

Correlation of Serum Calcium with Acute Ischemic Stroke

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ABSTRACT

Background: Stroke or cerebrovascular accident is the most common cause for disability and third leading cause of mortality worldwide. Stroke not only accounts for leading reason for mortality and morbidity, but also puts a great economic burden on the family as well as on society.

Aim: To determine the relationship between blood calcium levels and the severity of patients with acute ischemic stroke presented to the medical department HMC Peshawar.

Methodology: From July 2019 to January 2020, the Department of Medicine at the Hayatabad Medical Complex in Peshawar carried out this descriptive (cross-sectional) study. 137 patients fulfilling the inclusion criteria were selected for this study. Appropriate history regarding presenting neurological deficit, occupational and socioeconomic history were taken to dig out the confounding factors. After taking history, appropriate physical examination was performed study the relationship between blood calcium levels and the severity of acute ischemic stroke

Results: Out of 137 patients, 71 were males and 66 females with age range of 35-80 years (Mean 56.42 years + 12.44SD). Pearson correlation coefficient shows that severity of stroke and serum calcium have negative correlation of -0.236. Majority of patients in our research sample had ischemic strokes, as evidenced by NIHSS scores of greater than 20, followed by scores of 6-10 individuals. To support the treatment recommendation of hypercalcemia in patient who presented with electrolyte imbalance should be treated early on time to prevent stroke and its severity.

Conclusion: Smoking habits of the trial participants were evenly distributed amongst the intervention groups, and they had no impact on the outcome of patients with acute ischemic stroke. Patients with ischemic stroke consistently had lower blood calcium levels than non-diabetic patients with diabetes mellitus. In order to support the treatment advice for hypercalcemia, patients who first presented with electrolyte imbalance should receive therapy as soon as possible in order to reduce the risk of stroke and its severity.

Keywords: Ischemic stroke, serum calcium, hypertension, diabetes mellitus.

INTRODUCTION

The second-leading cause of death globally and the third-leading cause in the developed world is stroke¹. In the United States it is the most prevalent reason for adult disability (US)². About 152,000 strokes occur in the UK each year³. In the UK, one stroke occurs every 3 minutes and 27 seconds. Stroke's incidence is increasing in Asia, this is having a terrible effect on patients, their families, and the healthcare system, and is responsible for tremendous economic burden⁴. 16.3 million new stroke cases occur worldwide each year.

Based on data from the World Health Organization (WHO) estimates⁵, the prevalence of neurological complication in acute ischemic stroke varies between 13% and 38%. Stroke patients are toward most astounding danger of death in the 1st week after the event. The first few weeks following a stroke are the high risk for patients with the condition, and within the first month, between 20% to 50% die. And those who do survive can still have no impairment or a slight, moderate, or severe condition. It can take around six months for significant spontaneous healing⁶. However, individuals who have already experienced a stroke run a higher chance of experiencing another one, with a first-year risk of 10% and a second-year risk of 5%⁷. By one year following a stroke, 60% to 83% of patients are independent in self-care. Around 60% to 83% of patients achieve independence in self-care by one year after a stroke⁸.

According to data on causes of death from the 1990s, cerebrovascular diseases continue to be a major cause of mortality. Globally, 5.5 million deaths from cerebrovascular diseases (stroke) were anticipated in 2001, accounting for 9.6% of all deaths⁹. Stroke is one of the main health issues in the UK. Over 56,000 deaths or 11% of all deaths in England and Wales

in 1999, were attributed to it¹⁰. Ischemic heart disease was the leading cause of death among the 135 disorders included in the Global Burden of Disease (GBD) research, with cerebrovascular diseases coming in second¹⁰. The global burden of stroke and absolute number of stroke-related deaths are great and increasing¹¹.

Barker-Collo et al¹², highlight that ischemic stroke has a higher incidence in men but a lack of sex differences in hemorrhagic stroke incidence. As compared to women, men and in especially younger age, are at a 25% higher risk of having a stroke¹³. A study done in the US has revealed that after acute ischemic stroke, low serum calcium is markedly as measured by the National Institute of Health Stroke Score (NIHSS), with a correlation coefficient value of -0.3 compared to individuals with high calcium levels¹⁴. High blood calcium levels at the time of hospital admission are related with a less severe stroke and a better functional result after release, according to a further US study¹⁵. Low blood Ca levels have been linked, according to a Turkish study, to more severe clinical signs and symptoms in acute stroke patients at the time of admission¹⁶.

According to a Japanese study, eating a diet high in calcium especially from dairy products was linked to a lower risk of stroke¹⁷, among the 138 patients, 51.4% of them were women and 48.6% were males. The mean age was 61.09±11.93 years. The average stroke score from the National Institutes of Health was 17.77±7.73. All patients' blood calcium levels were tested and corrected for serum albumin levels. The mean serum calcium concentration was 8.82±0.69 mg/dl. For continuous data on blood calcium and the National Institutes of Health Stroke Score, bivariate correlation was performed. Overall, the Pearson's correlation value was negative ($r=-0.237$; $p=0.005$)¹⁸. The risk of experiencing an overt stroke by the time a person reaches the age of 80 is anticipated to be one in four, while the likelihood of experiencing a silent or covert stroke is more likely to be close to 100%. Stroke affects both men and women equally and has a

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significant negative financial and social impact on society, with direct costs in Canada surpassing \$3 billion annually. Acute coronary syndromes and acute stroke have several things in common¹⁹.

Patients in higher calcium quartiles (Q3,Q4) had significantly fewer severe 24-48-hour strokes than those in lower calcium quartiles (Q1,Q2), with 72.73% in Q3 and 42.86% in Q4 being in the moderate NIH scale category, as opposed to 7.69% in Q2 and 0% in Q1. At the time of discharge and at the three-month follow-up, functional outcome was significantly better in the higher calcium quartile group than in the lower quartile (>3 mRS score suggestive of poor outcome in 91.66% of Q1, 76.93% of Q2, 27.27% of Q3, and 7.14% in Q4 at the time of discharge, and 83.32% in Q1, 76.93% in Q2, 27.27% in Q3, and 7.14% in Q4 at the three months follow up. This link was statistically significant (p-value 0.01), according to the correlation analysis²⁰.

Acute ischemic stroke is the major cause of mortality and morbidity. Since there hasn't been a recent research on the local population, this one will show how imbalanced serum calcium levels relate to the frequency and severity of strokes. This will help us treat our patients more quickly and prevent complications.

METHODOLOGY

July 2019 to January 2020, the Department of Medicine at the Hayatabad Medical Complex in Peshawar carried out this descriptive (cross-sectional) study. Inclusion criteria: both genders, male and female, range in age from 35 to 80 years and with acute ischemic stroke. While patient not willing for study, patients with previous cerebrovascular accident or recurrent stroke, Renal failure, Hemorrhagic stroke as evidenced by hyper dense lesion on CT brain and aspiration pneumonia as evidenced by consolidation on Chest X-RAY were excluded from this study.

Ethical approval was obtained from hospital ethical committee and research committee before performing the study. Patients who have been referred from the A&E Department and fulfil the inclusion criteria. The patients' attendants were told of the study's advantages and goal, and each patient provided written informed permission. All patients had thorough examinations and histories. NIHSS was used to determine the stroke's severity. Within 72 hours after the beginning of symptoms, a sample of 5cc of blood was collected from each patient without using a tourniquet under strict aseptic conditions, and submitted to the hospital's laboratory to assess serum calcium. Under the guidance of a pathologist, the serum calcium level was tested. The study proforma included the names, ages, genders, and residences of all the patients who provided the aforementioned information.

Table 2: Stratification of serum calcium

		Serum Calcium				p-value
		<= 9.00		9.01+		
		Count	N %	Count	N %	
Gender	Male	17	23.9%	54	76.1%	0.402
	Female	20	30.3%	46	69.7%	
Residence	Urban	22	24.7%	67	75.3%	0.411
	Rural	15	31.2%	33	68.8%	
Smoking	Yes	20	24.4%	62	75.6%	0.400
	No	17	30.9%	38	69.1%	
Diabetes mellitus	Yes	22	28.2%	56	71.8%	0.717
	No	15	25.4%	44	74.6%	
Hypertension	Yes	19	23.8%	61	76.2%	0.309
	No	18	31.6%	39	68.4%	
Alcoholism	Yes	2	40.0%	3	60.0%	0.505
	No	35	26.5%	97	73.5%	
Family history	Yes	14	43.8%	18	56.2%	0.015
	No	23	21.9%	82	78.1%	
Prior Strokehistory	Yes	13	26.0%	37	74.0%	0.840
	No	24	27.6%	63	72.4%	

RESULTS

In this study, 137 patients having detected ischemic stroke had observed. The mean age of the patients was 56.42 years ±12.44SD with range of 35-80 years. Majority of the patients presented with stroke were follow in age range of 56-70 years. There were 24 (17.5%) patients in the age range of less than 40 years, 41 (29.9%) patients in the age range of 41-56 years, 52 (38%) patients in the age range of 56-70 years and 20 (14.6%) patients in the age range of more than 70 years.

There were 71 (51.82%) male patients and 66 (48.18%) female patients while the male to female ratio was observed as 1.07:1.

Majority of the patients have ischemic stroke having NIHSS of more than 20 were observed followed by NIHSS of 6-10 in our study sample.

Pearson correlation coefficient shows that severity of stroke and serum calcium has negative correlation of -0.221. Which means that low level of calcium causes high level of stroke. The correlation coefficient is low but it is significant with p-value=0.006 (Table 1).

Age wise distribution of serum calcium in severity of ischemic stroke was found a little bit high in older age group and the rest of age group have almost same pattern it was insignificant with p-value=0.218. Similar results were found when serum calcium was stratified among gender, residence, family history, previous stroke, diabetes, and hypertension (Table 2).

Table 1: Correlation between severity of ischemic stroke and serum calcium

Spearman's rho		Severity of Stroke	Serum Calcium
Severity of Stroke	Correlation Coefficient	1.000	-.221
	P-value	.	.009
	N	137	137
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DISCUSSION

The most frequent cause of admission to a General Medicine unit in our region of the world is stroke³. The World Health Organization defines a stroke as the sudden onset of a new neurological deficit caused by an obstruction or rupture in the cerebral artery system that lasts for at least 24 hours and had to include specific localising findings that were confirmed by neurological testing and a computed tomography (CT) scan of the brain, with no indication of an underlying non-vascular cause⁴. A stroke may be transient if full recovery takes place within 24 hours, developing if a neurological deficiency worsens after 6 hours, and complete when a fixed, non-evolving deficit is identified. Nearly two-thirds of strokes are ischemic in nature, while the other third are either thrombotic or embolic in nature⁵. Ischemic stroke (70.1%) is far more common than the hemorrhagic type (29.9%) in Pakistan as well⁴.

The patients in our study had a mean age of 56.42±12.44 years. The average age of the patients was 619.7 years, which was older than the research conducted by Barech et al²¹. It is similar to our study. In another study conducted by at Agha Khan University Hospital Karachi Pakistan²² and found that mean age of the patients was 57±13.9 years, the average age is low as that study as we have limited the study up to 60 years of age.

There were 48.18% female patients and 51.82 % male patients in our study. In the study, there were 60.3% male patients and 39.7% female patients conducted by Barech et al²¹, which is comparable to our findings. In another study conducted by Khan et al²³ there were 78% male patients and 22% female patients, which is also comparable with our study. In a study conducted at Pakistan²² and revealed that there were 34.6% women and 65.4% men, which is similar to our study's findings.

NIHSS-measured stroke severity ($r = -0.236$, p) Pakistan²⁴ similarly to Turkey, the study's findings²⁵ There was evidence of a negative correlation between NIHSS score and calcium level. Since the majority of the participants in our study arrived at the emergency room after experiencing their first symptoms after travelling from far locations, blood calcium levels were tested between 48 and 72 hours after the stroke. The calcium levels that we measured were comparable to the group with "delayed calcium," therefore this was helpful for our study of Ovbiagele et al²⁶ this was linked to a greater three-month recovery and a stroke that was less severe. Although serum calcium did correlate with stroke severity as previously reported, albumin adjusted serum calcium did not connect with stroke severity in the same way by Erasmo et al²⁷.

Higher blood calcium levels upon admission have been reported to be linked to lower cerebral infarct sizes in individuals with acute ischemic stroke. Acute ischemic stroke clinical outcomes have been explored in relation to both early and delayed Ca²⁺ levels, but no discernible changes in clinical outcomes between early and delayed Ca²⁺ levels have been found²⁸⁻³⁰.

The link between relatively low calcium levels and severe stroke and a bad prognosis has been explained in a number of different ways. A tissue ischemia condition that results in intracellular calcium accumulation might be the cause of low calcium levels. Numerous mechanisms contribute to neuronal cell death brought on by ischemia, including the excitatory route, oxidative stress, apoptosis, and necrotic cell death¹⁸. Recent studies suggests that these processes are brought about by calcium influx via the N-methyl-D-aspartate (NMDA) receptor^{31,32}. Reduced incidence of stroke has been linked to high dietary calcium consumption. 13 Another argument is that low calcium levels are a reflection of low vitamin D levels, which themselves are directly linked to unfavourable results³³. Stroke risk is also enhanced by low vitamin D levels³.

CONCLUSION

This study's findings suggest that the negative correlation between serum calcium level and severity of ischemic stroke patients, which seems to be major risk factor of acute ischemic stroke. The

clinicians will continue to be challenged by this patient counselling and good management are necessary. This risk factor can be changed, but doing so requires knowledge, education, the eradication of poverty, consistent medicine usage, and a change in lifestyle. When compared to male patients, ischemic stroke patients consistently had lower blood calcium levels in female patients. The intervention groups' prognosis for patients with acute ischemic stroke is unaffected by the study participants' alcohol consumption status, which is normally distributed among them. Smoking habits of the trial participants were evenly distributed amongst the intervention groups, and they had no impact on the outcome of patients with acute ischemic stroke. The prognosis for patients with acute ischemic stroke is affected by the distribution of diabetes mellitus among trial participants in the intervention groups. Patients with ischemic stroke consistently had lower blood calcium levels than non-diabetic patients with diabetes mellitus. The intervention groups' normal distribution of hypertension among the trial participants had no impact on the outcome of acute ischemic stroke patients NIHSS score. Further randomize control trials to confirm it as independent prognostic factor while managing acute ischemic stroke patients.

Conflict of interest: Nil

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