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Examining the Correlation between Serum Calcium Levels in Individuals Experiencing Acute Myocardial Infarction and those in a Healthy Control Group

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Abstract:
Background: *Acute myocardial infarction (AMI) is a major cause of illness and death globally, especially in East Asian countries. AMI is a life-threatening condition, with its incidence influenced by risk factors for atherosclerosis, including age, sex, hypertension, hyperlipidemia, obesity, diabetes mellitus, and smoking. In addition to measuring blood pressure, height, and weight, BMI was also calculated. Elevated serum calcium levels have been identified as another risk factor associated with AMI.* ***Objective:*** *The aim of the study was to examine the relationship between serum calcium concentrations and acute myocardial infarction in patients.* ***Methods:*** *This case-control study was carried out in the Department of Cardiology in Mymensingh Medical College Hospital, from July 2017 to June 2018. The study included Hundred patients diagnosed with acute myocardial infarction (AMI) and Hundred age- and sex-matched healthy controls, selected purposively based on the selection criteria. Blood pressure, height, and weight were recorded, and body mass index (BMI) was calculated. Biochemical parameters, including serum calcium, blood glucose, and lipid profile, were assessed using fasting blood samples. All results were presented as mean ± SD, with a P value of <0.05 considered statistically significant. Statistical analyses of the results were be obtained by using window-based Microsoft Excel and Statistical Packages for Social Sciences (SPSS-24).* ***Results****: The present study found that serum calcium levels were significantly higher (P < 0.05) in the case group (2.61±0.15 mmol/L) compared to the control group (2.13±0.15 mmol/L). Additionally, there was a significant difference in systolic blood pressure (SBP) between the case group (137.8±14.92 mmHg) and the control group (124.7±11.35 mmHg). The study also revealed that the mean BMI was significantly higher in the case group (27.34±3.37 kg/m²) compared to the control group (25.30±3.42 kg/m²). Moreover, a positive correlation was observed between serum calcium and SBP (r=0.083), diastolic blood pressure (DBP) (r=0.207), LDL-C (r=0.204), BMI (r=0.021), and total cholesterol (TC) (r=0.391) in the case group. However, a negative correlation was found between serum calcium and HDL-C (r=-0.021) in the case group.* ***Conclusion:*** *This study suggests that elevated serum calcium levels are associated with acute myocardial infarction (AMI). Regular monitoring of serum calcium, along with other atherogenic biochemical markers, may help in early detection and prevention of AMI.*

Keywords: *Correlation, serum calcium, acute myocardial infarction and healthy control.*

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I. Introduction

Cardiovascular mortality has significantly decreased in developed countries over the past four decades due to improved risk factor management and advancements in treatment. However, despite substantial progress in managing cardiovascular disease with cardiovascular disease remaining a leading cause of death. [1, 2] First incident acute myocardial infarction (AMI), a severe form of cardiovascular disease, is defined as the first occurrence of AMI in a patient. Patients experiencing a first incident AMI among those with coronary artery disease (CAD) tend to have more cardiovascular risk factors. [3, 4] Effective risk factor management has been fundamental in preventing and treating first incident AMI.

Calcium, one of the most vital cations, plays a crucial role in various biological processes, including cardiac contraction, blood pressure regulation, and blood coagulation. Maintaining a proper balance of calcium flux is especially important for the myocardium. Hypocalcemia is a common electrolyte disturbance in critically ill patients and has been linked to poor outcomes.1 Additionally, adequate calcium intake has been shown to reduce the incidence of myocardial infarction. [5] Conversely, elevated serum calcium levels significantly increase the risk of coronary artery disease (CAD), particularly acute myocardial infarction (AMI). [6] However, calcium intake within the tolerable upper limits of 2000 to 2500 mg/day has not been associated with an increased risk of cardiovascular disease in generally healthy adults. [7]

Recent research has increasingly indicated that serum calcium levels are linked to cardiovascular disease. [8] Despite this, total serum calcium seems to serve as a marker for cardiovascular diseases, including acute myocardial infarction. This study conducted a case-control analysis to investigate the relationship between serum calcium concentrations in patients with acute myocardial infarction and healthy individuals.

II. Methodology

This case control study caried out Department of Cardiology in Mymensingh Medical College Hospital, Mymensingh, Bangladesh from July 2017 to June 2018. Total 200 diagnosed were taken in this study. Data was collected and recorded in a predesigned data collection sheet including particulars of the subjects, history and relevant investigations. A complete physical and relevant clinical examination was performed. Fasting blood sample was collected to estimate lipid profile and calcium. Height and weight were measured to calculate BMI. Blood pressure was measured on the right arm with a standard sphygmomanometer. Hypertension was defined as a DBP ≥90 mm of Hg and /or SBP ≥140 mm of Hg. Diabetes mellitus was defined as fasting blood glucose ≥7 mmole/L. Calcium level above2.60 mmol/L was considered as high. Hyperlipidemia was defined as total cholesterol ≥200 mg/dl, triglyceride ≥150 mg/dl, LDL-c ≥100mg/dl, or HDL-c<40mg/dl for men and <50 mg/dl for women. The parameter of lipid profile may deviate from normal individually or in combination. By all aseptic precaution 5 ml venous blood from each study subject was drawn from antecubital vein after overnight fasting (12 hours) with a disposable plastic syringe and immediately transferred to a dry clean test tube which was allowed to clot. Then serum was separated after centrifuging at 3000 rpm for 10 minute and was collected in Eppendorf tube and labeled appropriately. Preservation was done at -180C.All the biochemical test was performed in the Department of Cardiology in Mymensingh Medical College Hospital, Mymensingh, Bangladesh. After meticulous checking and re-checking data were compiled and expressed as mean ± SD (Standard Deviation). All data were analyzed using statistical package for social science (SPSS) version 25.0, using Student "t" test, Pearson's correlation coefficient 'r' test was done to see the statistical significance. The p value <0.05 was taken as the minimum level of significance.

III. Result

Table 1: Distribution of the subjects according to Sex (n=200)

Characteristics	Case (n=100)		Control (n=100)	
	No	**%**	**No**	**%**
Age in years				
31-40	24	24	44	44
41-50	26	26	30	30
51-60	54	54	24	24
>60	16	16	2	2
Mean±SD	53.40±6.78		43.44±9.46	
Range	35-64		30-62	

Table-1 shows distribution of the subjects according to age, it was observed that, (24%) patients were belonged to age 31-40 years, (26%) were in 41-50 years, (54%) were in 51-60 years and (16%) were in >60 years in case group respectively. And in control group (44%) patients were belonged to age 31-40 years, (30%) were in 41-50 years, (24%) were in 51-60 years and (2%) were in >60 years in case group respectively.

Table 2: Distribution of the subjects according to Gender (n=200)

Characteristics	Case (n=100)		Control (n=100)	
	No	**%**	**No**	**%**
Sex				
Male	74	74	64	64
Female	26	26	36	36

Table-2 shows distribution of the subjects according to Sex, it was observed that, (74%) patients were male and (26%) patients were female in case group. And in control group (26%) patients were male and (36%) patients were female.

Table 3: Mean of serum calcium of the study subjects (n=200)

	Case (n=100)	Control (n=100)	P value
Serum calcium (mmol/L)	2.61±0.16	2.13±0.15	0.001
Range	1.80-2.85	1.70-2.40	

Table-3 shows mean of serum calcium of the study subjects, it was observed that, (2.61±0.16) were Serum calcium and range 1.80-2.85 in case group. And in control group (2.13±0.15) were Serum calcium and range 1.70-2.40.

Table 4: Distribution of the subjects according to BMI (n=200)

BMI	Case (n=100)		Control (n=100)		P value
	No	**%**	**No**	**%**	
Under weight (<18.5)	4	4	2	2	0.001
Normal (18.5-24.9)	4	4	44	44	
Over weight (25-29.9)	68	68	42	42	
Obese (≥30)	24	24	12	12	
Mean±SD	27.34±3.37		25.30±3.42		

Table-4 shows distribution of the subjects according to BMI, it was observed that, (4%) patients had underweight, (4%) had normal, (68%) had over weight and (24%) had Obese respectively. And in control (2%) patients had underweight, (44%) had normal, (42%) had over weight and (12%) had Obese respectively.

Table 5: Level of lipid profile of the study subjects (n=200)

Level of lipid profile	Case (n=100)		Control (n=100)		P value
	No	**%**	**No**	**%**	
TC					
Normal (<200 mg/dl)	62	62	84	84	
Raised (≥200 mg/dl)	38	38	14	14	
Mean±SD	196.80±53.03		171.22±29.11		0.004
TG					
Normal (<150 mg/dl)	50	50	86	86	
Raised (≥150 mg/dl)	50	50	14	14	
Mean±SD	181.82±128.54		112.96±52.85		0.002

LDL-c					
Normal (<100 mg/dl)	18	18	34	34	
Raised (≥100 mg/dl)	82	82	66	66	
Mean±SD	129.62±37.08		110.83±27.07		0.005
HDL-c					
Normal (≥40 mg/dl)	84	84	40	40	
Below (<40 mg/dl)	16	16	60	60	
Mean±SD	34.88±10.19		40.99±6.43		0.208

Table-5 shows the level of lipid profile of the study subjects, it was observed that, according to TC normal and raised were 62% and 38% in case group and 84% and 14% in control group respectively. Whereas, according to TG normal and raised were 50% and 50% in case group and 86% and 14% in control group respectively. And according to HDL-c normal and raised were 18% and 82% in case group and 34% and 66% in control group respectively.

Table 6: Correlation coefficient between s. calcium and lipid profile

S. calcium	TC		TG		LDL-c		HDL-c	
	r value	**p value**	**r value**	**p value**	**r value**	**p value**	**r value**	**p value**
Case	0.391	0.005	0.09	0.252	0.204	0.156	-0.021	0.441
Control	0.001	0.996	-0.027	0.427	-0.104	0.236	0.304	0.016

Table-6 shows the correlation coefficient between s. calcium and lipid profile, it was observed that, in case group, according to TC the value of r was 0.391 and the value of p was 0.005 and according to TG the value of r was 0.09 and the value of p was 0.252. And in control group according to TC the value of r was 0.001 and the value of p was 0.996 and according to TG the value of r was -0.027 and the value of p was 0.427.

Table 7: Correlation coefficient between s. calcium and blood pressure& BMI

S. calcium	BMI		SBP		DBP	
	r value	**p value**	**r value**	**p value**	**r value**	**p value**
Case	0.021	0.435	0.083	0.284	0.207	0.075
Control	-0.178	0.408	0.186	0.098	0.230	0.054

Table-7 shows the correlation coefficient between s. calcium and blood pressure& BMI, it was observed that, in case group, according to BMI the value of r was 0.021 and the value of p was 0.435 and according to SBP the value of r was 0.083 and the value of p was 0.284. And in control group according to BMI the value of r was -0.178 and the value of p was 0.408 and according to SBP the value of r was 0.186 and the value of p was 0.098.

IV. Discussion

In this case control study, we have measured the serum Calcium, FBS, Lipid profile, Troponin I in 100 diagnosed AMI patients as cases (Group – I) a 100 healthy control subjects (Group –II) to evaluate the association of serum calcium levels along with other risk factors in AMI. This is because serum Calcium is associated with component of metabolic syndrome such as HTN, hypercalcemia. In the study, males were predominant among the 200 subjects, comprising 74% (n=74) of the case group (Group I) and 64% (n=64) of the control group.

The present study found that the mean serum calcium concentration in the case group was 2.61±0.16 mmol/L, with a range of 1.80–2.85 mmol/L. In contrast, the mean serum calcium concentration in the healthy control group was 2.13±0.15 mmol/L, with a range of 1.70–2.40 mmol/L. The serum calcium concentration was significantly higher in the case group compared to the control group; a finding consistent with observations from several other studies worldwide. [4]

The study found that abnormal systolic blood pressure (SBP) was more prevalent in the case group compared to the control group, with 64% versus 16%, respectively. The mean SBP in the case group was 137.8±14.92 mmHg, ranging from 95 to 160 mmHg, while in the control group, it was 124.7±11.35 mmHg, with

a range of 90 to 160 mmHg. Additionally, pre-hypertensive diastolic blood pressure (DBP) was more common in the case group than in the control group, at 86% versus 72%, respectively. The mean DBP in the case group was 90.30±16.42 mmHg, with a range of 60 to 110 mmHg, compared to 79.60±7.61 mmHg, with a range of 60 to 95 mmHg in the control group. The difference between the two groups was statistically significant ($P<0.05$), aligning with findings from previous studies. [9, 10]

The current study demonstrates a positive correlation between serum calcium and both systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Group I, with correlation coefficients of r=0.083 and r=0.207, respectively. In the control group, the correlations were r=0.186 for SBP and r=0.230 for DBP. These findings are consistent with those of Chowdhury et al. Additionally, Rolf Jorde et al. in Tromsø observed a significant linear relationship between serum calcium levels and blood pressure in both genders. [11, 12] The association between hypercalcemia and hypertension observed in this study is similar to that reported by Lutsey et al. and Wang et al. [12, 13]

Calcium in plasma exists in three major forms: approximately 50% is in the free or ionized form, which is the physiologically active fraction; 40% is bound to albumin; and the remaining 10% is in soluble complexes with anions such as bicarbonate, phosphate, and lactate. Therefore, total serum calcium reflects not only calcium physiology but also serum albumin levels. To account for this, various algorithms have been developed to correct for serum albumin. However, serum albumin data were not included in our study. In other epidemiological studies on calcium and blood pressure, some researchers have corrected for serum albumin concentration. For instance, Anderson et al. applied this correction, and in a Swedish study by Lind et al. involving over 18,000 men and women, the corrected values still showed a strong and highly significant association. [14, 15]

This study found that overweight and obesity were more prevalent in the case group than in the control group, with rates of 68% and 24% in Group I, compared to 42% and 12% in Group II. The mean±SD BMI in Group I was 27.34±3.37 kg/m², ranging from 17 to 35 kg/m², while in Group II, the mean±SD BMI was 25.30±3.42 kg/m², with a range of 18 to 32 kg/m². A positive correlation (r=0.021) was observed between BMI and serum calcium. A similar result was reported in a study by Lind et al. conducted at Uppsala University Hospital, Sweden, among 2,183 participants, where the mean±SD BMI was 26.2±3.7 kg/m² in the case group and 24.8±3.0 kg/m² in the control group, with a positive correlation also observed. [15]

In this current study, the mean±SD TC, TG, LDL-c, HDL-c was 164.88±42.41 mg/dl in case group and 171.22±29.11mg/dl in control group, Serum calcium was negatively related with TC, whereas other study showed positive significant association between serum calcium and TC. The mean±SD TG was 181.82±128.54 in case group, whereas mean±SD 112.96±52.85 in control group, this correlation of serum calcium and TG was non-significant. But Rolf Jorde et al. found weaker association between serum calcium and TG in men. mean±SD of LDL-c 103.81±34.87in case group and110.83±27.07 in control group, the correlation between serum calcium and LDL-c was positive. Mean ± SD of HDL-c was 34.88±10.19 in case group (I) and 40.99±6.43 in control group (II) which was higher in control group and negative correlation was found between serum calcium and HDL-c. This study showed similar result with Lind et al. But Rolf et al. found HDL-c was positively correlated with serum calcium in both sexes. Studies done on different population with larger size found significant positive relation between serum calcium and HDL-c that was differ from current study as this study was done with smaller size. [12, 15]

There are several limitations to this study that may have impacted the results. Due to time constraints and financial limitations, the study was conducted with a small sample size, which may not be sufficient to represent the entire population. The sample was selected purposively, introducing the possibility of bias that could influence the findings. Additionally, the study was a case-control design based on hospital records collected over a short period, preventing the examination of long-term outcomes.

Limitations of the study

The present study was conducted in a very short period due to time constraints and funding limitations. The small sample size was also a limitation of the present study.

V. Conclusion

This case-control study aimed to establish the association between serum calcium levels and acute myocardial infarction (AMI). The results showed that serum calcium was significantly higher in the case group ($P=0.001$). Based on these findings, it can be suggested that elevated serum calcium is an important risk factor for myocardial infarction (MI) and may also serve as a coronary marker. However, a combined assessment of

increased serum calcium, lipid profile, and BMI could be more effective in evaluating AMI risk. Routine estimation of serum calcium may help in early detection of MI, potentially reducing the incidence of death in AMI patients. Regular monitoring of serum calcium in individuals at risk for AMI could be beneficial for the prevention and improved management of AMI.

VI. Recommendation

This study can serve as a pilot to much larger research involving multiple centers that can provide a nationwide picture, validate regression models proposed in this study for future use and emphasize points to ensure better management and adherence.

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