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Correlation of serum calcium with blood pressure and Body Mass Index (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.
Objective: We sought to observe the correlation of serum calcium with blood pressure and BMI among stroke patients in Bangladesh.
Methods: We performed a case-control study using the Department of Biochemistry at Dhaka Medical College, Dhaka, Bangladesh from January 2014 to December 2014. The case were defined as patients diagnose with an acute ischemic stroke, and controls were defined as healthy subjects. In this identified population, 15 cases were matched on age and sex to 50 control subjects. The information regarding age, serum calcium level, height and weight of both cases and controls were taken to calculate BMI. Systolic and diastolic blood pressure (SBP and DBP) from the subject are taken to investigate the history of hypertension.
Result: Serum calcium has statistically significant with a negative correlation with DBP (r =-0.335, p=0.017) and BMI (r =-0.426, p=0.002). A negative correlation between serum calcium and SBP also can be observed (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 in Dhaka, Bangladesh.

Latar Belakang: *Stroke iskemik seringkali terjadi pada pasien dengan hipoglikemik dengan manifestasi klinis yang berat.*
Tujuan: *Untuk mengobservasi korelasi kalsium serum terhadap tekanan daranh dan indeks masa tubuh (IMT) pada pasien stroke di Bangladesh.*
Metode: *Penelitian ini adalah studi case-control yang dilakukan di Departemen Biokimia, Ddhaka Medical College, Dhaka, Bangladesh mulai January 2014 hingga Desember 2014. Kelompok kasus adalah pasien stroke iskemik akut. Kelompok kontrol adalah orang sehat dengan usia dan jenis kelamin yang sama dengan kelompok kasus. Informasi yang dikumpulkan adalah usia, kadar kalsium serum, berat badan dan tinggi badan, serta tekanan darah sistolik dan diastolik.*
Hasil: *Kalsium serum memiliki korelasi negatif yang signifikans terhadap tekanan darah diastolik (r =-0.335, p=0.017), IMT (r =-0.426, p=0.002), dan tekanan darah sistolik (r= - 0.194, p= 0.176).*
Kesimpulan: *Kadar kalsium darah berkorelasi negatif terhadap tekanan tekanan darah dan IMT pada pasien stroke iskemik di Dhaka, Bangladesh.*

INTRODUCTION

Acute stroke is characterized by the rapid appearance (usually over minutes) of a focal deficit of brain function most commonly 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. Between 1990 and 2010 the number of strokes decreased 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 (Morris and Schroeder, 2001).[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 dies 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. Elyas et al. (2012) reported,84% stroke patients are ischemic in Bangladesh and 42.16% are hemorrhagic.[9]

Generally, it is recognized that a stroke is a multifactorial condition. Risk factors that are 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 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. The mechanisms are an active extrusion of calcium from the cell by ATP-driven membrane pump, exchange of calcium for sodium at the cell membrane by cell membrane's Na^+K^+ pump, sequestration of intracellular calcium in the endoplasmic reticulum by an ATP-driven process and also the 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 and the remaining mechanism cause 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 cardiovascular disease (CVD).[15] Hypocalcemia may be associated with more severe clinical symptoms on admission in an acute stroke patient.[13] Highest calcium lowers 50% to 70% risk of poor functional outcome following stroke. Calcium administration also can reduce both infract size and stroke related mortality.[16] Another study suggests 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, when systolic blood pressure ≥ 160 mmHg and/ or diastolic blood pressure ≥ 95 mmHg the risk factor of stroke approximately.[18] Uncontrolled high blood pressure increase the risk for stroke incidence by four to six times.[18] The risk of stroke

is directly related to the increased blood pressure. 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 the weakening of blood vessels in the brain, causing them to balloon and burst.[19]

Most of the data about stroke and the risk factor are from the developed countries. Very few data are available in this country, especially about the hypocalsemia and stroke. Therefore, the purpose of the present study was to assess the correlation of hypocalcemia with anotherrisk factor of stroke (hypertension and BMI) among ischemic stroke patients.

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. 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 defined as the patients who clinically suffered from ischemic stroke confirmed by computerized tomography (CT) scan of brain attending in the Medicine unit of DMCH during the study period.

A preformed data collection sheet was used to collect information regarding age, family history of stroke, hypertension, diabetes mellitus, relevant drug history and the height and weight of individuals (for measuring the BMI). For the measurement of serum calcium level, 5 ml 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 (age, serum calcium, blood pressure and BMI were compared between case and control by unpaired student's t-test. Sex of the demographic characteristics from the subject was compared between case and control by using the Chi-square test. The correlation between serum calcium, blood pressure and BMI were analyzed by using Pearson's correlation test. P-value < 0.05 was considered as significant. The data were expressed as mean ± SD

RESULTS

RA total number of 100 subjects were recruited for this study. fifty subjects with an acute ischemic stroke (case groups) and 50 subjects were taken as healthy controls.

Table1. Demographic characteristics of the subjects

Variables	Case (mean+SD)	Control (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%)	

In this study, the mean 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 1 showed that the study subjects were sex matched and the difference between case and control was not statistically significant (p= 0.414).

Table 2. Mean serum calcium of the study subjects

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

*p<0.05 The serum calcium is lower in case groups compared with control groups. Mean differences of both groups are statistically significant (Table 2, p<0.05).

Table 3. Mean blood pressure and BMI of the subjects

Blood pressure (mmHg) and BMI (kg/m2)	Case (Mean ± SD)	Control (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*

Table 3 shows that SBP, DBP and BMI in case groups are higher compared with the control groups. Mean of SBP, DBP, and BMI was significantly significant (p<0.05).

Table 4. Correlation between serum calcium with blood pressure and BMI

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

Table 4 shows that 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.

DISCUSSIONS

Phytochemical screening of secondary in this case-control study, correlation of hypocalcemia with hypertension and BMI among ischemic stroke patients of Bangladesh has been studied at a tertiary care hospital.

Present study showed that mean of serum calcium was significantly lower in acute ischemic stroke cases compare with healthy control groups. This study shows the same result with Chaudhuri et al (2014).[20]

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 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 the data indicate that a higher serum calcium levels at admission are associated with better clinical outcomes after ischemic stroke.[21]

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.[22] 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 a toxic increase in intracellular calcium and other ions.[23] This increase in intracellular calcium activates multiple signalling 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 proteases, kinases, lipases and endonucleases, triggering the intrinsic apoptotic pathway and thus ending in cellular death.[24,25]

This study also shows that the BMI in acute ischemic stroke groups are higher compared with control groups. This BMI result are similar with shows the same with Farhangi et al (2011).[26] 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.[27]

This study also showed that both the SBP and DBP were significantly higher (0.001) in the acute ischemic stroke groups than that of controls. A study done by Abu-Odah et al (2014) found also that systolic blood pressure and diastolic blood pressure was significantly higher (0.000) among cases compared to controls.[28]

In the current study among cases of stroke, 40% of patients had SBP≥140 mmHg compared to 4% among controls (OR= 16.00, 95% C.I. 3.48 t0 73.40). In the case group, 46% patients had DBP≥90 mmHg 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 a 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.[28]

This present study found that serum calcium maintained significant ($p<0.05$) and have a negative correlation with DBP (r= -0.335) & BMI (r= -0.426). This result consistent with the other studies done by Kesteloot and Joossens; Alharbi et al.[29,30] In this study, serum calcium also maintained insignificant ($p>0.05$) negative correlation with SBP (r= -0.194) in case. But in the study of Lin et al found that serum calcium showed a significant inverse association with SBP.[31]

CONCLUSION

In conclusion, hypocalcemia is found to be negatively correlated with blood pressure and BMI among Bangladeshi stroke patients.

CONFLICT OF INTEREST

No conflict of interest

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