

ROLE OF SERUM CALCIUM IN PATIENTS OF METABOLIC SYNDROME: A CASE CONTROL STUDY

Yogita Joshi¹, Dr. Jaya Jain², Dr. Krishna Murari Lodha^{1*}

¹*PhD Research scholar, Department of Biochemistry, Index Medical College, Indore.

²Associate Professor, Department of Biochemistry, Index Medical College, Indore.

***Corresponding Author:** Dr. Krishna Murari Lodha

*Associate Professor, Dept of Biochemistry, Jhalawar Medical College, Jhalawar (Rajasthan)

Email: drkmlodha@gmail.com Mobile: 8949916071

ABSTRACT

Introduction: Metabolic syndrome is a group of physiological and metabolic abnormalities including obesity, abnormal glucose metabolism, dyslipidemia, and hypertension. Metabolic syndrome is known to be related with increased risk of cardiovascular disease, hypertension, and type II diabetes mellitus. There is growing evidence of close association between calcium and metabolic syndrome. This case-control study aimed to evaluate the association between serum calcium level and risk of metabolic syndrome.

Objectives: To evaluate the role of serum calcium level in patients with metabolic syndrome.

Methodology: We conducted an analytical case-Control study on Metabolic Syndrome patients (N=90) and age matched healthy controls (N=90). Estimation of serum calcium in healthy controls and metabolic syndrome patients done by spectrophotometric method.

Results: We found that serum calcium levels were significantly decreased (1.7 ± 5.25 Mg/dl) in patients having metabolic syndrome as compared to healthy controls (1.9 ± 10.05 Mg/dl).

Conclusions: Low serum calcium levels have been associated with risk factors of metabolic syndrome, such as hyperglycaemia, hypertension, hypertriglyceridemia and insulin resistance. Low levels of serum calcium are widely accepted as risk factors for hypertension and cardiovascular diseases.

Keywords: Calcium, Metabolic Syndrome, Hypertension, Obesity, Diabetes mellitus

INTRODUCTION:

Metabolic syndrome (MetS) is a combination of glucose intolerance, central obesity, a high triglyceride (TG) level, low high-density lipoprotein cholesterol (HDL-C) level, and hypertension. The prevalence rates of metabolic syndrome and its components are increasing worldwide, even in young adults. Moreover, metabolic syndrome is linked to cardiovascular mortality and all-cause mortality throughout world.¹

The serum calcium level plays an important role in glucose homeostasis, and it enhances the vascular resistance. Previous epidemiological studies have demonstrated that low serum calcium levels are associated with high blood pressure levels, high glucose levels, and dyslipidemia. Intracellular calcium plays an important role in the regulation of lipid metabolism and insulin sensitivity. Serum calcium homeostasis is regulated within a narrow range, and is under tight hormonal control. Several epidemiological studies have demonstrated that a high level of serum calcium is associated with increased risk for type 2 diabetes mellitus (T2DM), obesity, increased blood pressure, hypercholesterolemia, as well as metabolic syndrome.²

Serum calcium concentrations were also negatively correlated with increasing numbers of conventional metabolic syndrome components. Finally, decreases serum calcium concentration can predict increased all-cause and cardiovascular disease mortality in

patients.³

Research suggests that decreased serum calcium level is associated with an increased risk of metabolic syndrome. Previous studies have reported inconsistent results on the association between obesity and serum calcium level with some reporting a positive correlation between the two, while others an inverse correlation. Studies determining an association between the serum calcium level and metabolic syndrome in young adults.⁴

Therefore, this case-control study investigated the association between the serum calcium level and metabolic syndrome in adults.

Materials and Methods

Inclusion criteria: We conducted an analytical case-Control study on Metabolic Syndrome patients (N=90) and age matched healthy controls (N=90) who participated in health examinations at Index Hospital, Indore (Madhya Pradesh) in Central India from January 2023 to July 2023. We included participants aged 18 years and older in the analysis. Participants were asked to complete a self-administered questionnaire that included questions on lifestyle habits (average daily alcohol intake and cigarette smoking), medical illness, and current medications.

Height and weight were measured using a stadiometer and digital scale. The participants were asked to wear light clothes without shoes. Height was measured to the nearest 0.1 cm, and weight was measured to the nearest 0.1 kg. Body mass index (BMI) was calculated as the weight (kg) divided by the height in meters squared (m²). Waist circumference was measured midway between the lowest ribs and iliac crest in a horizontal plane in a standing position. Blood pressure was measured in the right arm with at least 10 min of rest in a sitting position using a mercury sphygmomanometer.

All blood samples were collected in the morning after an overnight fasting. Serum calcium levels were measured by spectrophotometer.⁵ The normal serum calcium levels ranged from 9.0 to 11.0 mg/dL. To define metabolic syndrome, we adopted the guidelines of 2005 revision of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) (19).

Exclusion criteria: Study subjects who were less than 18 years and above 60 years not participated in this study. We excluded participants who had history of taking medicines, known renal disease or patients with hepatic disorder or patients suffering any chronic illness.

RESULTS:

We found that serum calcium levels were significantly decreased (1.7 ± 5.25 Mg/dl) in patients having metabolic syndrome as compared to healthy controls (1.9 ± 10.05 Mg/dl).

STATISTICAL ANALYSIS:

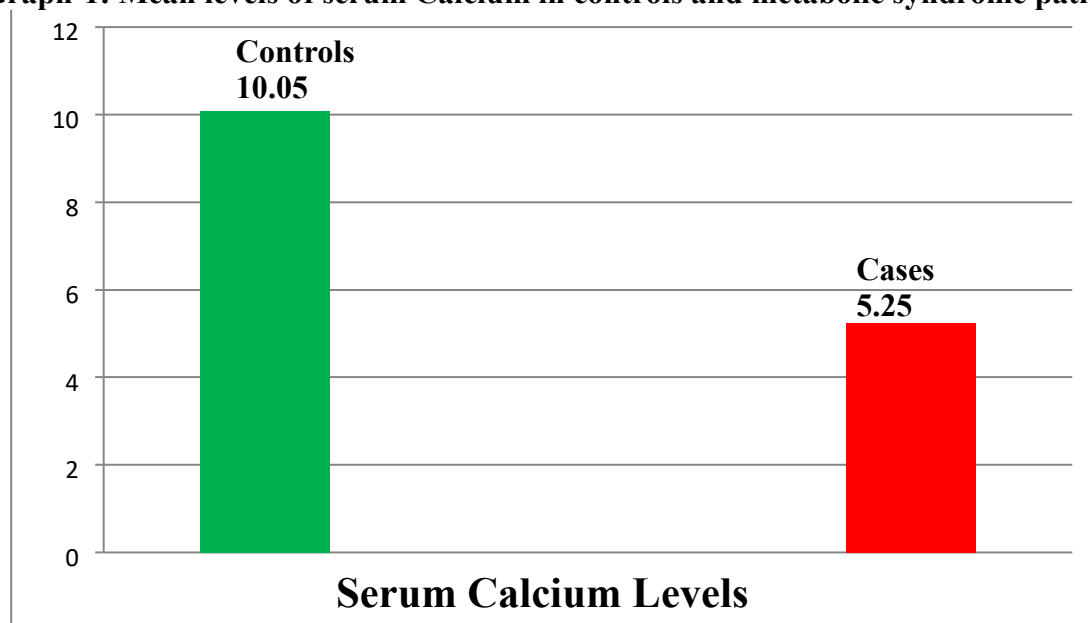
Unpaired student 't' test was used to compare serum calcium levels between cases and controls. Results were expressed as mean \pm S.D. A p-value 0.05 or less is considered to be statistically significant.

Table-1: Showing age and sex-wise distribution of controls and cases

Variables	Controls	Metabolic Syndrome cases	p-Value
Male (No.)	60	60	>0.05 NS
Female (No.)	30	30	>0.05 NS
Age in years (Mean \pm SD)	45 \pm 12	45 \pm 12	>0.05 NS

Table-2: Mean levels of serum Calcium in controls and metabolic syndrome patients

	Cases	Controls	
Parameters	Mean (\pm S.D.)	Mean (\pm S.D.)	p-Value
Serum Calcium	1.7 \pm 5.25 Mg/dl	1.9 \pm 10.05 Mg/dl	<0.0001

Graph-1: Mean levels of serum Calcium in controls and metabolic syndrome patients

DISCUSSION

Intracellular calcium plays an important role in the regulation of lipid metabolism and insulin sensitivity.⁶ Serum calcium homeostasis is regulated within a narrow range, and is under tight hormonal control.⁷ Several epidemiological studies have demonstrated that a low level of serum calcium is associated with increased risk for type 2 diabetes mellitus, overweight or obesity, elevated blood pressure, hypercholesterolemia, as well as Metabolic syndrome.⁸ Serum calcium concentrations were also negatively correlated with increasing numbers of conventional metabolic syndrome components.

The current study demonstrated that low serum calcium level was associated with higher levels of systolic blood pressure, increased blood glucose, higher levels of triglycerides and insulin resistance. Our findings suggest that the lower the serum calcium level, greater the risk of metabolic syndrome in overweight and obese young adults. Several studies have found that people with low serum calcium levels have a higher prevalence of metabolic syndrome and its components. Hazari MA et al⁶ reported decreased serum calcium levels with a higher prevalence rate of metabolic syndrome in a young adult population who underwent health examinations in 2012. Serum calcium plays a partial role in the regulation of energy metabolism. High-calcium diets attenuate adipocyte lipid accretion, increase lipolysis and preserve thermogenesis during caloric restriction.^{9,10}

Cho GJ, Shin JH, Yi KW et al¹¹ discovered that an intracellular calcium can also act directly on adipocytes to regulate lipid metabolism and insulin-stimulated glucose uptake and storage. Our study reported that the serum calcium level was negatively associated with the risk of a high systolic blood pressure, insulin resistance and elevated cardiovascular risk in metabolic syndrome patients. Metabolic syndrome predicts the onset of metabolic diseases, such as type 2 diabetes mellitus and cardiovascular diseases. A large cross-sectional study of 12,405 participants in the United States, reported that the Metabolic syndrome is linked to high cardiovascular mortality and mortality in young adults.^{12,13} Previous studies have reported inconsistent results on the association between obesity and serum calcium level with some reporting a positive correlation between the two, while others an inverse correlation.^{14,15} Additionally, limited studies have investigated the effect of obesity on the serum calcium level and metabolic syndrome.^{16,17} In the present study, a relationship was found between lower serum calcium levels and metabolic syndrome patients. Finally, decreased serum calcium concentration can predict increased all-cause and cardiovascular disease mortality in metabolic syndrome patients.

CONCLUSION

Serum calcium levels are potential indicators to estimate the severity of complications in metabolic syndrome patients. This marker should be included in diagnostic work-up to stratify disease severity. Therefore, full monitoring of metabolic syndrome patients and effective early intervention are the fundamental measures for reducing mortality. Our research work will be helpful in making novel strategies for diagnosis, treatment and prognosis of metabolic syndrome. This study may be helpful to reduce mortality and morbidity in metabolic syndrome patients.

In summary, we report an association between low serum calcium levels and a higher risk of metabolic syndrome and its components especially in obese participants. Further prospective research is necessary to fully determine the association between serum calcium levels and risk of developing metabolic syndrome in young adults.

REFERENCES

1. Wilson PW, Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type-2 diabetes mellitus. *Circulation*.2005;112:3066-72.
2. Baek JH, Jin SM, Bae JC, Jee JH, Yu TY, Kim SK, Hur KY, Lee MK, Kim JH. Serum Calcium and the Risk of Incident Metabolic Syndrome: A 4.3-Year Retrospective Longitudinal Study. *Diabetes Metab J*. 2017 Feb;41(1):60-68.
3. Becerra-Tomás N, Estruch R, Bulló M, Casas R, Díaz-López A, Fitó M, Serra-Majem L, Salas-Salvadó J. Increased serum calcium levels and risk of type 2 diabetes in individuals at high cardiovascular risk. *Diabetes Care*. 2014;37(11):3084-91.
4. Jer-min Chen, Tai-yin Wu, Yi-fan Wu, Kuan-liang Kuo. Association of the serum calcium level with metabolic syndrome and its components among adults in Taiwan. *Arch Endocrinol Metab*, 2023, v.67(5), 1-8.
5. S. Adeleh, Razavi Laleh, Hoghooghiraad Hoda, Golab-Ghadaksaz, Mehdi Hedayati. Calcium determination in EDTA treated plasma by colorimetric method and microplate reading format. *Zahedan Journal of Research in Medical Science* :17(2); 2013,209-213
6. Hazari MA, Arifuddin MS, Muzzakar S, Reddy VD. Serum calcium level in hypertension. *North American Journal of Medical Science*. 2012;4(11):569-72.
7. Ozsahin AK, Gokcel A, Sezgin N, et al. Prevalence of the metabolic syndrome in a Turkish adult population. *Diabetes Nutr Metab*. 2004;17:230-4.
8. Demiral Y, Soysal A, Can Bilgin A, et al. The association of job strain with coronary heart disease and metabolic syndrome in municipal workers in Turkey. *J Occup Health*.2006;48:332-8.

9. Gundogan K, Bayram F, Capak M, et al. Prevalence of metabolic syndrome in the Mediterranean region of Turkey evaluation of hypertension, diabetes mellitus, obesity, and dyslipidemia. *Metab Syndr Relat Disord*. 2009;7:427–34. doi: 10.1089/met.2008.0068.
10. Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR, Holman RR. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study. *BMJ*. 1998;14;316(7134):823-8.
11. Cho GJ, Shin JH, Yi KW, Park HT, Kim T, Hur JY. Serum calcium level is associated with metabolic syndrome in elderly women. *Maturitas*. 2011;68(4):382386.
12. Scott M. Grundy, Obesity, Metabolic Syndrome, and Cardiovascular Disease, *The Journal of Clinical Endocrinology & Metabolism*. 2004, (6):2595–2600.
13. Schumacher C, Ferucci ED, Lanier AP, Slattery ML, Schraer CD, Raymer TW, Dillard D, Murtaugh MA, Tom-Orme L. Metabolic syndrome: prevalence among American Indian and Alaska native people living in the southwestern United States.
14. Kunutsor SK, Laukkanen JA. Circulating active serum calcium reduces the risk of hypertension. *Eur J Prev Cardiol*. 2017;24(3):239-43.
15. Kim KN, Oh SY, Hong YC. Associations of serum calcium levels and dietary calcium intake with incident type 2 diabetes over 10 years: the Korean Genome and Epidemiology Study. *Diabetol Metab Syndr*. 2018;10:50.
16. Kirang K, Yang YJ, Kim K, Kim MK. Interactions of single nucleotide polymorphisms with dietary calcium intake on the risk of metabolic syndrome. *Am J Clin Nuts*. 2012; 95:231-40.
17. Brandão Lima PN, Carvalho GB, Santos RKF, Santos BDC, Dias Vasconcelos NL, Rocha VS, Barbosa KBF, Pires LV. Intakes of Zinc, Potassium, Calcium, and Magnesium of Individuals with Type 2 Diabetes Mellitus and the Relationship with Glycemic Control. *Nutrients*. 2018, 8;10(12):1948.