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ORIGINAL ARTICLE

Relationship of Serum Calcium Level with Clinical Severity of Acute Ischemic Stroke as Assessed by National Institute of Health Stroke Score (NIHSS)

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ABSTRACT

Introduction: Calcium (Ca^{2+}) plays an important role in the pathogenesis of ischemic cell damage. Different studies have shown that lower serum calcium leads to more clinical severity of stroke as assessed by National Institute of Health Stroke Scale (NIHSS).

Materials & Methods: Stroke patients who met the inclusion criteria were evaluated using NIHSS and their serum calcium levels were checked at presentation. Pearson's correlation was determined between serum calcium levels and NIHSS score.

Results: There were 200 patients in the study with mean age 61.58 ± 12.4 years. The male to female ratio was 1 : 1.15. The mean calcium level of the study population was 8.95 ± 0.75 mg/dL. The mean NIHSS score was 18.01 ± 7.91. The overall Pearson's correlation coefficient between serum calcium level and NIHSS score came out to be r = - 0.413 ($p < 0.001$). The value was r = -0.396 ($p = 0.29$) among men and r = -0.416 among women ($p = 0.12$).

Conclusion: Lower serum calcium levels is associated with more severe clinical findings at the onset of stroke.

Keywords: Ischaemic stroke, Stroke severity, NIHSS score, Serum calcium

INTRODUCTION

A stroke is a disease marked by abnormal brain function that occurs quickly with no other recognized cause, other than a vascular disorder[1, 2]. Sometimes, the loss of function can involve the whole brain such as in deep comas or subarachnoid hemorrhage[1]. The disorder might result in a patient getting well in one day, having incomplete improvement, becoming severely restricted or dying. The World Health Organization reports that there are approximately 16.3 million stroke cases every year[3]. Official numbers about Pakistan are rare, but since stroke risk factors are so common, it is reasonable to assume that stroke affects many people[4].

NIHSS is a tool physicians use to rate the amount of damage caused by a stroke[5]. It has numerous times been shown to measure how severe a stroke is and to predict how well a patient will recover[6]. One of the triggers for cell damage in strokes is calcium (Ca2+). A rise in Ca2+ within neurons causes them to suffer damage by setting off a series of harmful reactions[7]. Ischemia/hypoxia quickly allows calcium to move from the outside of cells into the inside of cells in the brain. Knowing that Ca2+ is involved in the ischemic cascade has inspired scientists to develop kinds of medications that target this ion's effect in brain injury[8].

The role of Ca2+ in stroke risk factors and occurrence of stroke has been looked at as well. According to research, having high amounts of Ca2+ in your diet may lower your risk of stroke[9]. A number of reasons may connect serum calcium to the amount of energy-deficient tissue found in acute ischemic stroke patients. These mechanisms can be organized into 2 major and non-exclusive groups. Raised calcium in the blood often keeps ischemic tissue from swelling and serum calcium levels also drop when tissue ischemic occurs[9]. A drop in serum calcium during ischemia allows calcium-sensing nonselective channels to become more active which simultaneously increases membrane depolarization and raises the level of calcium inside the cell[10].

Rodents fed a high-calcium diet had smaller areas of brain damage after experiencing an ischemic stroke[8]. Other epidemiological research shows that raising dietary calcium may lower the risk of dying from ischemic and hemorrhagic stroke; in these studies, researchers did not check blood calcium levels. Diet is just a part of calcium homeostasis, so it's tricky to know if the epidemiological evidence really relates to blood calcium levels. Very limited research has tried to establish a link between serum calcium levels and how severe an acute ischemic stroke is. By learning the results of the study, we could help patients at risk of stroke decide on the right amount of calcium in their diet which would perhaps reduce both the frequency and the intensity of stroke incidences. The objective of the study was to find out if there is any relationship between serum calcium and the level of impairment seen in acute ischemic stroke assessed using the National Institute of Health Stroke Scale.

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MATERIALS AND METHODS

To study the relationship between serum calcium levels and acute ischemic stroke scores, a cross-sectional study was done at the department of medicine in Central Park Teaching Hospital Lahore from October 2022 to April 2023 after approval by the Institutional Review Board of Central Park Medical College. It was decided to have 200 participants and recruitment was random non-convenient sampling. All people in the age range of 20 to 70 years who had a stroke within seventy two hours were studied, except those who suffered from more than one stroke, intracerebral hemorrhage, myocardial infarction within the past 3 months and unstable supraventricular tachycardia and arrhythmias.

The researchers obtained approval before starting the study, then enrolled 200 subjects who met the required criteria after the patients gave written consent. Since the patient could not give consent, a written informed consent was gotten from the patient's next of kin. Next, the following sociodemographic factors were written down: age and gender. Later, specific questions about possible causes of stroke, including hypertension, diabetes, coronary artery disease, peripheral vascular disease, etc. and about any medicines they had been prescribed such as warfarin or aspirin, were asked. Sphygmomanometer was used to measure blood pressure and doctors evaluated stroke severity using the NIHSS questionnaire. Blood was taken from the patient by a skilled phlebotomist and the samples were sent to check the serum calcium level and all the standard tests. We put all the information which included the NIHSS and serum calcium values, into a pre-built proforma.

Statistical Analysis: With SPSS version 26.0, the assembled data was analyzed. Numerical variables like age, NIHSS score, blood pressure, serum calcium levels were shown in means and standard deviations. Gender, history of hypertension, diabetes and

smoking were shown as frequencies and percentages. The relationship between serum calcium levels and NIHSS scores was assessed with Pearson's correlation coefficient and $p < 0.05$ was considered statistically significant. Age, gender, BMI, hypertension, diabetes mellitus and smoking were used to deal with factors that might affect the results. Post-stratification Person's chi-square test was used, with a p-value less than or equal to 0.05 seen as statistically significant.

RESULTS

In the study, there were 200 subjects and their average age was 61.58 ± 12.4 (the age range was 34 to 85 years). Of the 199 patients, there were 93 males (46.5%) and 107 females (53.5%) and the ratio of males to females was 1: 1.15. The average calcium level measured in the patients was 8.95 mg/dL with a range of 0.75 mg/dL. All patients were sorted into 4 groups dependent on their serum calcium levels. Out of all 198 people, 47 (23.5%) had a serum calcium level under 8.70 mg/dL, 60 (30.0%) had levels between 8.71 and 9.0 mg/dL, 42 (21.0%) had levels between 9.01 and 9.30 mg/dL and 51 (25.5%) were above 9.30 mg/dL as depicted in figure 1.

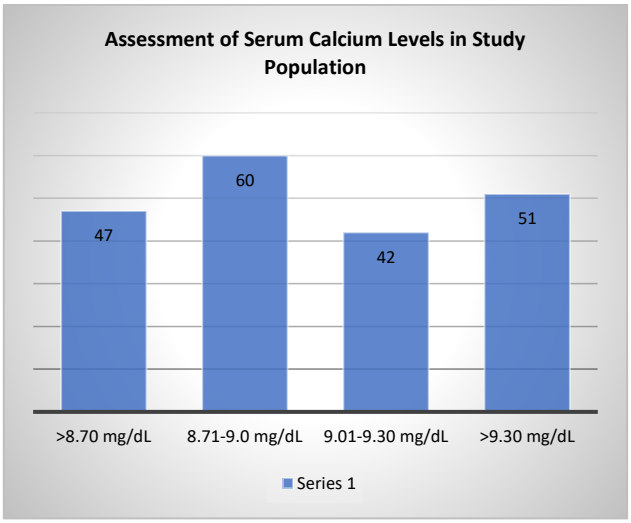

Figure 1: Assessment and Comparison of Serum Calcium Levels in Study Population.

After performing Pearson's chi-square tests, no strong relationship was found between measured calcium and hypertension, diabetes and smoking, as they are baseline variables for the study patients (p=0.93, 0.87 and 0.53 respectively). The inhabitants had an average systolic blood pressure of 144.1 ± 10.3 mmHg and diastolic blood pressure of 98.4 ± 8.8 mmHg. The systolic and diastolic blood pressure varied in ways that were not specific to the level of serum calcium found in patients. For this reason, the analyses did not show any significant relationship between systolic and diastolic blood pressure and serum calcium (p = 0.631 and 0.874, respectively).

The research calculated the mean NIHSS score for everyone in the study sample. It was found to have an average of 18.01 ± 7.91 (out of 42). Numerous patients with weak serum calcium indicators at the beginning showed much higher NIHSS scores than those with better calcium. The average NIHSS score for patients with low, medium, high and very high serum calcium was 21.02 ± 7.17, 20.72 ± 7.68, 19.95 ± 5.98 and 14.23 ± 8.11, respectively. Serum calcium level and NIHSS stroke severity scale were connected using the bivariate correlation method. The total Pearson's correlation coefficient was r = - 0.413 (p = 0.00001). The value declined for men, with r = -0.396 (p = 0.29) and women, with r = -0.416 (p = 0.12). In accordance with the table, the internetwork Pearson's correlation coefficient r = - 0.413 proves that the trend of decreased NIHSS score with increased Ca2+ concentration does exist and supports that stroke severity drops as Ca2+ goes up and vice versa.

Table 1: Correlation Between Stroke Severity Score (NIHSS Score) with Calcium Levels

Variables	Mean ± SD	Pearson's Correlation (r-value)	P-value
NIHSS Score	18.01 ± 7.91	- 0.413 [a]	0.00001
Calcium Level (mg/dL)	8.62 ± 0.76		

DISCUSSION

Source of much mortality and morbidity in the global community, stroke ranks among the highest. Hypertension, hyperlipidaemia, diabetes, smoking, atrial fibrillation, valvular heart diseases and vasculitis are risk factors for stroke. Assessing how bad an ischaemic stroke is can be done through examination, imaging to measure the damaged area and certain lab tests[11]. Biochemical markers have been examined using studies to learn about their involvement in the seriousness of stroke.

The ratio of women to men in our study (1.15:1) is the same as the ratio reported by Guven et al (1:1.13) in their international research. In their study, Buck BH et al. have noted that there are 1.4 more female than male patients (89). But according to Appel and team, there is a larger number of male patients, with a male-to-female ratio of 1.35:1.15 (93). We found similar findings to the only known local study which reported a 1: 1.06 male to female ratio[12].

Ages 61 to 70 were the most common among our patients (40.0%). As we have learned before, this is in line with what has been found in other studies[13]. The average age of those treated was 61.58 with a standard deviation of 12.4 years. According to Guven H. et al., the cases in their study were mostly affect people older than 67 years of age[14]. Appel SA and his colleagues found that the average age was 70.7 years (93). Ishfaq et al found that the average age in their Karachi, Pakistan population was 61.09 ± 11.93[15]. The athletes in our study had a low average age which agrees with the reality that many proper stroke prevention guidelines are not followed in our country because of poverty. People in our nation live fewer years on average than people in more developed countries.

The mean serum calcium we found was 8.62 ± 0.76 mg/dL compared to 8.82±0.69 mg/dl in a study from Pakistan[16]. Another study by Appel et al showed that albumin adjusted calcium levels were 9.2±0.5 mg/dl[17]. We think that lower mean calcium is due to various factors. First, our patients were generally of lower income and lower calcium levels compared to other studies could be because of poor nutrition. The lower calcium is also likely due to limited sunlight exposure which is common among women whose mean calcium was 8.60 ± 0.65 mg/dl in our study since many women in our community remain indoors and wear veils. Most patients in our study who had lower calcium were females which is similar to what has been seen in previous studies[18]. The patient group with low serum calcium levels had a higher average age. In their study, Guven H. et al. reached the same conclusions[19]. According to Ovbiagele B. et al. (20), patients with low mean age tended to have elevated blood calcium[20]. The average NIHSS during the first 48 to 72 hours of symptoms was 18.01 and was more common in people with calcium levels below 2.2, 2.2 to 2.6 and 2.6 to 3.0. Other research studies have supported this finding[21].

Research comparing serum calcium levels and how severe a stroke is or its impact on prognosis in acute ischaemic stroke, is very scarce. Calcium levels are usually low in transient ischaemic attack, while a major reduction happens in ischaemic cerebral infarction compared to TIA[22]. There was a significant relationship between lower calcium in the blood and a more severe stroke as measured by NIHSS (r = -0.413, p < 0.001). A low level of albumin adjusted calcium measured early after ischaemic stroke occurs

together with more severe symptoms. Another study by Guven H. et al. also found the same association, but here the serum calcium measurements were done within the first 24 hours[23].

Different ideas have been proposed to explain how low calcium relates to stroke being more severe and the patient doing less well after the stroke. When tissues become ischaemic, calcium is held inside cells which may lead to low calcium. Dying neuronal cells during ischaemia have different reasons such as overstimulation, too much reactive oxygen, programmed death or necrosis (99, 100). Current research points to the fact that calcium influx from N-methyl-D-aspartate (NMDA) receptors prompt these events[8]. People who consume plenty of calcium in their diet may be less likely to have a stroke[10]. Another possible reason is that low calcium indicates low levels of vitamin D which by itself is linked to worse outcomes[11]. A shortage of vitamin D is related to a higher possibility of suffering a stroke[18]. Should low calcium promote ischaemic injury, then lifting the calcium levels might be neuroprotective. Studies should be conducted to observe this possible impact.

CONCLUSION

Based on our study, people with lower levels of Serum Calcium during onset of their stroke often have more severe symptoms. Serum Calcium levels can show the severity of the stroke and may be a useful target for better treatment.

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