

Research ARTICLE

## Serum calcium in association with ischemic heart disease: a case-control study in the coronary care unit at Al-Diwaniyah Teaching Hospital

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### ABSTRACT:

**Background:** Growing bulk of data inferred from medical literature favors the significant association between serum calcium and vascular disorders. Some of this literature has been collected and analyzed globally in meta-analysis studies. It has been shown that the rate of death is higher with higher serum calcium concentrations. However, some studies have shown that higher calcium levels are associated with other cardiovascular risk factors such as dyslipidemia, hypertension, and obesity, questioning the direct contribution of raised serum calcium as a risk factor for cardiovascular disorders. **Aim of the study:** To compare mean serum calcium between patients with ischemic heart disease and individuals known to be free of ischemic heart disease. **Patients and methods:** The current study was conducted at Al-Diwaniyah Teaching Hospital in Al-Diwaniyah Province, Iraq. The study started on January the 2<sup>nd</sup> 2018 and ended on June the 15<sup>th</sup> 2018 and it was designed to be a case-control study. The study group included a total of 40 patients with a diagnosis of ischemic heart disease, 20 patients with unstable angina (UA), and 20 patients with acute myocardial infarction (MI). Those patients were recruited for the pool of patients admitted to the coronary care unit at the hospital. The control group included 40 individuals who were not known to have ischemic heart disease with comparable age. **Results:** there was significant in mean serum calcium among patients and control subjects ( $P = 0.021$ ); the serum level of the control group was significantly lower than that of patients with unstable angina and patients with myocardial infarction ( $P < 0.05$ ), but, the level was not significantly different between patients with unstable angina and patients with myocardial infarction ( $P > 0.05$ ). **Conclusion:** the significantly higher serum calcium in patients with ischemic heart disease in comparison with individuals lacking ischemic heart disease may be an indicator of a possible role of serum calcium in the pathogenesis of ischemic heart disease.

**KEYWORDS:** Serum calcium, ischemic heart disease, Iraq

### INTRODUCTION:

Physiologically speaking, calcium plays significant roles in addition to its well-known contribution to bone formation [1]. From a pathological perspective, calcium has been recognized to be associated with several disorders such as hypocalcemia and hypercalcemia [2]. The concentration of calcium in extracellular fluid can regulate several cellular functions through receptors that are expressed by many cells in human tissues such as renal tubules and parathyroid gland [3]. Excitable tissues such as nervous tissue and muscular tissue are sensitive to calcium in extracellular fluid because of its direct effect on cell membrane potentials [4-6]. Contraction of muscle cells, including cardiac muscles, is a process in which calcium is an essential messenger [7]. Calcium also plays a role as a cofactor for several enzymes and it

is involved in the process of blood coagulation; therefore, calcium chelating agents such as ethylenediaminetetraacetic acid and citrate are commonly used as anti-coagulants when blood samples are collected [8, 9].

The compressive strength of bony tissues depends on the presence of hydroxyapatite crystals that exist between collagen fibers and these crystals are formed following deposition of calcium and phosphate between collagen fibers during the process of bone maturation [10, 11].

The calcium contribution to the health of vascular tissues is still under debate [1]. As has been stated previously, calcium is essential for cardiac muscle contraction, in addition to the existence of calcium receptors on platelets and smooth muscle cells [12-14]. One of the well documented risk factors for cardiovascular events is the deposition of calcium in vasculature [15-17]. Calcium may be deposited in other tissues such as the kidney and muscles and may impair their functions [18, 19]. The human body is provided by a complicated system that prevents calcium deposition and tissue mineralization and these systems include matrix GLA protein, fetuin-A, and pyrophosphate [20]. The mineralization of tissues is highly organized so that bone mineralization is allowed while that of soft tissues is prevented. However, aging leads to impairment of these anti-mineralization mechanisms and in particular in vascular tissues. Added to that, the changes in serum calcium levels appear to affect vascular health [1].

Growing bulk of data inferred from medical literature favors the significant association between serum calcium and vascular disorders. Some of this literature has been collected and analyzed globally in meta-analysis studies [21]. It has been shown that the rate of death is higher with higher serum calcium concentrations. However, some studies have shown that higher calcium levels are associated with other cardiovascular risk factors such as dyslipidemia, hypertension, and obesity, questioning the direct contribution of raised serum calcium as a risk factor for cardiovascular disorders [22].

Some studies have linked ischemic heart diseases such as myocardial infarction to raised serum calcium [21]. It has been shown that the risk of ischemic heart disease is increased by about 10 % when serum calcium rises by 0.1 mmol/L in regions of Australia, Europe, and North America [1]. However, some authors deny such association claiming that the rise of the risk is due to the associated higher rate of other risk factors such as dyslipidemia and hypertension rather than due to rising serum calcium level [1]. Furthermore, stroke has been

also linked to raised serum calcium by some authors [23].

The poverty of national studies in our country dealing with the problem of serum calcium in association with ischemic heart disease and the existing controversy in the available published article with this health issue justified to plan and conduct this study on a sample of Iraqi patients proved to have some form of ischemic heart diseases.

## PATIENTS AND METHODS:

The current study was conducted at Al-Diwaniyah Teaching Hospital at Al-Diwaniyah Province, Iraq. The study started on January the 2<sup>nd</sup> 2018 and ended on June the 15<sup>th</sup> 2018 and it was designed to be a case-control study. The study group included a total of 40 patients with a diagnosis of ischemic heart disease, 20 patients with unstable angina (UA), and 20 patients with acute myocardial infarction (MI). Those patients were recruited for the pool of patients admitted to the coronary care unit at the hospital. The control group included 40 individuals who were not known to have ischemic heart disease with comparable age. Demographic data including age, gender, residency, and occupation, bad habits including smoking and ethanol drinking, results of serum calcium, serum lipid profile, and history of hypertension and diabetes were the main variables included in the current study.

The study was approved by the institutional ethical approval committee and verbal consent was obtained from every participant. Statistical analysis was done using SPSS version 23. Quantitative data were expressed as mean, standard deviation, and range, whereas, qualitative data were expressed as number and percentage. Independent samples t-test was used to compare means between two groups and Chi-square was used to study the difference in proportion between the two groups. The level of significance was chosen at  $P \leq 0.05$ .

## RESULTS:

The current study included 40 control subjects with a mean age of  $65.48 \pm 7.34$  years and an age range of 52 - 83, 20 patients with unstable angina with a mean age of  $65.55 \pm 7.37$  years and an age range of 53 - 82 years and 20 patients with myocardial infarction with a mean age of  $65.85 \pm 8.46$  years and an age range of 55 - 86 years. There was no significant difference in mean age among groups ( $P = 0.948$ ), table 1. There was no significant difference in the frequency distribution of patients and individuals according to gender, residency, and occupation ( $P > 0.05$ ), as shown in table 1. There was also no significant difference in the frequency distribution of patients and individuals according to

smoking, hypertension, diabetes mellitus, and dyslipidemia ( $P > 0.05$ ), as shown in table 2. However, there was significant in mean serum calcium among patients and control subjects ( $P = 0.021$ ); the serum level of the control group was significantly lower than

that of patients with unstable angina and patients with myocardial infarction ( $P < 0.05$ ), but, the level was not significantly different between patients with unstable angina and patients with myocardial infarction ( $P > 0.05$ ), as shown in table 3.

**Table 1:** Demographic Characteristics of patients and control group

Characteristic	Control group <i>n</i> = 40	Unstable angina <i>n</i> = 20	Myocardial infarction <i>n</i> = 20	<i>P</i>
<b>Age</b>				
Mean $\pm$ SD	65.48 $\pm$ 7.34	65.55 $\pm$ 7.37	65.85 $\pm$ 8.46	0.984 †
Range	52 -83	53 -82	55 -86	NS
<b>Gender</b>				
Male, <i>n</i> (%)	24 (60.0 %)	14 (70.0 %)	15 (75.0 %)	0.470 ¥
Female, <i>n</i> (%)	16 (40.0 %)	6 (30.0 %)	5 (25.0 %)	NS
<b>Residency</b>				
Urban, <i>n</i> (%)	25 (62.5 %)	13 (65.0 %)	12 (60.0 %)	0.984 ¥
Rural, <i>n</i> (%)	15 (37.5 %)	7 (35.0 %)	8 (40.0 %)	NS
<b>Occupation</b>				
Housewife, <i>n</i> (%)	9 (22.5 %)	5 (25.0 %)	5 (25.0 %)	0.946 ¥
Employee, <i>n</i> (%)	13 (32.5 %)	8 (40.0 %)	6 (30.0 %)	NS
Retired, <i>n</i> (%)	18 (45.0 %)	7 (35.0 %)	9 (45.0 %)	

*n*: number of cases; SD: standard deviation; †: one way ANOVA test; ¥: Chi-square test; NS: not significant at  $P > 0.05$

**Table 2:** Smoking and chronic medical conditions in patients and control subjects

Characteristic	Control group <i>n</i> = 40	Unstable angina <i>n</i> = 20	Myocardial infarction <i>n</i> = 20	<i>P</i>
<b>Smoking</b>				
Smoker, <i>n</i> (%)	15 (37.5 %)	8 (40.0 %)	10 (50.0 %)	0.645 ¥
Not smoker, <i>n</i> (%)	25 (62.5 %)	12 (60.0%)	10 (50.0 %)	NS
<b>Hypertension</b>				
Hypertensive, <i>n</i> (%)	11 (27.5 %)	5 (25.0 %)	4 (20.0 %)	0.819 ¥
Not hypertensive, <i>n</i> (%)	29 (72.5 %)	15 (75.0 %)	16 (80.0 %)	NS
<b>Diabetes mellitus</b>				
Diabetic, <i>n</i> (%)	6 (15.0 %)	3 (15.0 %)	5 (25.0 %)	0.595 ¥
Not diabetic, <i>n</i> (%)	34 (85.0 %)	17 (85.0 %)	15 (75.0 %)	NS
<b>Lipid profile</b>				
Dyslipidemia, <i>n</i> (%)	9 (22.5 %)	5 (25.0 %)	6 (30.0 %)	0.819 ¥
Normal lipid profile, <i>n</i> (%)	31 (77.5 %)	15 (75.0 %)	14 (70.0%)	NS

*n*: number of cases; SD: standard deviation; ¥: Chi-square test; NS: not significant at  $P > 0.05$

**Table 3:** Comparison of serum calcium level between patients and control subjects

Serum calcium	Control group <i>n</i> = 20	Unstable angina <i>n</i> = 20	Myocardial infarction <i>n</i> = 20	<i>P</i>
Mean $\pm$ SD	9.56 $\pm$ 1.00	10.17 $\pm$ 0.78	10.07 $\pm$ 0.71	0.021 †
Range	B 7 -10.9	A 8.3 -11.4	A 8.7-10.9	S

*n*: number of cases; SD: standard deviation; †: one way ANOVA test; S: significant at  $P \leq 0.05$ ; Capital letters were used to indicate the level of significance so that similar letters denote no significant difference; whereas, different letters indicate significant difference; letter (A) takes the highest value

## DISCUSSION:

The search for a possible association between ischemic heart disease and newly suggested risk factors may provide a medical approach to reduce the rate of mortality and morbidity resulting from these common disorders. The growing bulk of data during the last 3 decades has suggested a possible association between higher serum calcium and increased risk of both mortality and ischemic heart disease. Local Iraq studies contain little if any information about such an association, therefore, we planned the current study and conducted it in the coronary care unit at Al-Diwaniyah

teaching Hospital, a mid-Euphrates region of Iraq to explore the association between high serum calcium and ischemic heart disease, namely acute coronary syndromes. It has been shown by the results of the current study that serum calcium of patients with acute coronary syndromes, unstable angina, and acute myocardial infarction, is higher than that of control subjects with comparables age, gender, residency, occupation, smoking, and chronic medical illnesses. Thus, we concluded that high serum calcium may somehow play a significant role in the pathogenesis of ischemic heart disease.

Jin *et al.*, have also shown that serum calcium is higher in patients with coronary disease [24]. The question about the causative role of high serum calcium in coronary artery disease arises from the correlation between serum calcium with subsequent mortality and vascular disease events. One possible explanation for such suggested causation is the development of vascular calcification as it is observed in previous large sample size studies that showed a clear association between coronary artery calcification and high serum calcium level [25, 26]. However, the risk is attenuated when other risk factors are adjusted such as body mass index, high blood pressure, advancing age, hypertension, smoking, dyslipidemia, and diabetes mellitus [1, 27-29]. However, statistically wise these attenuations might be less important since that we can postulate that ischemic heart disease is a multifactorial disorder and that the higher number of risk factors, the greater the chance for having these disorders.

### CONCLUSION:

The association between high serum calcium and coronary artery disorders has been questioned by other authors and a solid consensus needs further research work; however, based on current study findings and the findings of several previous studies, we suggest a possible role for high serum calcium in the causation of ischemic heart disease at least partially.

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