International Journal of Medical and Pharmaceutical Research
Available on: https://ijmpr.in/ | Print ISSN: 2958-3675 | Online ISSN: 2958-3683
NIH NLM ID: 9918523075206676
Volume: 5 Issue:1 (Jan-Feb 2024); Page No: 30-35

OPEN ACCESS ORIGINAL ARTICLE

Serum Calcium and Serum Magnesium Levels in Newly Detected Hypertensive Patients

Dr. Rajeev Agarwal[1], Dr. Suhas M[2*], Dr. Abhi G M[2]

[1] MD, DNB (Nephrology), Professor, Department of General medicine, JJM Medical College, Davangere
[2] Junior resident, Department of General medicine, JJM Medical College, Davangere

ABSTRACT

Background: Hypertension is a complex cardiovascular disorder with multifactorial etiology. This study aimed to investigate the association between serum calcium and magnesium levels and hypertension.

Methods: A prospective observational study was conducted with 100 newly diagnosed hypertensive patients and 100 normotensive controls. Serum calcium and magnesium levels were measured, and their correlation with blood pressure was analyzed.

Results: Hypertensive patients exhibited significantly higher serum calcium levels (9.8 ± 0.6 mg/dL) compared to normotensive controls (9.4 ± 0.5 mg/dL, $p < 0.001$). Conversely, serum magnesium levels were lower in hypertensive patients (1.9 ± 0.2 mg/dL) than in controls (2.1 ± 0.2 mg/dL, $p = 0.003$). A positive correlation was found between serum calcium levels and blood pressure severity (systolic: $r = 0.28$, $p = 0.004$; diastolic: $r = 0.19$, $p = 0.03$), while an inverse correlation was observed for magnesium (systolic: $r = -0.31$, $p = 0.002$; diastolic: $r = -0.25$, $p = 0.01$).

Conclusion: The study highlights the significant association of serum calcium and magnesium levels with hypertension. These findings suggest the potential of serum mineral levels as predictive markers and therapeutic targets in hypertension management.

Key Words: *Hypertension, Serum Calcium, Serum Magnesium, Blood Pressure, Cardiovascular Disease.*

***Corresponding Author**

Dr. Suhas M
Junior resident, Department of General medicine, JJM Medical College, Davangere.

Received: 02-12-2023 / Accepted: 04-01-2024

INTRODUCTION

Hypertension, a prevalent cardiovascular disorder, poses a significant public health challenge globally. It is a major risk factor for coronary heart disease, stroke, and kidney failure, affecting approximately 1.13 billion people worldwide [1]. The pathophysiology of hypertension is multifactorial, involving complex interactions between genetic, environmental, and physiological factors. Among these, the roles of serum calcium and magnesium levels have garnered increasing attention in recent years.

Calcium and magnesium are essential minerals that play vital roles in various physiological processes. Serum calcium is crucial for vascular smooth muscle function, and its imbalance is implicated in vascular contractility and hypertension [2]. Hypertension has been associated with alterations in calcium metabolism, and several epidemiological studies suggest a negative correlation between dietary calcium intake and blood pressure [3]. Conversely, hypercalcemia is linked to increased vascular resistance and arterial stiffness, contributing to elevated blood pressure [4].

Magnesium, on the other hand, is a natural calcium antagonist. It regulates vascular tone and endothelial function, and its deficiency has been correlated with hypertension [5]. Magnesium dilates arteries, reducing peripheral resistance and, consequently, blood pressure [6]. Low serum magnesium levels are commonly observed in hypertensive patients, and supplementation has shown potential in lowering blood pressure [7].

Despite the established roles of calcium and magnesium in blood pressure regulation, the relationship between their serum levels and newly diagnosed hypertension remains inadequately explored. This prospective study aims to investigate serum calcium and magnesium levels in newly detected hypertensive patients. Understanding this relationship can provide insights into the pathophysiology of hypertension and potentially guide therapeutic strategies.

Calcium's role in hypertension is multifaceted. It is involved in the regulation of vascular smooth muscle tone, a key factor in blood pressure control. Increased intracellular calcium in vascular smooth muscle cells leads to vasoconstriction and elevated blood pressure [8]. Additionally, calcium is essential for the release of neurotransmitters and hormones that regulate blood pressure, such as renin and angiotensin II [9]. Genetic studies have identified polymorphisms in calcium-regulating genes, such as the calcium-sensing receptor (CaSR), associated with hypertension [10].

Magnesium acts as a natural calcium channel blocker, influencing vascular tone and endothelial function. It modulates cellular processes involved in vascular reactivity and integrity [11]. Magnesium deficiency has been linked to endothelial dysfunction, increased vascular resistance, inflammation, and oxidative stress, all of which are conducive to hypertension [12]. Clinical trials have demonstrated the efficacy of magnesium supplementation in lowering blood pressure, especially in individuals with magnesium deficiency or insulin resistance [13].

Investigating serum calcium and magnesium levels in newly detected hypertensive patients is crucial for several reasons. Firstly, it may elucidate early changes in mineral metabolism associated with the development of hypertension. Secondly, it could identify individuals at increased risk for hypertension, potentially leading to early intervention strategies. Finally, understanding these relationships can inform dietary and pharmacological interventions to manage hypertension [14].

The investigation of serum calcium and magnesium levels in newly detected hypertensive patients is a promising area of research with significant clinical implications. This study aims to shed light on the mineral imbalances associated with the early stages of hypertension and contribute to a better understanding of its pathophysiology. Findings from this research may pave the way for new preventive and therapeutic approaches in hypertension management.

This prospective study hypothesizes that alterations in serum calcium and magnesium levels are associated with newly detected hypertension. The primary objective is to compare these serum mineral levels in newly diagnosed hypertensive patients with normotensive controls. Secondary objectives include assessing the correlation between serum calcium/magnesium levels and the severity of hypertension, and evaluating the potential predictive value of these minerals in hypertension development.

MATERIALS AND METHODS

Study Design

A prospective, observational study was conducted, involving two cohorts: newly diagnosed hypertensive patients and normotensive control participants. The duration of the study spanned 12 months, facilitating a thorough analysis of serum calcium and magnesium levels in relation to blood pressure.

Sample Size and Statistical Considerations

For the sample size calculation, the primary endpoint was set as the detection of a significant difference in serum calcium and magnesium levels between hypertensive patients and normotensive controls. A confidence interval (CI) of 95% and a margin of error of 5% were employed. The sample size of 200 (100 normotensive, 100 hypertensive) was determined using these parameters, alongside the standard deviation values obtained from preliminary studies in this area.

Population and Sampling

Participants were recruited from outpatient clinics of a tertiary care hospital. The inclusion criteria for the hypertensive group were adults aged 30-65 years, diagnosed with hypertension within the past six months. The exclusion criteria encompassed secondary hypertension, chronic kidney disease, any form of cardiovascular disease, diabetes, and current use of calcium or magnesium supplements.

For the normotensive group, the inclusion criteria were adults aged 30-65 years with no history of hypertension, and blood pressure readings within the normal range during the screening phase. The same exclusion criteria applied to this group as to the hypertensive participants.

Data Collection

Serum calcium and magnesium levels were measured using standardized laboratory procedures. Blood samples were collected after a 12-hour fast and analyzed in a central laboratory to ensure consistency. Blood pressure was measured using sphygmomanometers, following the American Heart Association guidelines, with three readings taken at five-minute intervals and averaged for analysis.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Review Board. Informed consent was acquired from all participants, ensuring they were aware of the study's purpose, procedures, and their right to withdraw at any time without consequence.

Statistical Analysis

Data were analyzed using statistical software. The comparison of serum calcium and magnesium levels between hypertensive and normotensive groups was performed using independent t-tests. Correlation analyses were conducted to explore the relationship between mineral levels and blood pressure severity. A p-value of less than 0.05 was considered statistically significant.

Limitations

Potential limitations of the study included the reliance on single-time-point measurements of serum calcium and magnesium levels and blood pressure, which may not reflect chronic status. Additionally, dietary intake of calcium and magnesium was not controlled or monitored, which could have influenced serum levels.

RESULTS

The findings from the presented tables provide comprehensive insights into the serum calcium and magnesium levels in newly detected hypertensive patients compared to a normotensive control group, along with their correlation with blood pressure severity and other baseline characteristics.

Table 1 detailed the baseline characteristics of both groups. The mean age was comparable between the hypertensive (52.3 ± 6.7 years) and normotensive groups (51.8 ± 7.1 years). Gender distribution was slightly male-dominant in both groups, with 60% males in the hypertensive group and 58% in the normotensive group. A notable difference was observed in the Body Mass Index (BMI), with the hypertensive group having a higher mean BMI (28.5 ± 4.2 kg/m²) compared to the normotensive group (24.7 ± 3.8 kg/m²). Regarding lifestyle factors, 30% of the hypertensive group were smokers, compared to 20% in the normotensive group. Alcohol consumption was reported by 40% of hypertensive and 35% of normotensive participants. A significant contrast was noted in the family history of hypertension, with 65% of hypertensive participants reporting a positive family history, in contrast to 30% in the normotensive group.

Table 2 focused on the baseline blood pressure readings. The hypertensive group had a significantly higher mean systolic blood pressure (142.3 ± 10.5 mmHg) and diastolic blood pressure (90.7 ± 8.3 mmHg) than the normotensive group, which recorded 122.5 ± 9.6 mmHg and 76.4 ± 7.5 mmHg, respectively.

In Table 3, the serum calcium levels were compared between the groups. The hypertensive group exhibited a higher mean serum calcium level (9.8 ± 0.6 mg/dL) than the normotensive group (9.4 ± 0.5 mg/dL), with the difference being statistically significant ($p < 0.001$).

Table 4 presented data on serum magnesium levels. The mean serum magnesium level was lower in the hypertensive group (1.9 ± 0.2 mg/dL) compared to the normotensive group (2.1 ± 0.2 mg/dL), and this difference was also statistically significant ($p = 0.003$).

The correlation between serum calcium levels and blood pressure severity was shown in Table 5. There was a positive correlation between serum calcium levels and both systolic ($r = 0.28$, $p = 0.004$) and diastolic blood pressure ($r = 0.19$, $p = 0.03$) in the hypertensive group.

Table 6 revealed a negative correlation between serum magnesium levels and blood pressure. The correlation coefficients were -0.31 ($p = 0.002$) for systolic blood pressure and -0.25 ($p = 0.01$) for diastolic blood pressure, indicating an inverse relationship between serum magnesium levels and hypertension severity.

In Table 7, multivariable analysis highlighted several predictors of hypertension. Serum calcium showed a significant association with hypertension (odds ratio 1.4, 95% CI 1.1-1.8, $p = 0.01$), as did serum magnesium (odds ratio 0.7, 95% CI 0.5-0.9, $p = 0.04$). Age and BMI were also significant predictors, with odds ratios of 1.03 (95% CI 1.01-1.05, $p = 0.007$) and 1.09 (95% CI 1.04-1.14, $p < 0.001$), respectively. Smoking status, however, was not a significant predictor (odds ratio 1.2, 95% CI 0.8-1.7, $p = 0.35$).

Finally, Table 8 provided a subgroup analysis based on age. In the 30-45 years subgroup, the mean serum calcium level in hypertensive patients was 9.7 ± 0.5 mg/dL, and the mean serum magnesium level was 1.8 ± 0.3 mg/dL. The differences in calcium and magnesium levels were statistically significant ($p = 0.02$ and $p = 0.05$, respectively). In the 46-65 years subgroup, the differences were more pronounced, with mean serum calcium at 9.9 ± 0.6 mg/dL and serum magnesium at 2.0 ± 0.2 mg/dL, and both differences were highly significant ($p < 0.001$ and $p = 0.01$, respectively).

Overall, the findings suggest that newly detected hypertensive patients have significantly different serum calcium and magnesium levels compared to normotensive individuals, with these differences correlating with the severity of hypertension. Additionally, age and BMI emerged as significant predictors of hypertension, underscoring the multifactorial nature of this condition.

Table 1: Baseline Characteristics of Participants

Characteristics	Hypertensive Group (n=100)	Normotensive Group (n=100)
Age (years), mean ± SD	52.3 ± 6.7	51.8 ± 7.1
Gender (M/F)	60/40	58/42
BMI (kg/m²), mean ± SD	28.5 ± 4.2	24.7 ± 3.8
Smoking status (Smokers/Non-smokers)	30/70	20/80
Alcohol consumption (Yes/No)	40/60	35/65
Family history of hypertension (Yes/No)	65/35	30/70

Table 2: Baseline Blood Pressure Readings

Group	Systolic BP (mmHg), mean ± SD	Diastolic BP (mmHg), mean ± SD
Hypertensive	142.3 ± 10.5	90.7 ± 8.3
Normotensive	122.5 ± 9.6	76.4 ± 7.5

Table 3: Serum Calcium Levels in Hypertensive and Normotensive Participants

Group	Serum Calcium (mg/dL), mean ± SD	p-value
Hypertensive	9.8 ± 0.6	<0.001
Normotensive	9.4 ± 0.5	

Table 4: Serum Magnesium Levels in Hypertensive and Normotensive Participants

Group	Serum Magnesium (mg/dL), mean ± SD	p-value
Hypertensive	1.9 ± 0.2	0.003
Normotensive	2.1 ± 0.2	

Table 5: Correlation Analysis between Serum Calcium Levels and Blood Pressure Severity

Blood Pressure Measurement	Correlation Coefficient (r)	p-value
Systolic BP	0.28	0.004
Diastolic BP	0.19	0.03

Table 6: Correlation Analysis between Serum Magnesium Levels and Blood Pressure Severity

Blood Pressure Measurement	Correlation Coefficient (r)	p-value
Systolic BP	-0.31	0.002
Diastolic BP	-0.25	0.01

Table 7: Multivariable Analysis for Predictors of Hypertension

Variable	Odds Ratio (95% CI)	p-value
Serum Calcium	1.4 (1.1-1.8)	0.01
Serum Magnesium	0.7 (0.5-0.9)	0.04
Age	1.03 (1.01-1.05)	0.007
BMI	1.09 (1.04-1.14)	<0.001
Smoking status	1.2 (0.8-1.7)	0.35

Table 8: Subgroup Analysis (Age Group)

Age Group	Serum Calcium (Hypertensive), mean ± SD	Serum Magnesium (Hypertensive), mean ± SD	p-value (Calcium)	p-value (Magnesium)

Age Group	Serum Calcium (Hypertensive), mean ± SD	Serum Magnesium (Hypertensive), mean ± SD	p-value (Calcium)	p-value (Magnesium)
30-45 years	9.7 ± 0.5	1.8 ± 0.3	0.02	0.05
46-65 years	9.9 ± 0.6	2.0 ± 0.2	<0.001	0.01

DISCUSSION

The findings of this study contribute significantly to the understanding of mineral metabolism in hypertension. The observed higher serum calcium levels in hypertensive patients compared to normotensive controls align with previous research indicating a potential role of calcium in the pathogenesis of hypertension. The mean serum calcium level in the hypertensive group was 9.8 ± 0.6 mg/dL, significantly higher than the 9.4 ± 0.5 mg/dL observed in the normotensive group ($p < 0.001$). These results are consistent with the study by Resnick et al. [15], which demonstrated elevated serum calcium levels in hypertensive patients. However, they contrast with the findings of Forman et al. [16], who reported no significant difference in serum calcium levels between hypertensive and normotensive individuals.

The study also found lower serum magnesium levels in hypertensive patients (1.9 ± 0.2 mg/dL) compared to normotensive controls (2.1 ± 0.2 mg/dL), with a p-value of 0.003. This is in agreement with the study by Barbagallo and Dominguez [17], which found that lower serum magnesium levels were associated with hypertension. This inverse relationship suggests a protective role of magnesium against hypertension, a notion supported by Guerrero-Romero and Rodriguez-Moran [18], who observed an improvement in blood pressure control with magnesium supplementation.

The positive correlation between serum calcium levels and blood pressure severity (systolic: $r = 0.28$, $p = 0.004$; diastolic: $r = 0.19$, $p = 0.03$) adds to the growing evidence that calcium metabolism might influence blood pressure regulation. This finding is consistent with the work of Zemel et al. [19], which indicated that calcium might play a role in the modulation of blood pressure. In contrast, the negative correlation between serum magnesium levels and blood pressure severity (systolic: $r = -0.31$, $p = 0.002$; diastolic: $r = -0.25$, $p = 0.01$) aligns with the hypothesis that magnesium has a vasodilatory effect, as suggested by Houston [20].

Multivariable analysis in this study highlighted serum calcium and magnesium, along with age and BMI, as significant predictors of hypertension. These findings are in line with the research by Peacock et al. [21], emphasizing the multifactorial nature of hypertension. However, the lack of a significant association between smoking status and hypertension in our study contrasts with the findings of Halimi et al. [22], who reported a significant relationship between smoking and elevated blood pressure.

The subgroup analysis based on age groups further underscores the variability in mineral metabolism with age. The significant differences in both calcium and magnesium levels in different age groups (p-values ranging from 0.02 to <0.001) are reflective of the findings by Cappuccio et al. [23], who noted age-related differences in hypertension risk factors.

This study supports the hypothesis that serum calcium and magnesium levels are significantly associated with hypertension. The data aligns with existing literature suggesting a role for these minerals in blood pressure regulation, although some contrasts exist, highlighting the complexity of hypertension pathophysiology. Future research should focus on longitudinal studies to better understand the causal relationships and explore the potential therapeutic implications of modifying serum calcium and magnesium levels in hypertensive patients.

CONCLUSION

The study's findings provide substantial evidence for the role of serum calcium and magnesium levels in the pathophysiology of hypertension. The observed higher serum calcium levels in hypertensive patients (9.8 ± 0.6 mg/dL) compared to normotensive controls (9.4 ± 0.5 mg/dL, $p < 0.001$) align with existing literature, suggesting a potential contributory role of calcium in hypertension. Conversely, the lower serum magnesium levels in the hypertensive group (1.9 ± 0.2 mg/dL) as opposed to the normotensive group (2.1 ± 0.2 mg/dL, $p = 0.003$) support the hypothesis of magnesium's protective role against hypertension.

The study also demonstrated a positive correlation between serum calcium levels and blood pressure severity, and an inverse relationship for magnesium levels, further emphasizing the importance of these minerals in blood pressure regulation. Multivariable analysis indicated that serum calcium and magnesium, along with age and BMI, were significant predictors of hypertension, highlighting the multifactorial nature of this condition.

These findings suggest that monitoring and possibly modifying serum calcium and magnesium levels could be integral to hypertension management strategies. However, the complex nature of hypertension, influenced by a myriad of

genetic, environmental, and physiological factors, necessitates a comprehensive approach to its management. Future studies should focus on longitudinal assessments to unravel the causal relationships further and explore the therapeutic implications of these findings.

REFERENCES

1. Zhou B, Bentham J, Di Cesare M, et al. (2017). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19·1 million participants. *Lancet*. 389(10064):37-55. doi:10.1016/S0140-6736(16)31919-5
2. McCarron DA, Morris CD, Henry HJ, Stanton JL. (1984). Blood pressure and nutrient intake in the United States. *Science*. 224(4656):1392-8. doi:10.1126/science.6729451
3. Dickinson HO, Nicolson DJ, Campbell F, et al. (2006). Calcium supplementation for the management of primary hypertension in adults. *Cochrane Database Syst Rev*. (2):CD004639. doi:10.1002/14651858.CD004639.pub2
4. Ma J, Folsom AR, Melnick SL, et al. (1995). Associations of serum and dietary magnesium with cardiovascular disease, hypertension, diabetes, insulin, and carotid arterial wall thickness: the ARIC study. *J Clin Epidemiol*. 48(7):927-40. doi:10.1016/0895-4356(94)00200-A
5. Barbagallo M, Dominguez LJ, Galioto A, et al. (2003). Role of magnesium in insulin action, diabetes and cardio-metabolic syndrome X. *Mol Aspects Med*. 24(1-3):39-52. doi:10.1016/S0098-2997(02)00090-0
6. Kisters K, Barenbrock M, Louwen F, et al. (1999). Membrane, intracellular, and plasma magnesium and calcium concentrations in preeclampsia. *Am J Hypertens*. 12(5):519-25. doi:10.1016/S0895-7061(99)00010-3
7. Jee SH, Miller ER 3rd, Guallar E, et al. (2002). The effect of magnesium supplementation on blood pressure: a meta-analysis of randomized clinical trials. *Am J Hypertens*. 15(8):691-6. doi:10.1016/S0895-7061(02)02964-3
8. Resnick LM. (1999). Calcium and hypertension: the emerging connection. *Ann Intern Med*. 131(4):311-3. doi:10.7326/0003-4819-131-4-199908170-00011
9. Sowers JR, Zemel MB. (1988). The role of calcium in the regulation of renin secretion. *Am J Hypertens*. 1(3 Pt 2):337S-342S.
10. Thakker RV. (1995). Genetics of blood pressure regulation and its disorders. *Ann N Y Acad Sci*. 758:1-11. doi:10.1111/j.1749-6632.1995.tb24817.x
11. Altura BM, Altura BT. (1995). Magnesium and cardiovascular biology: an important link between cardiovascular risk factors and atherogenesis. *Cell Mol Biol Res*. 41(5):347-59.
12. Maier JA. (2012). Endothelial cells and magnesium: implications in atherosclerosis. *Clin Sci (Lond)*. 122(9):397-407. doi:10.1042/CS20110505
13. Guerrero-Romero F, Rodríguez-Morán M. (2009). The effect of lowering blood pressure by magnesium supplementation in diabetic hypertensive adults with low serum magnesium levels: a randomized, double-blind, placebo-controlled clinical trial. *J Hum Hypertens*. 23(4):245-51. doi:10.1038/jhh.2008.129
14. Houston M. (2011). The role of magnesium in hypertension and cardiovascular disease. *J Clin Hypertens (Greenwich)*. 13(11):843-7. doi:10.1111/j.1751-7176.2011.00538.x
15. Resnick LM, Militianu D, Cunnings AJ, et al. (1999). Direct relation of dietary calcium and blood pressure. *Ann Intern Med*. 130(9):707-11.
16. Forman JP, Giovannucci E, Holmes MD, et al. (2007). Plasma 25-hydroxyvitamin D levels and risk of incident hypertension. *Hypertension*. 49(5):1063-9.
17. Barbagallo M, Dominguez LJ. (2007). Magnesium and hypertension. *Curr Opin Cardiol*. 22(4):310-5.
18. Guerrero-Romero F, Rodriguez-Moran M. (2009). The effect of lowering blood pressure by magnesium supplementation in diabetic hypertensive adults with low serum magnesium levels: a randomized, double-blind, placebo-controlled clinical trial. *J Hum Hypertens*. 23(4):245-51.
19. Zemel MB. (2002). Regulation of adiposity and obesity risk by dietary calcium: mechanisms and implications. *J Am Coll Nutr*. 21(2):146S-151S.
20. Houston M. (2011). The role of magnesium in hypertension and cardiovascular disease. *J Clin Hypertens (Greenwich)*. 13(11):843-7.
21. Peacock M, Liu G, Carey M, et al. (2000). Effect of calcium or magnesium supplementation on blood pressure: a meta-analysis of randomized controlled trials. *J Hum Hypertens*. 14(9):573-8.
22. Halimi JM, Giraudeau B, Vol S, et al. (2002). The risk of hypertension in men: direct and indirect effects of chronic smoking. *J Hypertens*. 20(2):187-93.
23. Cappuccio FP, Kalaitzidis R, Duneclift S, et al. (2000). Unravelling the links between calcium excretion, salt intake, hypertension, kidney stones and bone metabolism. *J Nephrol*. 13(3):169-77.