The myocardial concentrations of creatine phosphate and inorganic phosphate are significantly reduced during a phosphate depletion period, along with the mitochondrial and myofibrillar creatine phosphokinase activity, which has a crucial role in skeletal and cardiac muscle contractility [6]. Studies have shown that the creatine phosphate to ATP ratio is reduced in heart failure and is a strong predictor of prognosis [7-11]. Furthermore, cytoplasmic phosphate increases drastically with work rate in skeletal muscle and in the heart [12]. Therefore, phosphate levels are associated with ejection fraction [13]. Hypophosphatemia has been associated with ventricular arrhythmias additionally; low phosphate serum levels are common in the early stages of sepsis [14]. Due to the low ejection fraction and arrhythmias cerebral circulation may be adversely affected. In this study, 86 patients with acute ischemic stroke were examined with respect to phosphorus level in neurology intensive care unit in a tertiary hospital.

## Materials and Methods

This study was performed at Adana City Training and Research Hospital between September 2017 and July 2018. A total of 86 patients with acute ischemic stroke were included in this retrospective study. Patients who stayed at least 24 hours in NICU were included the study. Patients with haemorrhagic stroke, chronic renal failure, hepatic failure, hearth failure were excluded from the study. In all cases, measurements were taken of the participants 'serum phosphorus, magnesium, glucose, lipids, AST, ALT, creatinine levels and complete blood counts. Phosphorus levels were analysed using the phosphomolybdate method, with the Beckman Coulter Synchron LX20 (Danvers, MA), and the reference range was from 2.5-4.6 mg/dL. Magnesium levels were analysed with the Roche C-501 (Japan) using the colorimetric method. The reference levels range was between 1.9-2.6 mg/dL. Glucose, lipids, ASTs, ALTs, creatinine levels were analysed on the Beckman Coulter Synchron LX 20 (Massachusetts, USA). Complete blood counts were measured by on the Sysmex XE 2100i (Japan). For statistical evaluation MedCalc 15.8 software program (MedCalc Belgium) was used. Mean standard deviation values of the data were recorded. 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. Pearson correlation coefficient was used to analyse the degree of association between two variables. A log transformation was used for the variables that were not normally distributed. Chi-square test was used to compare qualitative data. Data were assessed at 95% confidence interval and p<0.05 values were considered as significant.

## Result

The data of 86 patients with acute ischemic stroke who were admitted to the NICU for a period of approximately one year were examined retrospectively. There were 50 (65.7%) patients who survived while there were 36 (34.3%) patients who died. Of the survivor patients and died patients, 29 (58.0%) and 23 (63.9%) patients were female retrospectively (p=0.583). The mean age of survivors was 71.6 ± 13.9 and the mean age of deaths was 72.56 ± 13.6 years. The difference was not statistically significant (p= 0.762). There was no significant difference in mortality rates between sexes. Furthermore; there was no statistically significant difference between the groups according to the blood glucose (118.2 ± 18.7 vs. 122.0 ± 40.8) (p=0.564), creatinine (0.75 ± 0.22 vs. 0.66 ± 0.23) (p=0.054), haemoglobin (11.6 ± 1.9 vs. 12.3±2.1) (p=0.135), white blood cells (11.4 ± 4.5 vs. 12.3 ± 4.2) (p=0.360), red blood cells (4.35 ± 0.77 vs. 4.16 ± 0.48) (p=0.184), platelets (274.8 ± 115.6 vs. 240.5 ± 94.5) (p=0.147). The mean magnesium value of the patients who died (1.73 ± 0.14) was significantly lower than that of the living patients (2.1 ± 0.18) (p<0.001). Mean Glasgow coma score (GCS) was 5.3 ± 1.6 of died, 9.3 ± 1.1 of the survived patients (p<0.001). Phosphorus levels were correlated with GCS score (p<0.001, r=0.491) **(Table 1 and Figure 1).**

**Table 1** Demographical and biochemical data of the groups.

|  | Survived (N=50) | Ex (N=36) | P |
|---|---|---|---|
| Age (years) | 71.6 ± 13.9 | 72.5 ± 13.6 | 0.762 |
| Female N (%) | 29 (58.0%) | 23 (63.9%) | 0.583 |
| Creatinine mg/dL | 0.75 ± 0.22 | 0.66 ± 0.23 | 0.054 |
| Phosphorus mg/dL | 3.14 ± 0.2 | 2.77 ± 0.39 | <0.001 |
| Glucose mg/dL | 118.2 ± 18.7 | 122.0 ± 40.8 | 0.564 |
| Glasgow coma score | 9.3 ± 1.1 | 5.3 ± 1.6 | <0.001 |
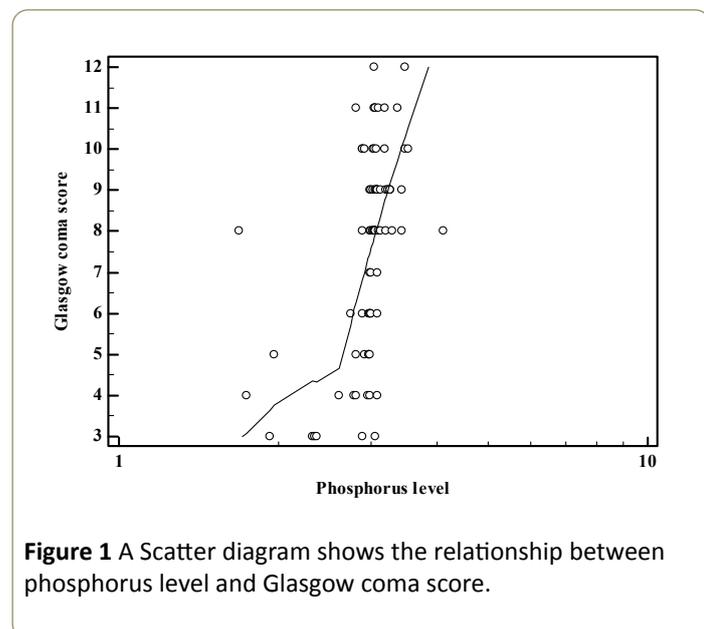


**Figure 1** A Scatter diagram shows the relationship between phosphorus level and Glasgow coma score.

## Discussion

In this study, we analysed 86 patients with acute ischemic stroke according to the phosphorus level. Moreover, we investigated GCS phosphorus association. We have found low levels of phosphorus in died patients. The relationship between ischemic stroke and phosphorus has not been extensively reviewed in previous publications. Massry has shown the clinical syndrome of phosphate depletion. According to Massry's study on phosphate depletion, the syndrome can lead to disturbances in the central nervous system, hematopoietic system, parathyroid glands, cardiac function, renal function, and also in muscles and bones [15]. The low levels of phosphorus affect the organs; a decrease in 2,3-diphosphoglycerate in red blood cells leads to tissue hypoxia, mitochondrial energy production decreases due to low tissue content of ATP. Correspondingly, hypoxia in the tissue and energy deficiency in the cells may lead to organ failure [16]. Studies examining acute ischemic stroke and phosphorus levels have produced only a few results. Wannamethee et al. [2] concluded that their study find a relationship between raised serum phosphorus levels and increased total mortality of stroke cases. Li et al. [3] concluded that there is no association between serum level of phosphate and stroke. Aronson et al. [4] reported that higher phosphorus levels were also associated with increased risk of heart failure, but not the risk of myocardial infarction or stroke.

The results of studies evaluating the relationship between phosphorus and stroke prognosis are inadequate. The studies about the association between acute ischemic stroke mortality and hypophosphatemia are insufficient. In our study, we have found significant relationship between phosphorus levels and mortality in acute ischemic stroke. To our knowledge whether correlation between phosphorus levels with acute ischemic stroke mortality in NICU has not been described before.

This study had some limitations. First, it would have been beneficial if the sample size had been larger. Second, we did not measure the level of PTH (parathyroid hormone), fibroblast growth factor 23 (FGF23).

In conclusion, serum phosphorus level can be associated with mortality in patients with acute ischemic stroke. When working on strengthening intensive care scoring systems with laboratory parameters, the phosphorus levels need to be further examined. Presence of hypophosphatemia in the ICU patients may be a preliminary finding for other organ damage as brain.

## Significance of the Study

Inadequate results have been shown about the phosphorus levels and stroke. This study supports that low serum phosphorus level may be associated with mortality of cerebral infarction. Presence of hypophosphatemia in intensive care unit patients may be a preliminary finding for other organ damage such as brain.

## Acknowledgement

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