

Association of Serum Calcium Level with other Risk Factors of Ischaemic stroke

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Abstract

Introduction

Calcium (Ca²⁺) plays an important role in the pathogenesis of ischemic cell damage. Intracellular Ca²⁺ accumulation leads to neuronal damage by triggering the cycle of cytotoxic events, however the relationship of serum Ca levels and the pathways involved in ischemic injury is unclear.

Aim of Study

To investigate the relationship of serum Ca²⁺ levels with severity of acute ischaemic stroke, serum calcium (Ca²⁺) levels were measured within the first 48 hours and were compared with the clinical severity of acute ischaemic stroke.

Material and Methods

A hospital based cross sectional study was performed among 100 patients of acute ischaemic stroke who fulfilled the inclusion criteria. The Study was done from July 2020 to August 2021 in SPRC & Neurology Hospital Dhaka, Bangladesh And BSMMU Hospital Dhaka, Bangladesh. After hospitalization presenting complaints, physical findings of the patients were recorded. Severity of stroke was measured by NIHSS scale. Serum calcium level of every patient was measured. Calcium level was divided into 3 groups by weighted average. Statistical analysis was carried out by a non-parametric Ruska Wallis test.

Results

Among the 100 patients 59% were male. Among all patients 57% of patients were found to be smokers (98% male, 2% female). Among all patients 63% patients were found hypertensive and 21% of all patients (24% male, 17% female) were diabetic. Mean cholesterol level was 257.98mg/dl with standard deviation 55.49 which is above the reference range suggesting hypercholesterolemia, Triglyceride was borderline and LDL cholesterol was slightly higher and HDL cholesterol was slightly lower. Calcium level was divided into 3 groups and NIHSS score was calculated for every patient in each group. The median NIHSS score for group1 (calcium level ≤ 8.8 mg/dl) was 9(2-20), for group 2 (calcium level 8.9-9.6 mg/dl) was 6 (1-17) and for group 3 (calcium level ≥ 9.7 mg/dl) was 4 (1-16).

Conclusion

Commonest risk factor of ischaemic stroke is hypertension. Other risk factors are smoking, diabetes mellitus and hyperlipidemia, cardiac disease. Higher serum calcium level is associated with less severity of ischaemic stroke.

Background

Stroke is the leading cause of disability worldwide, the second most common cause of dementia and the third leading cause of death[1]. It has enormous clinical, social, and economic implications and demands a significant effort from both basic scientists and clinicians in the quest for understanding the underlying pathogenic mechanisms and thereby adopting suitable preventive measures and successful therapies, beyond thrombolysis, which is but available to <5% of all patients[2].Owing to its high prevalence, high burden of illness and economic cost, well-defined modifiable risk factors, and effective prevention measures stroke is well suited for prevention. However, unfavorable trends in stroke risk factor profile; lack of awareness among public and medical fraternity; misapplication or underutilization of stroke preventative programs; and lack of emphasis on preventive training in medical school and postgraduate programs throughout

the world, have precipitated high stroke rates and culminated into widening the stroke prevention gap[3].Given the immense burden that ischemic stroke exerts, the need to develop more precise estimates of a stroke severity and survivor's prognosis remains an important goal. Calcium (Ca^{2+}) plays an important role in the pathogenesis of ischemic cell damage. Intracellular Calcium accumulation leads to neuronal damage by triggering the cycle of cytotoxic events. Very few attempts have been made to investigate the impact of serum Ca^{2+} level on clinical outcomes after ischemic stroke[4-5]. A recent study suggested that calcium levels obtained within 24 hours of stroke onset are associated with better hospital discharge clinical outcomes.[5] This study was conducted in all units of the Neurology department and SPRC and Neurology Hospital. Serum Calcium level was measured in all patients within 48 hours of onset of symptoms. Clinical severity was determined according to the NIHSS scale. Data was collected from patients and their attendants and statistical analysis was done by SPSS.

Objectives

General Objective

To measure the serum calcium level in acute ischaemic stroke.

Specific Objectives

To find out the association of serum calcium level with clinical severity.

To look for the common comorbidities associated with ischaemic stroke and their association with serum calcium.

Materials and Methods

A hospital based cross sectional study was performed among 100 patients of acute ischaemic stroke who fulfilled the inclusion criteria. The Study was done from July 2020 to August 2021 in SPRC & Neurology Hospital Dhaka, Bangladesh And BSMMU Hospital Dhaka, Bangladesh.. After hospitalization presenting complaints, physical findings of the patients were recorded. Severity of stroke was measured by the NIHSS scale. Serum calcium

level of every patient was measured. Calcium level was divided into 3 groups by weighted average. Statistical analysis was carried out by a non-parametric kruskal wallis test.

Inclusion Criteria

1. Patients aged >18years.
2. Ischaemic stroke confirmed by brain imaging within 48 hours of onset of Symptoms.

Exclusion Criteria

1. Patient who presented 48 hours after onset of symptoms.
2. Patients who can't give the history properly or no attendant available to give history.
3. Patients who failed to complete the investigations required for the study.
4. Known patient with hypercalcemia.
5. Patients who will refuse to give informed consent.
6. Patients diagnosed with hemorrhagic stroke.
7. Female pregnant patient.

Data Collection Procedure

Patients were selected according to inclusion and exclusion criteria. Detailed history was taken from patients or their attendants. With proper consent clinical examination was done and clinical severity was measured according to NIHSS scale. After that blood was collected with all the precaution for measurement of serum calcium level. All the data were recorded in the data collection sheet.

Data Processing and Analysis

All the data were checked after collection. Then data entered into the computer, with the help of SPSS 17 for Windows 7 program version. An analysis plan was developed keeping in view the objectives of the study. Frequency distribution and normal distribution of all continuous variables was calculated.

Procedure of Blood Drawing

1. The patient was lying down. Arm was extended.
2. The median cubital vein of the stronger arm was generally the vein of choice, although other veins were used when needed.
3. Tourniquet was avoided
4. The patient was advised to make a fist without pumping the hand.
5. Venipuncture site was selected and cleansed with antiseptic in a circular fashion, beginning at the site and working outward and allowed to air dry.
6. Needle was inserted swiftly, but gently through the skin and into the lumen of the vein.
7. Using the plunger 5 mL of whole blood was withdrawn.
8. Blood is then transferred to the appropriate tube or vial for the test.
9. Needle from the patient's arm was removed using a swift backward motion.
10. Adequate pressure was applied to avoid formation of hematoma.
11. Specimens were promptly delivered to the laboratory or processing area.

Results

Among the 100 patients 59% were male. Among all patients 57% of patients were found to be smokers (98% male, 2% female). Among all patients 63% patients were found hypertensive and 21% of all patients (24% male, 17% female) were diabetic. Mean cholesterol level was 257.98mg/dl with standard deviation 55.49 which is above the reference range suggesting hypercholesterolemia, Triglyceride was borderline and LDL cholesterol was slightly higher and HDL cholesterol was slightly lower.

Figure 1 shows gender of patients, a total of 59% of the patients were Male and the rest 41% were female.

Figure 2 shows 63% patients were hypertensive (known and newly diagnosed).

Table 1 Showed the occupational status of the patients. Large numbers of respondents were businessmen (21%) followed by service holders (14%). A considerable portion of the respondents (13%) were retired from their jobs. Most of the female patients were housewives (39%).

Table 2 showing the association of smoking in ischaemic stroke, among 59 male patients 56 patients (95%) were smokers. But among 41 female patients only 1 patient (2.43%) was found to be a smoker which is 2.43% of total females. Overall 57% of patients were smokers.

Table 3 showing the results of Lipid profiles. It showed that the total cholesterol level was much higher than normal. It also showed that LDL cholesterol was high and Triglyceride was borderline.

Table 4 showed distribution of Diabetes Mellitus in the study population. About 24% of all male stroke patients were diabetic from DM whereas 17% of the female patients were diabetic.

Table 5 showing Relationship of serum calcium level with severity of acute ischaemic stroke as assessed by NIHSS score showed 31% patients with median score of 9 with calcium level below 8.8, 37% patients in 8.9-9.6 serum calcium level with median score of 6 and 32% patients having calcium level above 9.6 had median NIHSS score 4. Comparison was done between groups by non parametric method (kruskal wallis test). P value was below .05 which is statistically significant.

Table 6 showing association of serum calcium levels with common risk factors of stroke. In group I 18 patients were hypertensive, in group II and III it was 27 and 18 respectively. In case of Diabetes Melitus the results in group I, II&III were 6,10&5 respectively whereas in case of atrial fibrillation results were 5,9 and 6 in group I,II&III respectively. Results were compared by Pierson chi-square test and found to be insignificant in all cases.

Discussion

A study on 100 acute stroke patients was

undertaken to see the serum calcium level in acute ischaemic stroke and its association with clinical severity in medicine in the patient department of Dhaka Medical College Hospital from June 2013 to December 2013. 100 patients were enrolled in the study through a non probability sampling technique. Fifty nine percent of the patients were male and the rest were female. Table 1 showed mean age of the patients. The mean age of the patients was 62.3 years with a SD of 9.078 years. Patients from the age group 51-60 years formed the main bulk followed by 61-70 years group (36% and 33% respectively). These findings were consistent with the fact that the incidence of stroke increases rapidly with age.[6] In this study (table 2) it was found that 57% patients were smoker which is consistent with other study.[7] This study also shows that most of the smokers (95%) are male and small fraction (2.43%) which may be due to the fact that female population in our country smokes less or they hide their smoking history. Lipid profile done in this study showed that that the Cholesterol level was much higher than normal value, Triglyceride was borderline, LDL was higher and HDL was slightly below normal (Table 3). These findings are consistent with studies done elsewhere.[8] In this study 63% the patients were found to be hypertensive (known and newly diagnosed) which matches with study in other parts of the world[9] and in our country.[10] The study revealed that about 21% of all stroke patients (24% male, 17% female) were suffering from DM whereas (Table 4). This is consistent with the fact that between 15% and 33% of ischemic stroke patients have diabetes mellitus.[11] this is also consistent with other other studies done elsewhere[12,13]. Though there is not much study in our country, these findings are in line with a study in our country. [14] The primary goal of this study was to assess serum calcium with severity of acute ischaemic stroke. In this study the highest serum calcium was 10.4 and lowest was 8.1. Calcium levels were divided into three groups by using weighted average. Severity of ischaemic stroke was assessed clinically by NIHSS score (Table 5). The patients were divided into three groups according to serum total Ca levels. Patients with

Table 1. Occupational status of the patients.

Occupation	Frequency	Percent
Business	21	21
Service Holder	14	14
Retired/Aged person	13	13
Farmer	5	5
Daily worker	4	4
Teacher	2	2
Housewife	39	39
total	100	100

Table 2. Association of smoking with ischaemic stroke.

Smoking	Sex				Total	
	Male (59)		Female (41)			
	n	%	n	%	n	%
Positive	56	95%	1	2.43%	57	57%
Negative	3	5%	40	97.57%	43	43%
Total	59	100%	41	100%	100	100%

Table 3. Lipid profile of ischaemic stroke patient.

Serum Lipid Profile	N	Mean	SD
Total Cholesterol	100	257.98 mg/dl	55.491 mg/dl
TG	100	186.66 mg/dl	45.207 mg/dl
LDL	100	140.08 mg/dl	18.045 mg/dl
HDL	100	37.89 mg/dl	34.79 mg/dl

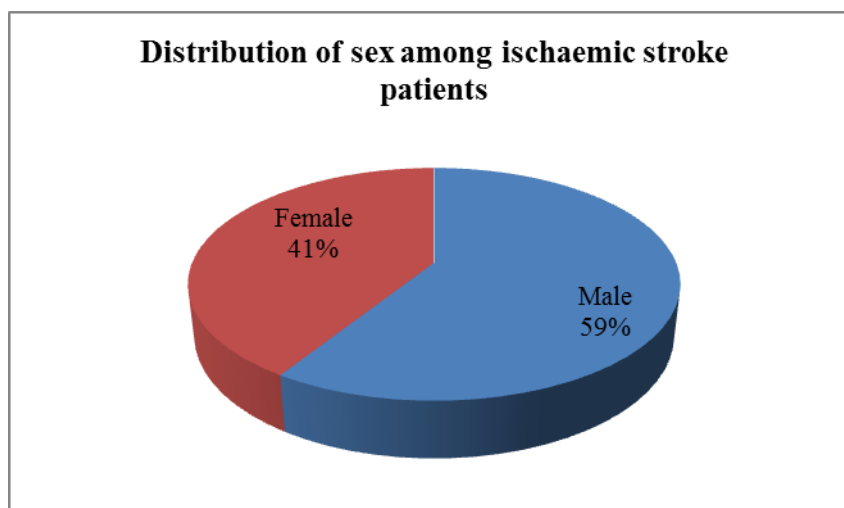


Figure 1. Distribution of sex among ischaemic stroke patients.

Table 4. Distribution of diabetes mellitus in the studied patients.

Diabetes Mellitus	Sex				Total	
	male		Female			
	n	%	n	%	n	%
Positive	14	23.73	7	17.07	21	21
Negative	45	76.27	34	82.93	79	79
Total	59	100	41	100	100	100

Table 5. Serum calcium in ischaemic stroke patients.

Group	n(100)	Serum Calcium	NIHSS score	Significance
I	31	≤8.8	9(2-20)	<.05
II	37	8.9-9.6	6(1-17)	
III	32	≥9.7	4(1-16)	

Table 6. Association of serum calcium level with other risk factors of ischaemic stroke

	Group I (n=31) Ca ≤8.8	GroupII (n=37) Ca 8.9-9.6	Group III (n=32) Ca ≥9.6	Significance
Hypertension	18 (58%)	27 (73%)	18 (56%)	>.05
Diabetes Melitus	6 (19.35%)	10 (27.2%)	5 (15.6%)	>.05
Atrial fibrillation	5 (16.1%)	9 (24.32%)	6 (18.75%)	>.05

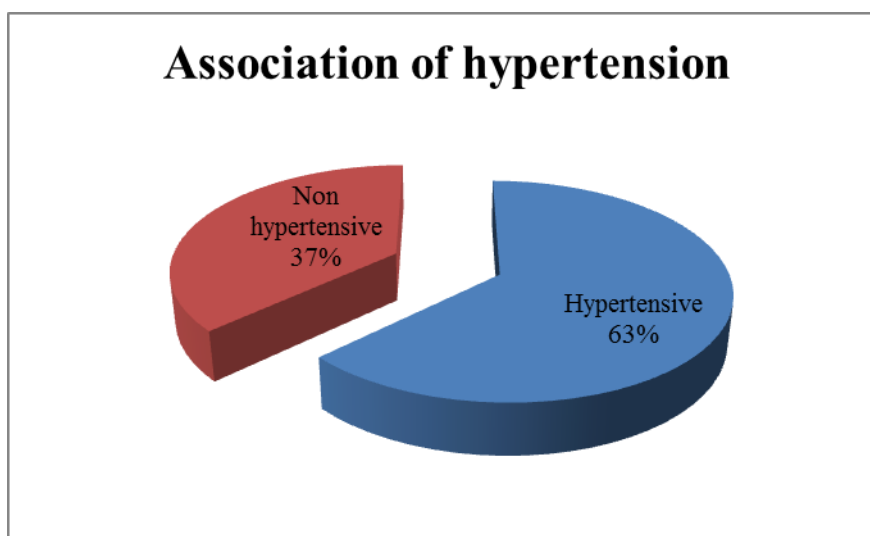


Figure 2. Association of hypertension in the study population.

Ca \leq 8.8mg/dl were included in group I, Ca levels between 8.9 and 9.6 mg/dl were included in group II, and Ca \geq 9.7 mg/dl were included in group III. NIHSS scores on admission were higher in group I (median 9) than group II (median 6) and group III (median 4) ($p < 0.05$), and they were found to be higher in group 2 than group 3 ($p < 0.05$). These results are consistent with a similar study done by Gueven et al. in 2011. This study results are also found to be consistent with a study done by Brian H. Buck, MD et al. in 2007. Though there are several biomarkers for acute ischaemic stroke there are only few markers for severity of stroke like CRP[15], early CT scan changes, serum S-100. The association of serum calcium and severity of acute ischaemic stroke could not be analyzed along with these factors. Common risk factors found to be associated with ischaemic stroke were smoking, diabetes mellitus, hypertension, hyperlipidemia and atrial fibrillation. There were several studies regarding the association of serum calcium level with hypertension. These studies yield different results. In this study (Table 6) in group I 18 patients were hypertensive, in group II and III it was 27 and 18 respectively. These results are neither significant nor consistent with other studies done previously. In case of Diabetes Mellitus the results in group I,II&III were 6,10&5 respectively whereas in case of atrial fibrillation results were 5,9 and 6 in group I,II&III respectively. These results were not also significant.

Conclusion

In this study 100 patients with acute ischaemic stroke were included. Majority patients were aged and male. Hypertension was found to be the commonest comorbidities. A significant number of patients were diabetic and hyperlipidemic. It was found that higher serum calcium level was related with less clinical severity. But there was no relationship of serum calcium level with other common risk factors of ischaemic stroke.

Limitation of the Study

1. Small sample size
2. This study did not use univariate or multivariate analysis. So it was not able to prove any association

between serum calcium level and severity of ischaemic stroke.

Recommendations

Calcium may be used as a prognosticator of ischaemic stroke and potential therapeutic agent to reduce severity of ischaemic stroke. But exact recommendations about these facts can be given only after large scale study and trials. Multicentre trials with large samples can be done in future to have a consolidated result about these findings.

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