

Original Article

CORRELATION BETWEEN SERUM CALCIUM LEVEL WITH BLOOD PRESSURE LEVEL IN PATIENTS PRESENTING WITH TYPE 2 DIABETES MELLITUS

Dur Muhammad Khan , Imran Mahfooz Khan, Fawad Ahmad Randhawa and Muhammad Shahid

Objective: To study the relationship between serum calcium level and blood pressure level in patients presenting with type 2 diabetes mellitus.

Methods: This cross sectional study was conducted at East Medical Ward, Department of Medicine Mayo Hospital Lahore. This study was done in six months period from March 10, 2015-Sep 10, 2015. The non-probability consecutive sampling technique was used in this study. Informed consent and demographic information like name, age and address was recorded. Systolic and Diastolic Blood pressure was measured by using standard and absolute sphygmomanometer. 3ml Blood sample of each patient was taken with informed consent and was sent to the laboratory of the hospital to assess serum calcium level (as per operational definition). Reports were assessed and calcium level was recorded. Pearson correlation coefficient was calculated to measure the relationship between serum calcium level and systolic & diastolic blood pressure. pvalue ≤ 0.05 was considered statistically significant.

Results: In our study the mean age of the patients was 59.42 ± 11.02 years, 30% patients were males and 70% patients were females. The mean SBP value of the patients was 140.56 ± 11.35 mmHg and mean DBP value was 87.98 ± 6.11 mmHg. In this study the mean value of calcium level of the patients was 8.22 ± 1.24 mg/dl. The negative correlation was observed in our study between the calcium level and SBP, DBP of the DM patients i.e. $r = -0.665$ & -0.401 respectively

Conclusion: The study concluded that negative correlation was observed between the serum calcium level and the blood pressure level in patients presenting with type 2 diabetes mellitus.

Keywords: Serum Calcium, Type 2 diabetes mellitus, blood pressure.

Introduction

Hypertension is up to three times more common in patients with diabetes contributing its major effect in development of macro vascular complications.¹ Hypertension affects 34% of US adults and African American adults have among the highest rates of hypertension in the world at 44%.² At present, it is estimated that about 1 billion people worldwide have hypertension ($>140/90$ mmHg), and this number is expected to increase to 1.56 billion by 2025.³ According to WHO, the total prevalence of diabetes in 2011 in Pakistan was 12.9 million (10% of total population). It has been estimated that Pakistan is known as the 7th largest country in terms of highest prevalence of diabetes and will be 4th largest by the year 2030.⁴ In a report, it was shown that 18% of people in Pakistan suffer from hypertension with every third person over the age of 40 becoming increasingly vulnerable to a wide range of diseases. It was also mentioned that only 50% of the people with hypertension were diagnosed and that only half of those diagnosed

were ever treated. Thus, only 12.5% of hypertension cases were adequately controlled.⁵ Cardiovascular and kidney functions have a significant dependency on serum calcium levels and calcium homeostasis is an integral part in carrying out the physiologic functions of these systems.⁶ Studies have concluded that there is a significant difference in serum levels of calcium in hypertensive and normotensive individuals. Amongst the different forms of serum calcium that are present in the serum, it's the ionized form that is physiologically active.^{7,8} Extracellular calcium levels are in strict check under the effects of different endocrine systems and any alterations in its normal values may affect the intracellular calcium levels too and possibly can contribute towards development of hypertension.⁹ Behradmanesh S et al inferred a significant inverse correlation between serum calcium and diastolic blood pressure (DBP) ($r = -0.261$, $p = 0.046$). Interestingly, the statistically insignificant reverse relationship was observed with systolic blood pressure (SBP) and serum calcium levels ($r = -0.232$, $p = 0.080$).¹⁰ to make the matters more intriguing and

interesting, Phillips A et al reported way back in early 1990s a significant correlation between serum calcium and both SBP and DBP ($r = 0.15$ and 0.11 , respectively; $P < 0.0001$).¹¹ In order to make these associations more clear this research idea was launched on this relationship of both variables with a rationale to measure the relationship between calcium level and blood pressure (BP) in diabetic patients as hypertension control is of prime importance in diabetics and carries equal weightage as glycemic control to control microvascular and macrovascular complications. Previously mixed results have been noted and different criteria have been employed and the results of those studies few of them are already mentioned provided us with different results of the relationship of these variables. Very weak relationship has been observed which showed that decrease in calcium may cause elevation in BP (negative correlation), while other reported positive correlation (i.e. decrease in calcium may cause decrease in blood pressure). So to resolve this controversy, this study was conducted to study the relationship between BP and serum calcium in diabetic patients. This will help us to plan management option for such cases to prevent them from hazardous events like stroke or MI, as these are very common in diabetic patients.

Methods

A sample size of 150 cases were calculated with 5% type I error, 10% type II error and taking value of correlation coefficient i.e. $r = -0.232$ between serum calcium level and blood pressure of diabetic patients with non-probability consecutive sampling. Patients of age between 40-80 years of either gender with diabetes mellitus (as per operational definition) for at least 1 year were included in the study. Current smokers (>1 pack year), patients taking calcium or vitamin D supplements (on medical record), patients taking antihypertensive medicines (on medical record), patients with CKD patients stages 3 and 4 not taking calcium or vitamin D supplements.¹² were excluded. A total of 150 patients fulfilling the inclusion and exclusion criteria were included in the study from Outpatients Department of Medicine, Mayo hospital, Lahore. Informed consent was obtained. The demographic information like name, age and address was recorded. Systolic and Diastolic Blood pressure was measured by using standard and absolute sphygmomanometer. 3ml Blood sample of each patient was taken with informed consent and was sent to the laboratory of

the hospital to assess serum calcium level. Reports were assessed and calcium levels were recorded. Data was collected in a predesigned proforma. Data was analyzed in SPSS version 20. Mean \pm SD was calculated for age, systolic & diastolic blood pressure and serum calcium level. Frequency and percentage were measured for gender. Pearson correlation coefficient was calculated to measure the relationship between serum calcium level and systolic & diastolic blood pressure. P value ≤ 0.05 was considered statistically significant.

Results

In this study a total of 150 cases were enrolled.

Table-1: Descriptive statistics.

	SBP	DBP	Serum Calcium
Mean	140.56	87.98	8.22
SD	11.35	6.11	1.24
Minimum	120.00	80.00	6.00
Maximum	160.00	100.00	10.20

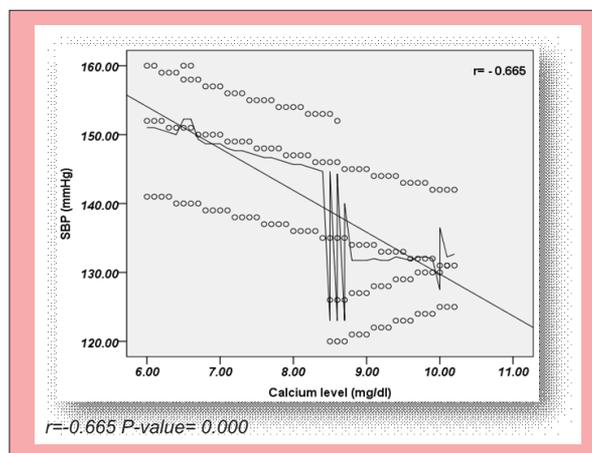


Fig-1: Correlation between the calcium level & SBP.

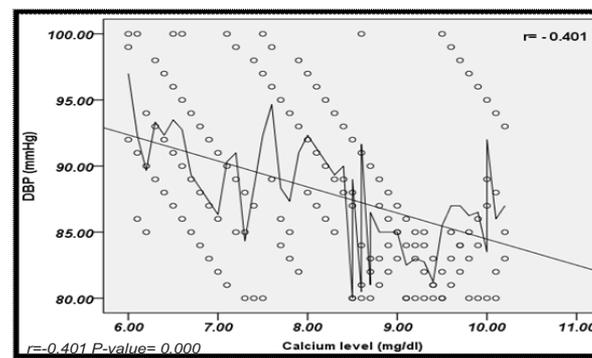


Fig-2: Correlation between the calcium level & DBP.

The mean age of the patients was 59.42 ± 11.02 years with minimum and maximum ages of 41 & 80 years respectively. Out of 150 cases, 70% patients were males and 30% patients were females. The male to female ratio of the patients was 2.3:1. In our study the mean duration of DM of the patients was 2.44 ± 0.92 years with minimum and maximum duration of 1 & 4 years respectively. The study results showed that 76% patients were on treatment of DM and 24% were treatment naive. Furthermore, the mean SBP value of the patients was 140.56 ± 11.35 mmHg with minimum and maximum SBP values of 120 & 160 mmHg respectively. The study results showed that the mean DBP value of the patients was 87.98 ± 6.11 mmHg with minimum and maximum DBP values of 80 & 100 mmHg respectively. In this study, the mean value of calcium level of the patients was 8.22 ± 1.24 mg/dl with minimum and maximum levels of 6 & 10.20 mg/dl respectively. (Table#1) The negative correlation was observed in our study between the calcium level and SBP of the DM patients i.e. $r = -0.665$. (Fig-1) The weak negative correlation was observed in our study between the calcium level and DBP of the DM patients i.e. $r = -0.401$. (Fig-2)

Discussion

This present cross sectional study was conducted at East Medical Ward, Department of Medicine, Mayo Hospital, Lahore to assess the correlation coefficient between serum calcium level and blood pressure level in patients presenting with type 2 diabetes mellitus. Diabetes mellitus is a systemic disease that adversely affects the quality and length of life by exerting its deleterious impact on cardiovascular events and sudden death. The prevalence of diabetes increases with age, with over 25% of the elderly having type 2 diabetes. Epidemiological studies have stated that interestingly there are up to 6 times more Non-Caucasians that are type 2 diabetics than Caucasians.¹³ In this study, the mean value of calcium level of the patients was 8.22 ± 1.24 mg/dl, the mean value of SBP & DBP were 140.56 ± 11.35 mmHg & 87.98 ± 6.11 mmHg respectively. There was an inverse relationship observed between the calcium level and systolic as well as diastolic blood pressures in diabetics i.e. $r = -0.665$, -0.401 respectively. Studies conducted around the globe have mixed results. A number of epidemiological studies suggested an inverse relationship between serum calcium and blood pressure level.¹⁴⁻¹⁶

Kesteloot et al inferred positive correlation between total serum calcium positively and blood pressure in male subjects, while 24-h urinary excreted calcium positively correlates with blood pressure. In a subgroup of 297 male subjects no correlation was found between the serum ionized calcium level and blood pressure.¹⁷ To make the things more controversial and at the same times intriguing, Folsom reported an inverse association between serum ionized calcium and hypertension though the sample size was small.¹⁸ One recent study found that a significant inverse correlation of serum calcium with level of DBP ($r = -0.261$, $p = 0.046$) was seen. In addition, a negative correlation of SBP with level of serum calcium was observed, however, this correlation was not significant ($r = -0.232$, $p = 0.080$). Vargas and coworkers, in a previous study using NHANES III data, reported an inverse association between serum ionized calcium and hypertension in the subgroup of younger Mexican-American men only.¹⁹ Hunt et al studied 875 normotensive patients and described a positive association between ionized calcium and BP among the high renin group and an inverse association between ionized calcium and BP among the low renin group.²⁰ On the contrary, some studies showed positive relationship between the serum calcium level and hypertension. A cross sectional study conducted by Philips and colleagues involving 7735 healthy middle-aged men, reported that higher serum total calcium was associated with hypertension. They demonstrated a small but significant correlation between serum calcium and both SBP and DBP ($r = 0.15$ and 0.11 , respectively) after adjusting for age. This association was diminished after adjustment for serum albumin, but remained significant ($r = 0.10$ and 0.07 ; P less than 0.0001).¹¹ Rinner and coworkers, in a small sample of 182 Dutch adults, reported that higher serum total calcium was positively associated with hypertension after adjusting for age, BMI, and albumin and in the subgroup analysis stratified by sex, the association was found to be stronger in women than in men.²¹ Gruchow et al showed in their study that the associations of age, BMI, gender, and alcohol with blood pressure were not affected by calcium levels.²² So it was worth an effort conducting this study to determine the reasons for these different results. May be gender, race and environments and genetic factors all play their part in this association.

Conclusion

The study results concluded that the negative correlation was observed between the serum calcium

Levels and the blood pressure level in patients presenting with type 2 diabetes mellitus. Further cohort studies need to be conducted to observe whether calcium replacement in hypocalcemic normotensive type 2 diabetic patients can prevent the development of hypertension and the study

should expand and should include non-diabetics as well to see the pattern.

*Department of Medicine
King Edward Medical University
www.esculapio.pk*

References

- Whalen KL, Stewart RD. Pharmacologic management of hypertension in patients with diabetes. *American family physician*. 2008;78(11):1277-82.
- Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation*. 2010 Feb 23;121(7):e46-e215.
- Sarafidis PA, Li S, Chen SC, Collins AJ, Brown WW, Klag MJ, et al. Hypertension awareness, treatment, and control in chronic kidney disease. *Am J Med*. 2008 Apr;121(4):332-40.
- Pakistan DI. Diabetes Statistics in Pakistan. [Online] 2013, May 8 [cited 2015 Mar 8] Available from:URL:(<http://diabetespakistans.com/treatment/2013/05/08/diabetes-statistics-in-pakistan/>)
- Vijan S. Type 2 diabetes. *Annals of internal medicine*. 2010;152(5):ITC3-1.
- Sabanayagam C, Shankar A. Serum calcium levels and hypertension among US adults. *The Journal of Clinical Hypertension*. 2011;13(10):716-21.
- Hazari MAH, Arifuddin MS, Muzzakar S, Reddy VD. Serum calcium level in hypertension. *North American journal of medical sciences*. 2012;4(11):569.
- Barret KE, Barman SM, Boitano S, Brooks H. Hormonal control of calcium and phosphate metabolism and the physiology of bone. In: Barret KE, Barman SM, Boitano S, Brooks H, editors. *Ganong's Review of Medical Physiology*. 23rd ed. New York: Mc-Graw Hill Companies; 2011. p.363-75.
- Baradaran A, Behradmanesh S, Nasri H. Association of body mass index and serum vitamin D level in healthy Iranian adolescents. *Endokrynologia Polska*. 2012;63(1):29-33.
- Behradmanesh S, Nasri H. Association of serum calcium with level of blood pressure in type 2 diabetic patients. *Journal of nephropathology*. 2013;2(4):254.
- Phillips A, Shaper A. Serum calcium and blood pressure. *Journal of human hypertension*. 1991;5(6):479-84.
- Clinical practice guideline. Vitamin D therapy in CKD patients. 2015 [cited 2015]; Available from:http://www2.kidney.org/professionals/KDOQI/guidelines_bone/Guide8A.htm
- med.umich.edu. Management of Type 2 Diabetes Mellitus. 2014 [cited 2015]; Available from: <http://www.med.umich.edu/1info/FHP/practiceguides/diabetes/dm.pdf>.
- Geleijnse J, Witteman J, Bak A, Den Breeijen J, Grobbee D. Long-term moderate sodium restriction does not adversely affect the serum HDL/total cholesterol ratio. *Journal of human hypertension*. 1995;9(12):975-9.
- Moore TJ, McKnight JA. Dietary factors and blood pressure regulation. *Endocrinology and metabolism clinics of North America*. 1995;24(3):643-55.
- Morris CD, Reusser ME, editors. Calcium intake and blood pressure: epidemiology revisited. *Seminars in nephrology*; 1995.
- Kesteloot H. Epidemiological studies on the relationship between sodium, potassium, calcium, and magnesium and arterial blood pressure. *Journal of cardiovascular pharmacology*. 1984;6:S192.
- Folsom AR, Smith CL, Prineas RJ, Grimm R. Serum calcium fractions in essential hypertensive and matched normotensive subjects. *Hypertension*. 1986;8(1):11-5.
- Vargas CM, Obisesan T, Gillum RF. Association of serum albumin concentration, serum ionized calcium concentration, and blood pressure in the Third National Health and Nutrition Examination Survey. *Journal of clinical epidemiology*. 1998;51(9):739-46.
- Hunt J, Dean R, Wolff S. Hydroxyl radical production and autoxidative glycosylation. Glucose autoxidation as the cause of protein damage in the experimental glycation model of diabetes mellitus and ageing. *Biochem J*. 1988;256:205-12.
- Rinner MD, Spliet-van Laar L, Kromhout D. Serum sodium, potassium, calcium and magnesium and blood pressure in a Dutch population. *Journal of hypertension*. 1989;7(12):977-81.
- Gruchow H, Sobocinski K, Barboriak J. Calcium intake and the relationship of dietary sodium and potassium to blood pressure. *The American journal of clinical nutrition*. 1988;48(6):1463-70.