Original Research Article

Serum calcium as a marker of severity in acute ischaemic stroke patients, a study in tertiary care centre of south eastern Rajasthan

[1]Dr. Laxmikant Tank, [2]Dr. Ashok Rathore, [3]Dr. Archana Dubey, [4]Dr. Piyush Baisla

[1]Assistant Professor, Department of General Medicine, Jhalawar Medical College, Jhalawar, Rajasthan, India

[2]Associate professor, Department of General Medicine, Jhalawar medical college, Jhalawar, Rajasthan, India

[3]Assistant professor, Department of General Medicine, Jhalawar medical college, Jhalawar, Rajasthan, India

[4]Assistant professor, Department of General Medicine, Jhalawar medical college, Jhalawar, Rajasthan, India

Corresponding Author:
Dr. Piyush Baisla (piyushbaisla@gmail.com)

Abstract

Introduction: The calcium ion (Ca2+) is a ubiquitous intracellular messenger during and immediately after an ischemic period. Clinical studies suggest that severity of clinical symptoms, prognosis and infarct volume are also associated with levels of serum calcium.

Aim: The aim of this study is to determine Serum calcium as a marker of severity in acute ischaemic stroke patients.

Methodology: This prospective observational study was conducted on 80 patients of acute ischemic stroke admitted in the department of medicine at Jhalawar medical college, Jhalawar during the period of 1 year. Adjusted serum calcium level was obtained within 72 hours from onset.

Results: Out of 80 patients of acute ischemic stroke, 49 (61.25%) had low serum calcium while 31 (38.75 %) participants had normal level of serum calcium. Most common age group was 61 to 70 years (36.7%). NIHSS score was higher with low serum calcium level. Out of the 49 patients who had low levels of calcium, 49% (24) had severe stroke with NIHSS score 21-42. Among 49 patients with low serum calcium, 91.5% (45) had poor outcome. MRS score was higher with low serum calcium level. Chi square analysis revealed lower adjusted serum calcium levels accompanied by poor outcome statistically significant (p= <0.0103).

Conclusion: Based on these results, we can conclude that low adjusted calcium levels in patients with acute ischemic stroke is an independent risk factor and have poor outcome than patients with normal serum adjusted calcium level.

Keywords: Modified Rankin score, national institutes of health stroke scale, adjusted calcium, stroke, severity

Introduction

The world health organisation defined stroke as "a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal neurological deficit and at times global loss of cerebral function, lasting for more than 24 hour or leading to death, with no apparent causes other than of vascular origin" [1].

The word 'stroke" first time used as a lay term in 1599, attributing the sudden onset of symptoms to a 'stroke of God's hande' [2, 3]. But medical lexicon of the time not adopted this

word and term "apoplexy' used by the physicians, as a diagnosis that had been in existence since the Hippocratic writings [4].

According to some recent studies prevalence rate of stroke in India is about 471.58/100000 population [5]. Recent study identified that 7% of medical and 45% of neurological admissions were due to stroke with a fatality rate of 9% at hospital discharge and 20% at 28 days [6].

The calcium ion (Ca2+) is a ubiquitous intracellular messenger during and immediately after an ischemic period, and it influences the cascade of events that lead to subsequent neuronal injury [7].

Increase in the Ca2+ following an event of stroke, are result of excessively activation of extracellular glutamates and NMDARs. In the excitotoxic cascade, Calcium plays a critical role, because either removing Ca2+ from extracellular medium or preventing Ca2+ from entering mitochondria by uncouplers protects neurons against excitotoxic injury.

Materials and Methods

Patients with acute ischemic stroke and >18 years old who were willing to sign informed consent included in this study. Exclusion criteria were: Patients age <18 years, history of malignancy, prior history of transient ischemic attacks, history of recent surgery and trauma, history of other brain disorders, acute infectious disease, history of chronic kidney diseases and chronic liver diseases, history of steroid intake.

This study was done on 80 patients of acute ischemic stroke admitted in the department of medicine at S.R.G hospital of Jhalawar medical college, Jhalawar during the period of 1 year. All the patients presenting with new onset neurological deficit following ischemic stroke within 48 hours of onset and confirmed by CT scan of brain, admitted in the medical wards (general ward / medical ICU) were included in the study. Clinical history was taken in detail, complete general physical and systemic examination was done and lab investigations were analyzed. Adjusted serum calcium level was obtained within 72 hours from onset. The NIHSS SCORE (National institutes of health stroke scale) and MRS (Modified Rankin Score) was used to access the severity of each subject. The results were analyzed by using appropriate statistical test.

Observations and Results

Study was conducted in the Department of Medicine at SRG Hospital, Jhalawar. Total number of patients studied were 80. Out of these 48 were males and 32 were females. Patients were distributed based on their calcium level as with low calcium and normal calcium level. Out of 80 patients, 49 (61.25%) had low serum calcium while 31 (38.75%) participants had normal level of serum calcium. [Table 1]

Table 1: Distribution of patients according to serum calcium levels

Study Subject	Low Serum Calcium	Normal Serum Calcium	Total
Number of Patients	49	31	80
Percentage (%)	61.25%	38.75 %	100%

Table 2: Distribution of patients according to age

Age Groups	Low Serum Calcium	(%)	Normal Serum Calcium	(%)	P-Value
<40 years	1	2%	1	3.2%	
41-50 years	5	10.2%	4	12.9%	
51- 60 years	9	18.4%	8	25.6%	
61- 70 years	18	36.7%	9	29%	0.909
71- 80 years	14	28.6%	7	22.6%	
> 80 years	2	4.1%	2	6.5%	
Total	49	100%	31	100%	

Out of 80 cases most of the patients with low serum calcium were in age group of 61-70

years with 36.7% (18) followed by 71-80 years with 28.6% (14). [Table 2]

Table 3: Distribution according to gender

Gender	Low Serum Calcium	(%)	Normal Serum Calcium	(%)	P value
Male	25	51.1%	23	74.2%	
Female	24	48.9%	8	25.8%	0.039
Total	49	100%	31	100%	

According to table 3, out of 49 patients with low serum calcium, 51.1% (25) were male and 48.9% (24) were female while out of 31 patients with normal calcium, 74.2% (23) were male and 25.8% (8) were female.

Table 4: Distribution according to NIHSS-Score

NIHSS Score	Low serum level	Percentage (%)	Normal calcium level	Percentage (%)	P Value
Minor stroke (1-4)	0	0%	21	67.8%	
Moderate stroke (5-15)	11	22.4%	7	22.6%	
Moderate to severe stroke (16-20)	14	28.6%	3	9.6%	<0.0001*
Severe stroke (21-42)	24	49%	0	0%	
Total	49	100%	31	100%	

In our study, out of the 49 patients who presented with low levels of calcium 49% (24) reported with severe stroke with NIHSS score 21-42 followed by 28.6 (14) with moderate to severe type of stroke with NIHSS score 16-20, and 22.4% (11) had score in the range 5-15 that is moderate score. In this study NIHSS score was higher with low level of serum calcium. There was a significant correlation of NIHSS score with serum calcium level (p value <0.0001). [Table 4]

Table 5: Distribution according to MRS (Modified Rankin Score)

Modified Rankin Score	Low Calcium Level	(%)	Normal Calcium Level	(%)	P Value
Good Outcome	4	8.5%	21	67.7%	
Poor Outcome	45	91.5%	10	32.3%	<0.0103
Total	49	100%	31	100%	

Study showed that out of 49 patients with low serum calcium, 91.5% (45) had poor outcome and 8.5% (4) had good outcome, while among 31 patients with normal calcium, 67.7% (21) had good outcome and only 32.3% (10) had poor outcome. In our study MRS score was higher with low levels of serum calcium. There was a significant correlation of MRS score with serum calcium level (p value<0.0103). [Table 5]

Discussion
In this study mean age of study population was 66.17±11.04 years. Out of 80 cases most of the patients with low serum calcium were in age group of 61-70 years with 36.7% (18) followed by 71-80 years with 28.6% (14). Least number of patients were noted in the age group less than 40 years with 2% (1). [Table 2]
In this study out of 48 male patients, 52.1% (25) were with low serum calcium and 47.9% (23) were with normal serum calcium, while out of 32 female patients, 75% (24) were with low serum calcium and 25% (8) were with normal serum calcium. The increased percentage of female patients with low serum calcium group (75%) and normal serum calcium group (25%), was found to be statistically significant (p =0.039) [Table 3]

Distribution according to NIHSS Score

In our study out of the 49 participants who presented with low levels of calcium, majority of them 49% (24) reported with sever stroke with NIHSS score 21-42 followed by 28.6 (14) with moderate to severe type of stroke with NIHSS score 16-20, and 22.4% (11) had score in the range 5-15 that is moderate score. After statistical analysis, higher NIHSS score (Severe Stroke category (21-42) was observed in low blood calcium group (49%) compared to normal blood calcium group (0.00%). The increased difference in percentage of NIHSS score presentation between low calcium group and normal calcium group was found to be statistically significant (p<0.0001) [Table 4]

A study done by Ishfaq et al. [8] and Guven et al. also reported negative correlation between calcium level and NIHSS score [9].

Abha Gupta, Umesh Dubey et al. (2015) in their study "Correlation of serum calcium levels with severity and functional outcome in acute ischemic stroke patients" stated that patients with high calcium had significantly less severity of the stroke and during follow up after 7 days the prognosis is better in patients with high calcium compared to the lower levels of calcium, which was statistically significant (p-value 0.01) [10].

Muhammed Ishfaq, Fahim Ullah et al., in their study, found that lower serum calcium is associated with more severe clinical finding at the onset of stroke and proved significant (P-value 0.005) [11].

The study conducted by Guven H, Cililier AE et al. in their study, inferred that NIHSS scores were higher in the patients with decreased calcium levels with P-value <0.05 [9]. We also observed the similar results in our study.

Distribution according to MRS (Modified Rankin Score)

In our study, out of 49 patients with low serum calcium, 91.5% (45) had poor outcome and only 8.5% (4) had good outcome, while out of 31 patients with normal serum calcium 67.7% (21) had good outcome and only 32.3% (10) had poor outcome. After analysis, poorer outcome was observed in low blood calcium group (91.5%) compared to normal blood calcium group (32.3%). The increased difference in percentage of poor outcome as per MRS score between low calcium group and normal calcium group was found to be statistically significant (p =0.0103).

A study done by Ganti et al. (2013) in which routine laboratory parameters such as serum calcium was a predictor of early mortality after acute ischemic stroke [12].

Apple et al. (2007) found that lower total serum calcium level was associated with higher mortality rates and poor outcome after 1 month and 1 year [13].

Gupta et al. (2015) found an independent association between levels of calcium to the severity of the stroke and functional outcomes [14]. Our results are similar to these studies.

In our study NIHSS score was higher with low serum calcium level. Out of the 49 patients who had low levels of calcium, 49% (24) had severe stroke with NIHSS score 21-42. NIHSS score had significant correlation with serum calcium level (p- value<0.0001)

In our study among 49 patients with low serum calcium, 91.5% (45) had poor outcome. MRS score was higher with low serum calcium level. MRS score had significant association with serum calcium level (p- value=0.0103).

In this study we found that CT scan infarct size is larger with low serum calcium levels. In our study there was a significant correlation found between CT scan infarct size and serum calcium level (p-value<0.0001)

Kasundra et al. (2014) in their study found that higher calcium levels were associated with a smaller size infarction [15].

Conclusion

Based on these results, we can conclude that low adjusted calcium levels in patients with acute ischemic stroke is an independent risk factor and have poor outcome than patients with normal serum adjusted calcium level. Regular evaluations of adjusted serum calcium levels are important in patients with acute ischemic stroke in an attempt to predict the occurrence of

a bad outcome, so a more targeted management can be done to increase outcome of stroke.

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