



Correlation between Calcium Phosphorus Product and Mean Arterial Pressure among Hemodialysis Patients with End Stage Renal Disease

Muhammad Nadeem^{1*}, Mansoor Abbas Qaisar², Ali Hassan Al Hakami³, Fateh Sher Chattah⁴, Muhammad Muzammil⁵ and Muhammad Kamran Ameer⁶

1. King Fahad Central Hospital, Gizan, Kingdom of Saudi Arabia
2. Diaverum, Hail, Kingdom of Saudi Arabia
3. King Fahad Central Hospital, Jazan, Kingdom of Saudi Arabia
4. Prince Sultan Military Hospital, Riyadh, Kingdom of Saudi Arabia
5. Bakhtawar Amin Medical and Dental College, Multan, Pakistan
6. Multan Medical and Dental College, Multan, Pakistan

*Correspondence: docmnadeem@gmail.com

Keywords: Calcium Phosphorous Product, Chronic Kidney Disease, End Stage Renal Disease, Mean Arterial Pressure

doi: 10.37978/tijfs.v5i1.324

Submitted: July 20, 2020
Accepted: August 19, 2020
Published Online: December 16, 2020

How to cite this: Nadeem, M. Qaisar, M.A., Al Hakami, A.H., Chattah, F.S., Muzammil, M. and Ameer, M.K. 2020. Correlation between Calcium Phosphorus Product and Mean Arterial Pressure among Hemodialysis Patients with End Stage Renal Disease. Int J Front Sci, 5(2).



Significance:

The mean arterial pressure serves as an expression of blood pressure in patients on chronic hemodialysis. Serum calcium phosphorus product is considered as a risk factor of vascular calcification that is associated with hypertension in the patients of end stage renal disease. The literature regarding this relationship is inconsistent therefore this study is designed to determine the correlation between calcium phosphorus product and mean arterial pressure among hemodialysis patients with end stage renal disease.

ABSTRACT

Background: The mean arterial pressure serves as an expression of blood pressure in patients on chronic hemodialysis. Serum calcium phosphorus product is considered as a risk factor of vascular calcification that is associated with hypertension in the patients of end stage renal disease. The literature regarding this relationship is inconsistent therefore this study is designed to determine the correlation between calcium phosphorus product and mean arterial pressure among hemodialysis patients with end stage renal disease.

Methods: A total of 110 patients of end stage renal disease on hemodialysis for at least one year, 20 to 60 years of age were included. Patients with primary or tertiary hyperparathyroidism, peripheral vascular disease, malignancy, hypertension secondary to any cause other than kidney disease were excluded. Mean arterial pressure was calculated according to the standard protocol in lying position. Blood samples for estimation of serum calcium and phosphorous were taken and was sent immediately to the laboratory for serum analysis.

Results: Mean age was 44.17 ± 10.94 years. Mean calcium phosphorous product was 46.71 ± 7.36 mg/dl and mean arterial pressure was 103.61 ± 12.77 mmHg. The values of Pearson correlation co-efficient (r) were 0.863 for age group 20 to 40 years and 0.589 for age group 41 to 60 years. This strong positive correlation means that high calcium phosphorous product goes with high mean arterial pressure (and vice versa) for both the age groups.

Conclusion: A strong positive relationship exists between the mean arterial pressure and calcium phosphorous product and is independent of patients' age.

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem. In the United States, chronic kidney disease is the ninth leading cause of death and recently there has been upsurge both in the incidence and prevalence of kidney failure (1). About 90% patients of CKD suffer from hypertension that is a major risk factor for progression towards end stage renal disease (ESRD) (2,3). Oppositely the progressive renal disease may also exacerbate uncontrolled hypertension due to volume expansion and increased systemic vascular resistance (4). The leading cause of mortality in patients with ESRD is cardiovascular disease (5). Compared with the general population, dialysis patients have a 3 to 30 folds increase in mortality, depending on the age group examined (6). Thus, it is of utmost importance to explore the causative agents of hypertension and exterminate them to halt the progression of both renal and cardiovascular ailments.

Blood pressure is multi-factorial, and its management is quite a challenge in patients with ESRD. In patients on chronic hemodialysis, hypertension is monitored in terms of Mean Arterial Pressure (MAP) instead of measuring systolic and diastolic blood pressure (7). Serum calcium phosphorus product is considered as an indicator of vascular calcification that aggravates hypertension in the patients of ESRD (8). These calcifications are equal to bone formation resulting from vascular smooth muscle differentiation as evident in patients of CKD and lead to higher mortality attributed to increased left ventricular after-load and disturbed coronary perfusion (9).

Jean et al. concluded that vascular calcifications are highly prevalent in hemodialysis patients and not linked to blood pressure (10). However, Adragao et al. conducted a prospective study and concluded that higher vascular calcification scores in dialysis patients were significantly associated with MAP and coronary artery disease (11). In another cross-sectional study conducted by Ashkar, it was cited that calcium phosphorous product (CPP) is positively associated with MAP and unrelated to pulse pressure (12). The inconsistency of the results regarding relationship between CPP and MAP is apparent in the existing literature thus this study is

designed to explore further evidence regarding the relationship between CPP and MAP and its dependency upon age.

Materials and Methods

Study was approved by Ethical Review committee of King Fahad Central Hospital, Gizan, Kingdom of Saudi Arabia. Total of 110 volunteer male and female patients with permitted range for age, 20 to 60 years with ESRD were selected by non-probability consecutive sampling at nephrology department of hospital. A detailed informed written consent was obtained from all the patients. Patients either having pre-dialysis glomerular filtration rate less than 15ml per minute or the patients requiring at least two session a week for last one year were declared cases of ESRD. Patients were excluded after being scrutinized for primary or tertiary hyperparathyroidism, diabetic mellitus, peripheral vascular disease, malignancy, calciphylax is and secondary hypertension unrelated to kidney disease.

MAP was determined by taking the resting systolic and diastolic blood pressure of the patients in lying position before and after dialysis. Averages of the pre-dialysis and post-dialysis systolic and diastolic blood pressures were taken as final reading. Mean arterial pressure was calculated using the formula:

$$\text{MAP} = 2/3 (\text{diastolic pressure}) + 1/3 (\text{systolic pressure})$$

Corrected serum calcium levels were used according to serum albumin.

Serum Calcium corrected= serum calcium + 0.8(4 – serum albumin mg/dl).

Serum calcium phosphorous product was calculated by multiplying the corrected serum calcium level in mg/dl with serum level of phosphorous in mg/dl. Blood samples for estimation of serum calcium and phosphorous were taken by using aseptic measures and was sent immediately to the laboratory for serum analysis.

Data was entered and analyzed using SPSS version 25. Numerical variable i.e. age, MAP and CPP were summarized as mean and standard deviation. Pearson correlation coefficient (r) was calculated to measure the correlation between CPP and MAP.

Results:

Age range in this study was from 20 to 60 years with mean age of 44.17 ± 10.94 years. 66 patients (60%) were between 41 to 60 years of age and 44 patients (40%) were between 20 to 40 years of age.

Mean calcium phosphorous product was 46.71 ± 7.36 mmHg and mean arterial pressure was 103.61 ± 12.77 mmHg. The values of Pearson correlation coefficient (r)

were 0.863 for age group 20 to 40 years (Figure 1) and 0.589 for age group 41 to 60 years (Figure 2).

Correlation between calcium phosphorous product and mean arterial pressure for both the age groups showed strong positive correlation. This correlation was stronger in age group 20 to 40 years than age group 41 to 60.

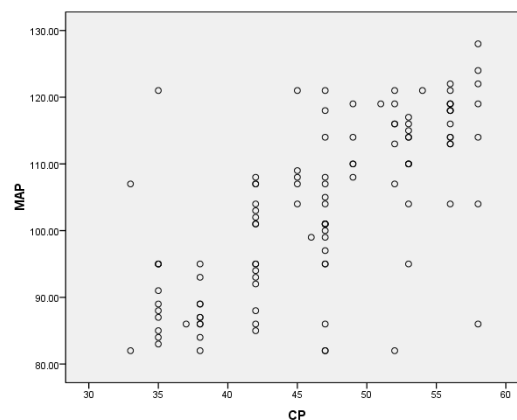


Figure 1: Correlation graph between Calcium phosphorous product and Mean arterial pressure with respect to age 41-60 years (n=66) (r =0.589)

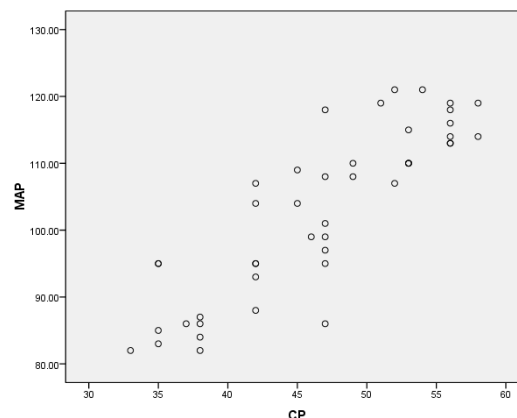


Figure 2: Correlation graph between Calcium phosphorous product and Mean arterial pressure with respect to age 20-40 years (n=44) (r = 0.863)

Discussion

In our study the value of Pearson correlation coefficient (r) is > 1 declaring a strong positive correlation between CPP and MAP thus higher the calcium phosphorous product higher will be the mean arterial pressure (and vice versa).

Our investigation was in agreement with Block et al., who analyzed a random sample of 2669 patients haemodialysed for more than 1 year (mean 4.5 years) and reported that higher the CPP higher is the mortality risk (13). In a cross-sectional study on fifty four hemodialysis patients during a 6-month period, linear

regression analysis as applied on the averages of CPP and blood pressures concluded that CPP was significantly associated with pre-dialysis systolic BP and diastolic BP, pre-dialysis MAP, and post-dialysis diastolic BP (12). Strozecki et al., investigated the predisposing factors for cardiac valve calcifications and revealed that no significant correlations were found with respect to calcium, phosphorus, and calcium-phosphorus product (14). Similarly, Menon et al., concluded in a randomized cohort study of renal disease that serum phosphate levels and CPP were statistically unrelated to cardiovascular disease linked mortality (15). However Petrovic et al., performed uni-variate regression analysis to confirm that serum phosphate levels and CPP are vital risk factors for the development of aortic valve calcifications (16). In contrast to our study Goodman et al., showed no significant differences in Blood Pressure among patients with or without calcifications (8). Jean et al., also reported similar results in dialysis patients (10). Adragao et al., have publicized that higher vascular calcification scores in dialysis patients were associated with higher mean arterial pressure (11). The total serum calcium x phosphate product is an indicator of the risk of mineral crystallization in soft tissues, (17) which can lead to cutaneous and systemic calciphylaxis, conjunctival precipitation, visceral and in particular, cardiovascular calcification (18). Lundin et al first identified an elevated CPP as a predictor of cardiac mortality along with age at onset of dialysis and sustained hypertension (19). In hemodialysis patients, the pathogenesis of vascular calcification is multifaceted and the process includes certain factors that may promote or inhibit calcification (16). An elevated Ca_xP combination is likely to be a predominant risk factor and Ca alone may also be problematic because, in general, a positive Ca balance may blood pressure and calcium phosphorous product, so maintaining a tight control of calcium phosphorous product will help to manage hypertension by administration of drugs, leading to improved management and decreased the mortality and morbidity associated with hypertension. Promote or accelerate soft-tissue and vascular calcification even in the absence of hypercalcemia (20). On the whole, it is concluded that there is a strong positive relationship between

Conclusion

The study concludes that in patients of ESRD there is a strong positive correlation between the serum calcium phosphorous product and mean arterial pressure in both age groups (20-40years and 41-60 years).

Conflict of interest: Authors do not have any conflict of interest to declare.

Disclosure: None

Human/Animal Rights: No human or animal rights are violated during this study.

References

- Guan G, Kramer SF, Bellinger LL, Wellman PJ, Kramer PR. Intermittent nicotine administration modulates food intake in rats by acting on nicotine receptors localized to the brainstem. *Life Sci.* 2004;74(22): 2725–37. Available from: <https://doi.org/10.1016/j.lfs.2003.10.015>
- Buffet L, Ricchetti T. Chronic Kidney Disease and Hypertension: A Destructive Combination. *Nephrol.* 2012;37(6):26-9.
- Kazancıoğlu R. Risk factors for chronic kidney disease: an update. *Kidney Int Suppl.* 2013;3(4): 368-71. Available from: <https://doi.org/10.1038/kisup.2013.79>
- Yudkin JS. World Kidney Day: hypertension and chronic kidney disease. *Lancet.* 2009;373: 1157-8. Available from: DOI:10.1016/S0140-6736(09)60355-X
- Thakar CV, Christianson A, Himmelfarb J, Leonard AC. Acute kidney injury episodes and chronic kidney disease risk in diabetes mellitus. *Clin J Am Soc Nephrol.* 2011;6(11):2567-72. Available from: <https://doi.org/10.2215/CJN.01120211>
- Tetta C, Gallieni M, Panichi V, Brancaccio D. Vascular calcifications as a footprint of increased calcium load and chronic inflammation in uremic patients: A need for a neutral calcium balance during hemodialysis? *Int J Artif Organs.* 2002;25(1):18–26. Available from: <https://doi.org/10.1177/039139880202500104>
- Sesso HD, Stampfer MJ, Rosner B, Hennekens CH, Gaziano JM, Manson JE et al. Systolic and diastolic blood pressure, pulse pressure, and mean arterial pressure as predictors of cardiovascular disease risk in men. *Hypertension.* 2000;36(5): 801-7. Available from: <https://doi.org/10.1161/01.HYP.36.5.801>
- Goodman WG, Goldin J, Kuizon BD, Yoon C, Gales B, Sider D, et al. Coronary artery calcification in young adults with end-stage renal disease who are undergoing dialysis. *N Engl J Med.* 2000;342(20):1478-83. Available from: DOI: 10.1056/NEJM200005183422003
- London GM, Marchais SJ, Guérin AP, Métivier F. Arteriosclerosis, vascular calcifications and cardiovascular disease in uremia. *Curroinnephrolhypertens.* 2005;14(6):525-31. Available from: doi: 10.1097/01.mnh.0000168336.67499.c0
- Jean G, Bresson E, Terrat JC, Vanel T, Hurot JM, Lorriaux C, et al. Peripheral vascular calcification in long-haemodialysis patients: Associated factors and survival consequences. *Nephrol Dial Transplant.* 2009;24(3):948–55. Available from: <https://doi.org/10.1093/ndt/gfn571>
- Adragao T, Pires A, Lucas C, Birne R, Magalhaes L, Goncalves M, et al. A simple vascular calcification score predicts cardiovascular risk in haemodialysis patients. *Nephrol Dial Transplant.* 2004;19(6):1480–8. Available from: <https://doi.org/10.1093/ndt/gfh217>
- Ashkar ZM. Association of Calcium-Phosphorus Product with Blood Pressure in Dialysis. *J Clin Hypertens.* 2010;12(2):96-103. Available from: <https://doi.org/10.1111/j.1751-7176.2009.00220.x>
- Block GA, Wheeler DC, Persky MS, Kestenbaum B, Ketteler M, Spiegel DM, et al. Effects of phosphate binders in moderate CKD. *J Am Soc Nephrol.* 2012;23(8):1407-15. Available from: doi: 10.1681/ASN.2012030223
- Stróżecki P, Odrowaz-Sypniewska G, Manitus J. Cardiac valve calcifications and left ventricular hypertrophy in hemodialysis patients. *Ren Fail.* 2005;27(6):733-8. Available from: <https://doi.org/10.1080/08860220500243296>
- Menon V, Greene T, Pereira AA, Wang X, Beck GJ, Kusek JW, et al. Relationship of phosphorous and calcium-Phosphorous Product with mortality in CKD. *Am J Kidney Dis.* 2005;46(3):455-63. Available from: <https://doi.org/10.1053/j.ajkd.2005.05.025>
- Petrović D, Obrenović R, Stojimirović B. Risk factors for aortic valve calcification in patients on regular hemodialysis. *Int J Artif Organs.* 2009;32(3):173-9. Available from: <https://doi.org/10.1177/039139880903200308>

17. Alfrey AC, Ibels LS. Role of phosphate and pyrophosphate in soft tissue calcification. *AdvExp Med Biol.* 1978;103:187–93. Available from: https://doi.org/10.1007/978-1-4684-7758-0_20
18. Braun J, Oldendorf M, Moshage W. Electron beam computed tomography in the evaluation of cardiac calcification in chronic dialysis patients. *Am J Kidney Dis* 1996;27(3):394–401. Available from: [https://doi.org/10.1016/S0272-6386\(96\)90363-7](https://doi.org/10.1016/S0272-6386(96)90363-7)
19. Lundin AP III, Adler AJ, Feinroth MV. Maintenance hemodialysis. Survival beyond the first decade. *JAMA.* 1980;244(1):38–40. Available from: [doi:10.1001/jama.1980.03310010024021](https://doi.org/10.1001/jama.1980.03310010024021)
20. Klemmer P. Calcium loading, calcium accumulation, and associated cardiovascular risks in dialysis patients. *Blood Purif.* 2005;23(1):12–9. Available from: <https://doi.org/10.1159/000083713>

