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PROGNOSTIC VALUE OF SERUM CALCIUM LEVELS IN PATIENTS WITHACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background: Ischemic heart disease is the leading cause of morbidity and mortality worldwide, and there is a growing evidence suggests that hypocalcemia is associated with poor prognosis in patients with acute myocardial infarction(AMI). **Aim:** The purpose of this study was to evaluate the impact of admission serumcalcium levels on final outcomes in patients admitted with myocardial infarction. **Materials and Methods:** This was an Analytic cohort study involved 72 patients with a diagnosis of AMI admitted at cardiac intensive care unit, Internal Medicine Department, Tishreen University Hospital, Lattakia, during one-year period 2022. Patients were divided into three groups based on admission serum calcium level, group 1(n=24) included patients with serum calcium<8.5 mg/dl, group 2(n=24) included patients with serum calcium in the range 8.5 to 10.2, and group 3(n=24) included patients with serum calcium≥10.2 mg/dl. **Results:** Ages of the study population range from 32 to 87 years, with a mean age of 58.54±10.2. Males represented 77.8% of the patients and STEMI type was observed in 61 cases (84.7%). Patients in group 1 were more likely to be older(p:0.001), with lower EF(p:0.001) and higher GRACE score(p:0.01). Duration of hospitalization increased significantly with decreasing serum calcium (9.2±6.1 in group 1 versus 3.8±1.2 in group 3,p:0.03) with higher rate of mortality (16.7% in group 1 versus 4.2 in group 2,p:0.0001). In multivariate regression analysis hypocalcemia was prognostic factor for arrhythmia (OR: 3.4,95% CI: 1.4-12.8, p: 0.0001),cardiac shock(OR:2.7,95% CI: 1.1-10.6,p:0.001) and mortality(OR:2.5,95% CI: 1.5-11.1,p:0.001). **Conclusion:** Hypocalcemia at admission is a bad prognostic factor formorbidity and mortality in patients with AMI.

KEYWORDS: Acute myocardial infarction, Hypocalcemia, Outcome.

INTRODUCTION

Acute myocardial infarction (AMI) is the leading cause of death worldwide, in which is associated with a 30% mortality rate and half of deaths occur prior to arrival to hospital.[1,2] It usually results from an imbalance in oxygen supply and demand which is caused mostly by plaque rupture with formation ofthrombus that obstructs an atherosclerotic coronary artery.[3] It is characterized by elevated ST segments and cardiac enzymes. Prognosis is variable and depends mainly on extent of infarct, residual left ventricular function, and performance of revascularization.[4] Identification of risk predictors of mortality and morbidity is considered important for tailoring more aggressive therapies that might improve survival in patients with cardiogenic shock.[5]

Serum calcium plays a crucial role in cardiac electrical activity and cardiac contraction.[6] Evidence demonstrated that hypocalcemia is a significant predictive index for poor prognosis in several acute illnesses including AMI. Several mechanisms have been proposed for the harmful effects of hypocalcemia in patients with AMI, which include an increase in ventricular action potential duration and prolongation of QTc interval which is associated with increased risk of arrhythmias.[7,8] However, it remains unclear whether low blood calcium levels are a marker of greater illness severity attributable to more extensive cardiac damage or a risk factor with a direct causal relationship to the observed adverse clinical outcome. Therefore, the aim of our study was to elucidate the impact of hypocalcemia on the final outcome in patients admitted with AMI.

PATIENTS AND METHODS

This is an Analytic cohort study of a group of patients older than 18 years with AMI was attending department of cardiac intensive care at Tishreen University Hospital in Lattakia-Syria during one-year period (2022). The exclusion criteria were presence one of the following: chronic kidney disease, liver disorders, severe acute infection, and vitamin D supplemental therapy.

Acute myocardial infarction was defined as presence of acute myocardial injury detected by abnormal cardiac biomarkers in the setting of evidence ofacute myocardial ischemia. It is divided into ST-elevation myocardial infarction(STEMI) and non-ST elevation infarction(NSTEMI).

Patients baseline characteristics as gender, age, cardiovascular factors such as smoking, hypertension, diabetes mellitus …. etc. were reported. Laboratory investigations were performed and patients were divided into three groups according to serum calcium; <8.5, 8.5-10.2, and ≤ 10.2 mg/dL.

The primary end point of this study was defined as occurrence of mortality for any cardiovascular etiology, whereas secondary end point included development of cardiogenic shock, heart failure, CVA, and malignant ventricular arrhythmias.

Ethical consideration

All patients were provided a complete and clear informed consent after discussion about the study. This study was performed following the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. To examine the relationships and comparisons between the two group, chi-square test was used. At first, Univariate analysis was done, factors with statically significance were put in multivariate analysis and odd ratio(OR) more than 2 considered significant. All the tests were considered significant at a 5% type I error rate($p<0.05$), β:20%, and power of the study:80%.

RESULTS

The baseline characteristics of the participants were as shown in (Table 1).Males represented 77.8% of the study population and females 22.2% with male: female ratio was 3.5:1. Ages range from 32 years to 87 years (mean 58.54±10.2 years) and majority of patients (84.7%) had ST-elevation myocardial infarction(STEMI).

Table 1: Demographic characteristics of the study population.

Variable	Result
Sex	
Male	56(77.8%)
Female	16(22.2%)
Age(years)	58.54±10.2
Myocardial infarction type	
STEMI	61(84.7%)
N-STEMI	11(15.3%)

As shown in table (2), there were no significant differences between three groups regarding gender, p:0.07. Patients in group 1 were significantly older (63.45±8.7) versus (58.44±9.4) in group 2 and (54.62±9.5) in group 3, p: 0.001.

Group 1 patients had higher prevalence of prognostic factors: diabetes mellitus(41.7% versus 20.8% in group 2 and 25% in group 3, p:0.02), hyperlipidemia (37.5% versus 16.7% and 16.7% in group 2 and 3 respectively), coronary artery diseases (25% versus 8.3% in group 2 and 4.2% in group 3, p:0.04), and CVA (16.7% versus 4.2% in group 2 and 0% in group 3, p:0.001).

Table 2: Baseline characteristics of the study population according toserum calcium levels.

Variable	serum calcium(mg/dL)			P value
	Group 1 <8.5	Group 2 8.5-10.2	Group 3 ≤10.2	
Sex Male Female	16(66.7%) 8(33.3%)	15(62.5%) 9(37.5%)	18(75%) 6(25%)	0.07
Age(years)	63.45±8.7	58.44±9.4	54.62±9.5	0.001
Risk factors				
Diabetes mellitus	10(41.7%)	5(20.8%)	6(25%)	0.02
Hypertension	8(33.3%)	11(45.8%)	9(37.5%)	0.08
Hyperlipidemia	9(37.5%)	4(16.7%)	4(16.7%)	0.03
Smoking	18(75%)	20(83.3%)	17(70.8%)	0.6
Coronary artery diseases	6(25%)	2(8.3%)	1(4.2%)	0.04

CVA	4(16.7%)	1(4.2%)	0(0%)	0.001
Family history of cardiovascular disease	13(54.2%)	10(41.7%)	14(58.3%)	0.1

There were no significant differences between groups regarding of heart rate (p:0.5), systolic blood pressure(p:0.8), diastolic blood pressure(p:0.09), type of myocardial infarction(p:0.3), and location of infarction(p:0.09). There was a significant decrease in mean EF as the levels of serum calcium decreased (41.81±9.3 in group 1 versus 45.28±8.2 in group 2 and 48.66±7.1 in group 3,p:0.001. In addition to, GRACE score was significantly higher in group 1(132.7±22.2) versus 114.2±23.4 in group 2 and 109.8±28.6 in group 3,p: 0.01.

Table 3: Clinical and echographic characteristics of the study populationaccording to serum calcium levels.

Variable	Serum calcium(mg/dL)			P value
	Group 1 <8.5	Group 2 8.5-10.2	Group 3 ≤10.2	
Heart rate(beat/minute)	79.8±14.3	81.9±10.2	82.5±13.5	0.5
Blood pressure(mm/Hg)				
Systolic Diastolic	132.4±22.8 80.2±13.5	134.9±17.5 80.9±15.4	134.2±18.9 82.1±12.2	0.8 0.09
Myocardial infarction type				
STEMI N-STEMI	21(87.5%) 3(12.5%)	19(79.2%) 5(20.8%)	21(87.5%) 3(12.5%)	0.3
Location of infarction				
Inferior Anterior	14(58.3%) 10(41.7%)	12(50%) 12(50%)	16(66.7%) 8(33.3%)	0.09
EF	41.81±9.3	45.28±8.2	48.66±7.1	0.001
GRACE score	132.7±22.2	114.2±23.4	109.8±28.6	0.01

The clinical outcomes in patients are listed in table (4). The duration of hospitalization was significantly longer in group 1 (6.1±9.2) versus (4.3±1.8) in group 2 and 3.8±1.2 in group 3, p: 0.03. Higher prevalence of mortality, cardiogenic shock, and arrhythmia, were reported more frequently in group 1 versus group 2 and group 3;(16.7% versus 4.2% and 0%), (12.5% versus 4.2% and 4.2%), (29.2% versus 8.3% and 12.5%) respectively.

Table 4: Outcome of the study population according to serum calcium levels.

Variable	serum calcium(mg/dL)			P value
	Group 1 <8.5	Group 2 8.5-10.2	Group 3 ≤10.2	
Duration of hospitalization(day)	6.1±9.2	4.3±1.8	3.8±1.2	0.03
Complications				
Cardiogenic shock	3(12.5%)	1(4.2%)	1(4.2%)	0.04
Arrhythmia	7(29.2%)	2(8.3%)	3(12.5%)	0.01
Cerebrovascular accident(CVA)	1(4.2%)	0(0%)	0(0%)	0.2
Mortality	4(16.7%)	1(4.2%)	0(0%)	0.0001

In multivariate analysis, hypocalcemia was independently associated with mortality (OR:3.5,95% CI:1.5-11.1, p:0.0001), arrhythmia(OR:3.4,95% CI:1.4-12.8, p:0.0001), and cardiogenic shock (OR:2.7,95% CI:1.1-10.6, p:0.001).

Table 5: Multivariate logistic regression analysis of hypocalcemia as a prognostic factor for Mortality and Cardiologic complications in patient with MI.

Variables	OR a	Confidence interval (95%)	p-value
Mortality	3.5	[1.5-11.1]	0.0001
Arrhythmia	3.4	[1.4-12.8]	0.0001
Cardiogenic shock	2.7	[1.1-10.6]	0.001

DISCUSSION

This Analytic cohort study of 72 patients with AMI assessed for predictive value of hypocalcemia on admission for in- hospital mortality, as well as complications resulting from infarction. This study showed the main findings: First, majority of the patients were elderly and males in which male gender represents a risk factor for coronary disease. Second, the mean age

of participants with lower serum calcium was higher compared to patients with normal range of calcium, which might be explained by poor regulation of serum calcium, high prevalence of vitamin D deficiency, renal failure and osteoporosis in elderly. Third, decreasing of serum calcium was associated significantly with reduced EF, increasing GRACE score, longer duration of hospitalization, with higher prevalence of complications. Finally, hypocalcemia was a prognostic factor for mortality, cardiogenic shock, and arrhythmia in AMI patients. These findings may be explained as follow: hypocalcemia prolongs duration of phase 2 of action potential of cardiac muscle leading to prolongation of QT interval which is considered an independent risk factor for mortality. In addition to, low levels of calcium could cause exaggerated calcium influx by increasing calcium channels on vascular cells, in which intracellular calcium is associated with increased cellular toxin damage, and activation of platelet, inflammation, lipid disposition, and increasing consumption of ionic calcium leading to defective cycle of hypocalcemia.

These findings are comparable with results of previous studies.

Lu et al (2014) demonstrated in a study conducted in China during the period 8 years and included 1431 patients with AMI that most of the patients were males and in advanced age group. Serum calcium levels were decreased significantly with increasing age of the patients, and hypocalcemia represented an independent risk factor for in-hospital mortality for STEMI patients.[9]

Shiyovich et al (2018) showed in a study performed in Italy during 10 years and included 11446 patients with AMI that majority of the patients were males with a mean age 67 years. Mortality rate was 6.9% with presence of association between mortality and serum calcium like U, in which serum less than 9.12, and greater than 9.86 were independent risk factors for mortality; OR: 2.4 and 1.7 respectively.[10]

Zhang et al (2020) performed a study in China during 2 years which included 1609 cases of AMI and 3252 controls. Serum calcium levels were significantly lower in patients with infarction and hypocalcemia was an independent risk factors for myocardial infarction OR:1.32.[11]

Schmitz et al (2021) demonstrated in a study conducted in Germany during six years and included 3732 patients with AMI the most of the patients were males and elderly. Hypocalcemia represented an independent risk factor for poor final outcome during 7 years after infarction. Mortality rate was significantly higher in patients with reduced serum calcium 16.2% versus 10.2% in normal group, p:0.001 and hypocalcemia was associated with the hazard of mortality(HR:1.53).[12]

In summary, low serum calcium is strongly related to poor outcome, so that serum calcium should be monitored in patients with AMI to predict mortality and cardiovascular complications.

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