Original Article

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Correlation of Serum Calcium with Blood Pressure and BMI among Ischemic Stroke Patients in Bangladesh

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ABSTRACT

Background: Ischemic stroke more commonly occurs in hypocalcemic patients and presented with more severe clinical symptoms. The purpose of the present study was to observe the correlation of serum calcium with blood pressure and BMI in stroke patients of Bangladesh.

Materials and methods: This case control study was carried out in the Department of Biochemistry at Dhaka Medical College, Dhaka, Bangladesh from January 2014 to December 2014 for a period of one (01) year. The patients presented with acute ischemic stroke, age ranges from 18 to 65 years of both sexes were taken as case group. Age and sex matched healthy individuals were selected as control group. The information regarding age, serum calcium level, history of hypertension, the height and weight of both cases and controls were taken to calculate BMI.

Results: A total number of 100 study subjects were taken of which 50 subjects presented with acute ischemic stroke were considered as case and the rest 50 healthy subjects were taken as control. Serum calcium has maintained significant negative correlation with DBP (r= - 0.335, p= 0.017) and BMI (r= - 0.426, p= 0.002) but insignificant negative correlation was maintained between serum calcium and SBP (r= - 0.194, p= 0.176).

Conclusion: Findings of this study concludes that hypocalcemia is found to be negatively correlated with blood pressure and BMI among ischemic stroke patients of Bangladesh.

KEY WORDS
Blood pressure; Hypocalcemia; Ischemic Stroke.

INTRODUCTION

Acute stroke is characterized by the rapid appearance (Usually over minutes) of a focal deficit of brain function most commonly a hemiplegia with or without signs of focal higher cerebral dysfunction (Such as aphasia) hemisensory loss, visual field defect or brain stem deficit.[1] Worldwide acute ischemic stroke is a major public health problem and is a leading cause of mortality and morbidity particularly in developing countries.[2] Between 1990 and 2010 the number of strokes decrease by approximately 10% in the developed world and increased by 10% in the developing world.[2] Stroke predominates in the middle and late years of life and it is ranked after heart disease and before cancer.[3, 4] Stoke was the second most frequent cause of death worldwide in 2011.[2]

In the United States, about 15% of strokes are hemorrhagic and 85% ischemic.[5] Each year, approximately 795,000 people in the US experience new (610,000 people) or recurrent (185,000 people) stroke. The stroke related annual cost is over $72 billion.[6]

According to the World Health Organization (WHO) 15 million people suffer from stroke worldwide each year. Of these, 5 million die and another 5 million are left permanently disabled.[7] In stroke survivors from the Framingham Heart Study, 31% needed help caring for themselves, 20% needed help when walking, 71% had impaired vocational capacity in long term follow up.[8] The incidence and mortality rates of stroke are still unknown in our country. But in a study, on Bangladeshi stroke patients revealed that 57.84% are ischemic and 42.16% are hemorrhagic.[9]

Generally, it is recognized that stroke is a multifactorial condition. A number of risk factors that have been shown to be associated with stroke are age, high blood pressure, diabetes mellitus, hypercholesterolemia, previous history of stroke or TIA, obesity and dietary factors, atrial fibrillation and cigarette smoking.[10] Risk

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of stroke increases with age, especially, in patients older than 64 years.[11]

Calcium plays an important role in the cellular and molecular pathways of ischemic neuronal death.[12] Intracellular Calcium accumulations lead to neuronal damage by triggering the cycle of cytotoxic events.[13] Normally Calcium homeostasis is maintained by four mechanisms:

i) Active extrusion of calcium from cell by ATP-driven membrane pump
ii) Exchange of calcium for sodium at the cell membrane by cell membrane's Na^+-K^+ pump
iii) Sequestration of intracellular calcium in the endoplasmic reticulum by an ATP-driven process
iv) Accumulation of intracellular calcium by oxidation-dependent calcium sequestration inside the mitochondria.[14]

During ischemia loss of cellular Na^+-K^+ gradient virtually eliminates 3 of the 4 mechanisms of cellular calcium homeostasis. Mitochondrial sequestration, the remaining mechanism, causes overloading of mitochondria with calcium and diminished capacity for oxidative phosphorylation. Elevated intracellular Calcium activates membrane phospholipases and protein kinases. Membrane degradation by phospholipases almost certainly damages membrane integrity, further reducing the efficiency of calcium pumping and leading to further calcium overload and a failure to regulate intracellular calcium levels following ischemic episode.[14]

Plasma calcium is a predictor of CVD.[15] Hypocalcemia may be associated with more severe clinical symptoms on admission in acute stroke patient.[13] Highest Calcium lowers 50% to 70% risk of poor functional outcome following stroke and calcium administration can reduce both infract size and stroke related mortality.[16] Another study suggest that high dietary intake of Calcium has been associated with reduced risk of stroke.[17]

Hypertension is one of the most important modifiable risk factors for ischemic stroke. Hypertension indicates a risk of stroke is approximately 4, when systolic blood pressure ≥160 mm of Hg and/ or diastolic blood pressure ≥95 mm of Hg.[18] Uncontrolled high blood pressure increase a person's stroke risk by four to six times.[18] Gradually hypertension leads to atherosclerosis and hardening of large arteries. This, in turn, can lead to blockage of small blood vessels in the brain. High blood pressure can also lead to weakening of blood vessels in the brain, causing them to balloon and burst. So that the risk of stroke is directly related to the increased blood pressure.[19]

However, most of these data are from developed countries. Very few data are available in this country. Therefore, the purpose of the present study was to assess the correlation of hypocalcemia with hypertension and BMI among ischemic stroke patients of this country.

MATERIALS AND METHODS

This case control study was carried out in the Department of Biochemistry at Dhaka Medical College, Dhaka, Bangladesh from January 2014 to December 2014 for a period of one (01) year. Ethical clearance from the concerned departments and authorities was taken. The ischemic stroke patients were considered as case and the age and sex matched healthy volunteers were taken as control. Cases were the patients who clinically suffered from ischemic stroke confirmed by Computerized Tomography (CT) scan of brain attending in the Medicine unit of Dhaka Medical College Hospital (DMCH) during the study period. A preformed data collection sheet was used to collect information regarding age, family H/O stroke, H/O HTN and DM, relevant drug history, the height and weight of individuals to calculate BMI. For the measurement of serum calcium level, 5ml of fasting venous blood sample were collected after all aseptic precautions by disposable plastic syringe without using any tourniquet from all the study subjects. Then mean values of the quantitative variables were compared between case and control by unpaired student's t-test. Results were analyzed statistically in SPSS version 20 for windows expressed as mean±SD. p value < 0.05 was considered as significant.

RESULTS

A total number of 100 subjects were recruited for this study of which 50 were acute ischemic stroke patients were considered as cases and the rest 50 were taken as healthy controls.

In this study, the mean±SD of age of case and control were 56.54±12.18 and 53.34±7.98 respectively. There was no statistically significant difference of mean age between groups (p= 0.124). Table I also showed that the study subjects were sex matched, the difference between case and control was not statistically significant (p= 0.414).

Table I Demographic characteristics of the subjects

Variables	Case (n=50) (mean+SD)	Control (n=50) (mean+SD)	p value
Age (years)	56.54±12.18	53.34±7.98	0.124*
Sex			
• Male	32 (64%)	28 (56%)	0.414**
• Female	18 (36%)	22 (44%)	

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* Student's t test was done to measure the level of significance, Significance = ($p<0.05$).

** Chi square test was done to measure the level of significance, Significance = ($p<0.05$).

Mean± SD of serum calcium of the study subjects were 1.99±0.25 mmol/L and 2.19±0.13 mmol/L in cases and controls respectively in Table II and it was significantly lower in cases (p=0.001).

Table II Mean serum calcium of the study subjects

Serum calcium (mmol/L)	Case (Mean ± SD)	Control (Mean ± SD)	p value
	1.99 ± 0.25	2.19 ± 0.13	0.001

Statistical analysis-unpaired student's t-test, Level of significance -$p<0.05$.

Table III shows mean±SD of SBP was significantly higher in cases when compared with that of controls (p=0.001) which were 139.20±29.12 mm of Hg and 117.40±12.08mm of Hg respectively. Mean±SD of DBP was also significantly higher in cases than that of controls (p=0.001) which were 86.20±17.59 mm of Hg and 77.20±8.33 mm of Hg respectively. Table- III also showed that mean BMI was significantly higher in cases when compared with that of controls (p=0.002) which were 27.25±3.25 kg/m2 and 25.38±2.57 kg/m2 respectively.

Table III Mean blood pressure and BMI of the subjects

Blood pressure (mm of Hg) and BMI(kg/m2)	Case (n=50) (Mean ± SD)	Control (n=50) (Mean ± SD)	p value
SBP	139.20 ± 29.12	117.40 ± 12.08	0.001
DBP	86.20 ± 17.59	77.20 ± 8.33	0.001
BMI	27.25 ± 3.25	25.38 ± 2.57	0.002

Unpaired student's t-test was done to measure the level of significance, Significance = ($p<0.05$).

Table IV shows the correlation between serum calcium with blood pressure and BMI among cases. It was found that there is a significant negative correlation between serum calcium and DBP (r= -0.335, p=0.017) and insignificant negative correlation between serum calcium and SBP (r= -0.194, p= 0.176) in cases. This table also showed significant negative correlation between serum calcium and BMI (r= -0.426, p=0.002) in cases.

Table IV Correlation between serum calcium with blood pressure and BMI

	Case	
Parameters	r value	p value
SBP	-0.194	0.176
DBP	-0.335	0.017
BMI	-0.426	0.002

Statistical analysis – Pearson's correlation test, Level of significance-$p<0.05$.

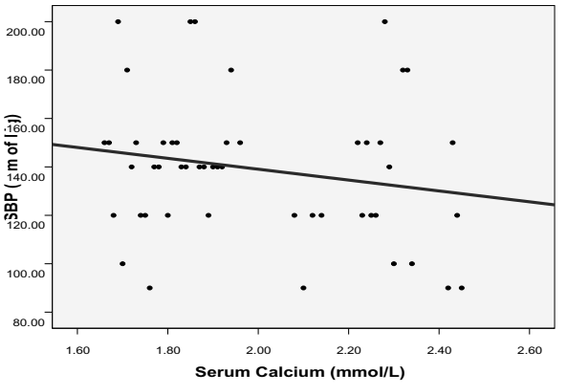

Figure 1 Correlation between serum calcium level and SBP in cases

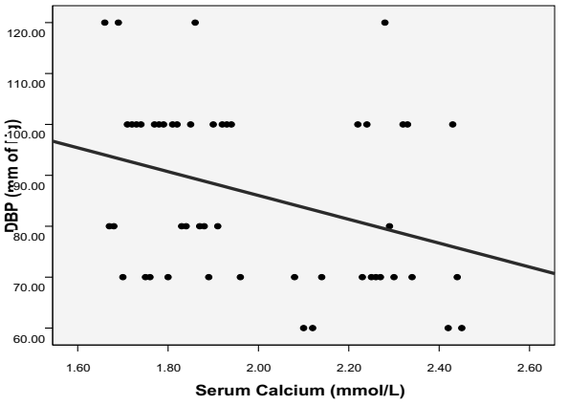

Figure 2 Correlation between serum calcium level and DBP in cases

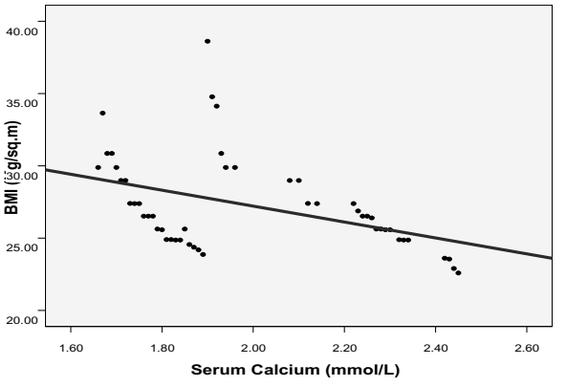

Figure 3 Correlation between serum calcium level and BMI in cases

DISCUSSION

In ischemic stroke, excessive intracellular serum calcium accumulation triggers a cascade of cytotoxic events that lead to the activation of enzymes involved in cell death.[1] In preclinical models, low extracellular serum calcium levels paradoxically enhance this

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overloading of intracellular serum calcium and potentiate cell death. Whether serum calcium levels affect serum calcium level-dependent excitotoxic pathways in the setting of human acute cerebral ischemia remains unclear, but mounting data indicate that higher serum calcium levels at admission are associated with better clinical outcomes after ischemic stroke.[20]

Ischemic neuronal death engages several terminal pathways including the loss of ionic homeostasis. Cell calcium metabolism during and immediately after a transient period of ischemia influences the cascade of events that lead to subsequent neuronal injury.[21] Events that occur following stroke include accumulation of excitatory amino acids, alterations in the genomic response, mitochondrial injury and secondary injury, often in the setting of reperfusion. It is well recognized that a significant portion of ischemia-induced neuronal damage is mediated by excessive accumulation of excitatory amino acids, leading to toxic increase in intracellular calcium and other ions.[22] This increase in intracellular calcium activates multiple signaling pathways, which ultimately leads to cellular death. Soon after reduction or termination of cerebral blood flow, energy-dependent cellular pumps fail due to a fall in glucose dependent ATP generation, resulting in the flow of numerous ionic species down their concentration gradient into the cell. This results in cellular swelling through osmosis and cellular depolarization. Calcium ions enter the cell through voltage-dependent and ligand gated ion channels, resulting in activation of a number of proteases, kinases, lipases and endonucleases, triggering of the intrinsic apoptotic pathway and thus ending in cellular death.[23, 24]

In the present case control study correlation of hypocalcemia with hypertension and BMI among ischemic stroke patients of Bangladesh has been studied at a tertiary care hospital. In this study, the mean age ±SD of case and control were 56.54±12.18 years and 53.34±7.98 years respectively. There was no significant (p= 0.124) difference between groups. Another study done by Abu-Odah et al in European Gaza Hospital, revealed that the mean age of cases were 54.74 years and that of controls were 53.22 years. Statistically no significant (p= 0.279) difference was found between case and control groups.[25] Among the study subjects there were, 32 male and 18 female in cases and 28 male and 22 female in controls. Study subjects were sex matched, the difference between case and control was not statistically significant (p>0.05). Similar result was found by Sorganvi et al.[26]

Present study showed that mean±SD of serum calcium was 1.99±0.25 and 2.19±0.13 mmol/L in acute ischemic stroke cases and healthy controls respectively. Serum calcium level was significantly lower in cases in comparison to controls. Chaudhuri et al was also revealed lowered serum calcium level in cases.[27]

The result of the current study showed that mean±SD of BMI was 27.27±3.25 and 25.38±2.57kg/m^2 in cases and controls respectively which was significantly higher in cases than that of controls (p= 0.002). Farhangi et al observed significantly higher (p< 0.001) BMI in cases compared to controls which were respectively 32.95±3.35 and 23.40±4.12 kg/m.[28]

Hypertension was found as a strong risk factor for ischemic stroke. Data from population studies indicate that an average reduction in blood pressure of just 9/5 mm of Hg results in a 34% reduction and 19/10 mm of Hg results in a 56% lower incidence of stroke.[29] This study showed that SBP±SD in case and control was 139.20± 29.12 and 117.40±12.08 mm of Hg respectively and the DBP±SD in case and control was 86.20±17.59 mm of Hg and 77.20±8.33 mm of Hg respectively. Both the SBP and DBP were significantly higher (0.001) in cases than that of controls. Study done by Abu-Odah et al found that both systolic blood pressure (159.92 mm Hg vs. 129.13mm Hg) and diastolic blood pressure (90.39 mm Hg vs. 77.01 mm Hg) was significantly higher (0.000) among cases compared to controls.[25]

In the current study among cases of stroke 40% patients had SBP≥140 mm of Hg compared to 4% among controls, (OR= 16.00, 95% C.I. 3.48 t0 73.40) and 46% patients of case group had DBP≥90 mm of Hg compared to 16% among controls (OR= 4.47, 95% C.I. 1.74 to 11.43). Statistically significant difference was observed between two groups regarding the presence of systolic and diastolic hypertension (p=0.001). Abu-Odah et al found similar result that 79% case and 31% control had SBP≥140mm of Hg and 59% of cases and 22% of controls had DBP≥90 mm of Hg.[25]

This present study found that serum calcium maintained significant (p<0.05) negative correlation with DBP (r= -0.335) & BMI (r= -0.426). This study result consistent with the other studies done by Kesteloot and Joossens; Alharbi et al.[30,31] In this study, serum calcium also maintained insignificant (p>0.05) negative correlation with SBP (r= -0.194) in case. But in the study Lin et al found that serum calcium showed significant inverse association with SBP.[32]

LIMITATION

The study was conducted in a selected Medical College, so the study population might not represent the whole community.

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CONCLUSION

In conclusion, hypocalcemia is found to be negatively correlated with blood pressure and BMI among Bangladeshi stroke patients. Hypertension, more specifically both systolic and diastolic hypertension and increased ranges of BMI are strongly correlated with increased risk of acute ischemic stroke.

RECOMMENDATION

General community should be made aware about these risk factors of stroke and therefore, this study suggests that hypertensive subjects should keep a keen eye on blood pressure monitoring, regular assessment of serum calcium level and if needed life style modification and weight reduction could be done which may reduce the incidence and morbidity of ischemic stroke.

DISCLOSURE

All the authors declared no competing interest.

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