

Serum Selenium levels in Essential hypertension among adults at the University Teaching Hospital, Lusaka, Zambia

AC Chisulo¹, N Lambwe², G Sijumbila³, M Mukosha^{4*}

¹University of Zambia School of Medicine Department of Physiological Sciences

²University Teaching Hospital Lusaka, Zambia.

³Mulungushi University School of Medicine Livingstone Campus

⁴University of Zambia School of Health Sciences Department of Pharmacy

ABSTRACT

In Zambia, essential hypertension is one of the commonest and prevalent non-communicable diseases. In the current medical literature it is not clear on the serum selenium levels among essential hypertensive patients in Zambia despite evidence in literature of its role in development of hypertension.

The present study investigated serum selenium levels in essential hypertensive adults. We hypothesized that serum selenium levels were significantly lower in this population and was a risk factor for developing hypertension. An analytical cross-sectional design was applied to a total of 245 participants. Blood was collected for serum levels of Selenium, glucose, urea, creatinine and electrolytes. Student t-test was used to compare the serum selenium levels between hypertensive and normotensive participants. Significant ($p < 0.0001$) lower levels of serum Selenium were observed in essential hypertensive adults ($0.093 \text{ mg/L} \pm 0.048$) than in healthy normotensive adults ($0.109 \text{ mg/L} \pm 0.047$). Regression results showed no significant relationship off Selenium levels with age ($p = 0.255$), BMI ($p = 0.232$), systolic blood pressure ($p = 0.175$) and diastolic blood pressure ($p = 0.195$). From these findings serum selenium

levels may not be a risk factor for essential hypertension in this population. Nevertheless, more studies in the same geographical area are needed to confirm this.

INTRODUCTION

Non-communicable diseases are on the rise worldwide with the highest burden in Sub-Saharan Africa. Hypertension affects about one billion people worldwide and about nine million people die annually. In Zambia hypertensive disorders are responsible for increased morbidity and mortality accounting for 18.39 % per 100000 deaths annually. The probability of dying from non-communicable disease in Zambia is currently at 18%. Lifestyle changes and nutritional aspects modification has been shown to play a significant role in prevention of cardiovascular disease. Selenium (Se) in particular has attracted attention for its role in cardiovascular diseases such as hypertension. A number of studies from literature have linked Selenium with hypertension thus indicating its possible role in this condition. Hypertension is systolic blood pressure ≥ 140 mmHg and/or a diastolic pressure ≥ 90 mmHg. 95% of all hypertensive cases are due to Essential hypertension (primary hypertension) while 5% are due to the secondary causes of hypertension. Essential hypertension refers to the majority high blood pressure with no known cause.

*Corresponding author

Mukosha Moses
University of Zambia,
School of Health Sciences
Department of Pharmacy
mukoshamoses@yahoo.com

Key words: Hypertension, Essential hypertension, Selenium and Reactive Oxygen species (ROS).

Hypertension can develop as a consequence of oxidative stress damage to the endothelium leading to increased peripheral resistance in the blood vessels.

In the cardiovascular system, ROS play a physiological role in controlling processes that contribute to endothelial dysfunction and cardiovascular remodeling in hypertension and other cardiovascular diseases. Selenium a co-factor of antioxidant enzyme is found incorporated in some antioxidant enzymes such as glutathione peroxidase (GPx). Antioxidant enzymes are crucial in prevention of oxidative stress and normal antioxidant signaling. Selenium is obtained from animal or plant food sources but mostly from a plant diet; Selenium plant content is dependent on the soil content of selenium. In Zambia, the soil selenium content is reportedly low which could explain the hypothesized deficiency in the Zambian population.

It is not clear from the current medical literature the serum selenium levels among the population at risk for cardiovascular diseases (CVDs) in Zambia a Low middle income country with a high burden of CVDs. Furthermore the high malnutrition levels and poor diet may be contributing to the observed high prevalence of these conditions. The current study aimed at establishing the serum selenium levels in essential hypertension in adults at UTH, Lusaka, Zambia. We are excited because the findings from this study can help the clinicians and the policy makers to develop simple cost effective interventions to better the outcomes of patients with CVDs.

MATERIALS AND METHODS

The study was conducted at the University Teaching Hospital (UTH), the largest tertiary hospital in Zambia. It receives referral cases from all over Zambia and provides treatment services for most of the population in Lusaka. The study was an analytical cross-sectional. The target population was hypertensive patients being attended to from clinic 5 and controls were participants who were healthy that

were coming to filter clinic (screening point for medical conditions) for minor ailments. Participants aged 18-65 years who were willing to take part in the study and signed informed consent forms were enrolled. Participants were systematically sampled where every 3rd person was selected and matched by age and sex. They were selected for the study only after thorough medical examination by the Physician on duty to rule out secondary causes of hypertension and chronic diseases. Those who were obese, chronically ill, pregnant, smokers or with secondary causes of hypertension were excluded from the study. A total of 245 participants were enrolled; 126 hypertensive and 119 control participants with 1 excluded from the study. The sample size was calculated based on comparison of two groups

8 mls of venous blood was collected from the antecubital vein for the purpose of establishing serum levels of Selenium, glucose, urea, creatinine and electrolytes. Two aliquots of blood in 4 mls vacutainers free from any elements were collected. The blood was first centrifuged to obtain serum and stored at - 20 °C if not analysed immediately. All blood samples were analysed within 24 hours of collection. The current age was noted. Weight (Kg) was measured using a beam balance, height (m) was determined using a height measuring scale. BMI (Kg/m²) was calculated from the weight and height.

Serum Selenium levels were determined by graphite furnace atomic absorption spectroscopy with Zeeman correction background using an ANALYTIK JENA –ContrAA700 AAS based on the method of Jacobson et al. Serum Selenium levels were determined at wavelength of 196 nm. Creatinine concentration was determined using the Jaffe method at 520 nm to 800 nm; urea by the enzymatic method of Talke and Schubert at 340 nm; and glucose based on developed by Stein at 340/380 nm using the Beckman coulter 480 clinical chemistry analyser. The concentration of electrolytes – sodium and potassium was determined using an ABX Pentra 400..

Means and standard deviations were used to describe normally distributed data as well as percentages and frequencies for non-parametric data. STATA software version 15 was used for the analysis and complimented with graph pad prism for graphical presentations.

Before conducting this study the protocol was first submitted for ethical consideration to ERES CONVERGE which reviewed and approved the study.

RESULTS

Demographic characteristics

Several demographic and other characteristics of the participants were captured. Among these include: age, gender, weight and height to mention a few. Gender was the only categorical variable and percentages and frequencies were used to describe the gender distribution (fig 1). The selenium levels was non parametric in the two groups and Mann Whitney test showed a significant ($p<0.0001$) difference in mean serum selenium levels between male and female participants. The majority slightly over 50% of the participants in both normotensive ($n=60$) and essential hypertensive ($n= 65$) cases were female adults and this was compared to males where about 50% ($n= 59$) were normotensive and about 48% ($n=61$) were hypertensive.



Figure 1: Mean serum selenium levels in male and female participants

There was no significant difference in age ($p=0.33$), height ($p=0.21$), creatine ($p=0.89$), potassium ($p=0.51$) and sodium ($p=0.52$) between normotensive and essential hypertensive (tab 1). However, there was a significant difference in systolic blood pressure ($p<0.001$), diastolic blood pressure ($p<0.001$), pulse ($p<0.001$), Urea ($p=0.001$), Glucose ($p<0.001$), BMI ($p<0.001$) and serum selenium ($p<0.0001$) between the two groups.

Table 1: Mean serum selenium levels in normotensive and essential hypertensive participants

Variables	Normotensive (n=119)	SD	Essential Hypertensive (n=119)	SD	Difference	P-value
Age (years)	46.98	10.00	46.98	10.00	0	1
Sys-BP (mmHg)	111.99	10.07	159.4	10.07	47.37	<0.001
Dias-BP (mmHg)	72.53	10.19	96.54	10.19	24	<0.001
Pulse (beats/min)	70.92	5.430	75.80	5.427	4.88	<0.001
Height (m)	1.67	0.092	1.65	0.092	-0.020	0.080
Weight (kg)	66.37	10.77	69.09	10.77	2.723	0.073
Selenium (mg/L)	0.109	0.047	0.093	0.048	-0.016	<0.0001
Urea (mmol/L)	3.71	1.070	4.09	1.070	0.379	0.008
Creatinine (umol/L)	70.71	9.770	70.38	9.770	-0.329	0.848
Potassium (mmol/L)	4.36	0.550	4.410	0.550	0.051	0.496
Sodium (mmol/L)	139.61	2.86	139.96	2.86	0.36	0.397
Glucose	4.26	0.67	4.52	0.668	0.265	0.010
BMI (kg/m ²)	23.88	3.40	25.42	3.40	1.54	<0.001

The paired t-test results of serum selenium levels between normotensive and hypertensive participants showed statistically significant difference in means between the two groups (table 2). Based on the p value of less than 0.0001, we were able to reject the null hypothesis that the difference was equal to zero

Table 2: mean serum selenium levels in hypertensive and normotensive participants matched cases

Paired t test

Variable	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf. Interval]
hypert-n	119	.0928992	.0044445	.0488839	.0840970 .1017005
normot-e	119	.1088493	.0043325	.0472625	.1002607 .11742
diff	119	-.0159412	.0066122	.0966782	-.0171535 -.0147289

mean(diff) = mean(hypertensioa - normotensive) t = -26.0397
 Ho: mean(diff) = 0 degrees of freedom = 118
 Ha: mean(diff) < 0 Ha: mean(diff) != 0 Ha: mean(diff) > 0
 Pr(T < t) = 0.0000 Pr(|T| > |t|) = 0.0000 Pr(T > t) = 1.0000

To determine the association between serum Selenium levels BMI, age, and blood pressure multivariate regression analysis was applied. Figure 2 presents the results from the regression model. There was no significant relationship among the variables (BMI ($p=0.232$), age ($p=0.255$), systolic blood pressure ($p=0.176$) and diastolic ($p=0.195$)), though we noted a negative correlation between systolic blood pressure and serum selenium levels.

DISCUSSION

The present cross-sectional study reports a significant difference in serum selenium levels between normotensive (0.109 ± 0.047 mg/L) and essential hypertensive (0.093 ± 0.048 mg/L) participants ($p<0.0001$). These results are in line with the findings by Babalola et al (2007) who reported lower levels of selenium in hypertensive individuals (0.136 ± 0.028 mg/L)) compared to normotensive (0.188 ± 0.026 mg/L). Similarly, Nawrot et al (2007) also reported low levels of selenium in hypertensive adults (97 ± 19.0 mg/L or 0.097 ± 0.019 mg/L) though he did not have comparative group. In addition, da Silva (2017) also reported serum selenium levels to be higher in the normotensive group (0.0564 ± 0.0153 mg/L) than in the hypertensive group (0.0532 ± 0.0152 mg/L) though the difference was not significant and the said study was conducted in pregnant women . In contrast, other studies have reported higher levels of selenium in hypertensive adults but with no comparative groups . The geographical location of an area determines the levels of Selenium in the soil and thus could be used to explain differences in the serum Selenium levels in adults from a given region.

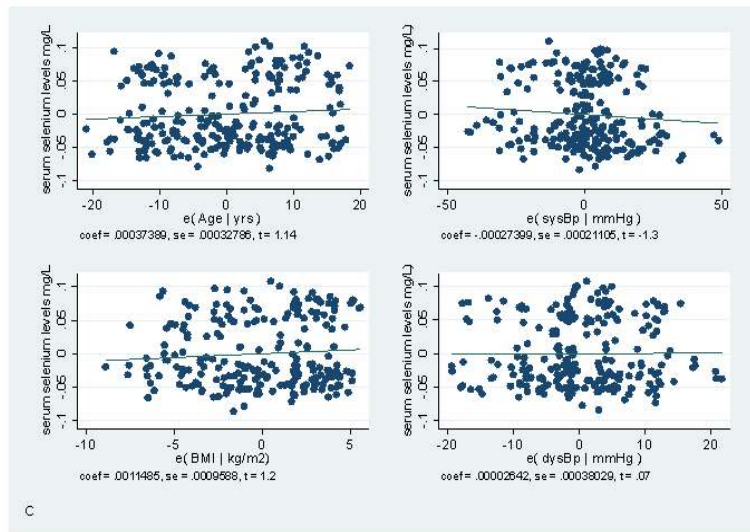


Figure 2: Regression analysis of serum selenium levels with BMI, age and blood pressure

Selenium levels in normotensives and essential hypertension were compared by gender and it was found that there were no significant differences between normotensive females and hypertensive females. These findings were similar to the finding of da Silva et al (2017) though this study was conducted in female pregnant women and had smaller sample size (73 participants). In contrast most studies have found differences in serum selenium levels in women who are normotensive and those

with hypertension but most of these studies have been conducted in pregnant women .

There was no significant relationship of selenium levels with BMI (p=0.232), age (p=0.255), systolic blood pressure (p=0.176) and diastolic (p=0.195). Similarly other studies did not find any relationship between these variables, though other studies did find a relationship. This current study found no association between essential hypertension and serum Selenium levels in adults. Similar findings were reported by studies conducted elsewhere . In contrast other studies have found a relationship between hypertension and serum selenium levels. BMI can predict serum selenium levels because of the volume of distribution that increase or cause dilutional effect. Shargorodsky et al (2010) reported that combined supplementation of Selenium with other antioxidants lead to lowered blood pressure. The study by Shargorodsky was a randomized controlled placebo study whilst the current study was not which could explain the differences in the findings. More studies are needed in Zambia in a larger population based to confirm the mean selenium levels in this population.

ACKNOWLEDGEMENT

We are grateful to the Lusaka Apex medical University for the financial help in conducting this study, Food and Drugs Control Laboratory and University Teaching Hospital clinical Chemistry Laboratory where samples were sent for analysis.

Disclosure of conflict of interest

The authors declare no conflicts of interest

REFERENCES

1. Hughes, G.D., et al., *The prevalence of traditional herbal medicine use among hypertensives living in South African*

communities. BMC complementary and alternative medicine, 2013. **13**(1): p. 38.

2. WHO. *A global brief on hypertension Silent killer, global public health crisis*. 2013 [cited 2017 20]; Available from: www.who.int/cardiovascular_diseases/publications/global_brief_hypertension/en/.
3. WHO. *Hypertension death rates by country*. 2014 [cited 2017 15 September]; Available from: <http://www.worldlifeexpectancy.com/zambia-hypertension>.
4. WHO. *Noncommunicable diseases country profiles 2014*. July 2014 [cited 2017; Available from: http://www.who.int/nmh/countries/zmb_en.
5. Eilat-Adar, S., et al., *Nutritional Recommendations for Cardiovascular Disease Prevention*. Nutrients, 2013. **5**(9): p. 3646-3683.
6. Nguyen, H., et al., *A review of nutritional factors in hypertension management*. International journal of hypertension, 2013. 2013.
7. Stranges, S., et al., *Associations of selenium status with cardiometabolic risk factors: an 8-year follow-up analysis of the Olivetti Heart study*. Atherosclerosis, 2011. **217**(1): p. 274-278.
8. da Silva, A.C., et al., *Comparison of serum selenium levels among hypertensive and normotensive pregnant women*. Hypertension in pregnancy, 2017. **36**(1): p. 64-69.
9. Grotto, D., et al., *Long-Term Excessive Selenium Supplementation Induces Hypertension in Rats*. Biological Trace Element Research, 2017: p. 1-8.
10. Chrissobolis, S., et al., *Role of Oxidative Stress in Hypertension*, in *Studies on Atherosclerosis*. 2017, Springer. p. 59-78.
11. Hu, X.F., K.M. Eccles, and H.M. Chan, *High selenium exposure lowers the odds ratios for hypertension, stroke, and myocardial infarction associated with mercury exposure among Inuit in Canada*. Environment International, 2017. **102**: p. 200-206.
12. Rodrigo, R., R. Brito, and J. González, *Oxidative Stress and Essential Hypertension*, in *Update on Essential Hypertension*. 2016, InTech.

13. Bolívar, J.J., *Essential hypertension: an approach to its etiology and neurogenic pathophysiology*. International journal of hypertension, 2013. 2013.
14. Montezano, A.C. and R.M. Touyz, *Molecular Mechanisms of Hypertension—Reactive Oxygen Species and Antioxidants: A Basic Science Update for the Clinician*. Canadian Journal of Cardiology, 2012. 28(3): p. 288-295.
15. Subash, P., et al., *Urinary 8-OHdG: a marker of oxidative stress to DNA and total antioxidant status in essential hypertension with South Indian population*. Indian Journal of Clinical Biochemistry, 2010. 25(2): p. 127-132.
16. Dharmashankar, K. and M.E. Widlansky, *Vascular Endothelial Function and Hypertension: Insights and Directions*. Current hypertension reports, 2010. 12(6): p. 448-455.
17. Rajendran, P., et al., *The Vascular Endothelium and Human Diseases*. International Journal of Biological Sciences, 2013. 9(10): p. 1057-1069.
18. Su, L., et al., *Longitudinal association between selenium levels and hypertension in a rural elderly Chinese cohort*. The journal of nutrition, health & aging, 2016. 20(10): p. 983-988.
19. Handy, D.E. and J. Loscalzo, *Selenoproteins in cardiovascular redox pathology*, in *Selenium*. 2016, Springer. p. 463-474.
20. Stranges, S., et al., *Associations of selenium status with cardiometabolic risk factors: An 8-year follow-up analysis of the Olivetti Heart Study*. Atherosclerosis, 2011. 217(1): p. 274-278.
21. Rayman, M.P., *Selenium and human health*. The Lancet, 2012. 379(9822): p. 1256-1268.
22. Benstoem, C., et al., *Selenium and its supplementation in cardiovascular disease—what do we know?* Nutrients, 2015. 7(5): p. 3094-3118.
23. Preedy, V.R., *Selenium : chemistry, analysis, function and effects*. 2015, Cambridge: Royal Society of Chemistry.
24. Zhang, M., et al., *Selenium uptake, dynamic changes in selenium content and its influence on photosynthesis and chlorophyll fluorescence in rice (Oryza sativa L.)*. Environmental and Experimental Botany, 2014. 107(Supplement C): p. 39-45.
25. Melse-Boonstra, A., P. Hogenkamp, and O.I. Lungu, *Mitigating HIV/AIDS in Sub-Saharan Africa through selenium in food*. 2007.
26. Eng, J., *Sample Size Estimation: How Many Individuals Should Be Studied?* Radiology, 2003. 227(2): p. 309-313.
27. Jacobson, B. and G. Lockitch, *Direct determination of selenium in serum by graphite-furnace atomic absorption spectrometry with deuterium background correction and a reduced palladium modifier: age-specific reference ranges*. Clinical Chemistry, 1988. 34(4): p. 709-714.
28. Delanghe, J.R. and M.M. Speeckaert, *Creatinine determination according to Jaffe—what does it stand for?* Nephrology Dialysis Transplantation Plus, 2011. 4(2): p. 83-86.
29. Talke, H. and G. Schubert, *Enzymatic urea determination in the blood and serum in the Warburg optical test*. Klinische Wochenschrift, 1965. 43: p. 174.
30. Laclaustra, M., et al., *Serum selenium concentrations and hypertension in the US population*. Circulation. Cardiovascular quality and outcomes, 2009. 2(4): p. 369-376.
31. Haque, M.M., et al., *Low serum selenium concentration is associated with preeclampsia in pregnant women from Bangladesh*. Journal of Trace Elements in Medicine and Biology, 2016. 33: p. 21-25.
32. Maduray, K., et al., *Elemental analysis of serum and hair from pre-eclamptic South African women*. Journal of Trace Elements in Medicine and Biology, 2017.
33. Ghaemi, S.Z., et al., *A prospective study of selenium concentration and risk of preeclampsia in pregnant Iranian women: a nested case-control study*. Biological trace element research, 2013. 152(2): p. 174-179.
34. Sakýz, D., A. Kaya, and M. Kulaksizoglu, *Serum Selenium Levels in euthyroid nodular thyroid diseases*. Biological trace element research, 2016. 174(1): p. 21-26.
35. Letsiou, S., et al., *Gender specific distribution of selenium to serum selenoproteins: Associations with total selenium levels, age, smoking, body mass index, and physical activity*. Biofactors, 2014. 40(5): p. 524-535.

36. Christensen, K., M. Werner, and K. Malecki, *Serum selenium and lipid levels: Associations observed in the National Health and Nutrition Examination Survey (NHANES) 2011–2012*. Environmental research, 2015. 140: p. 76-84.
 37. Nnodim, J., et al., *Membrane potential, serum calcium and serum selenium decrease in preeclampsia subjects in Owerri*. Universa Medicina, 2017. 36(2): p. 88-93.
 38. Babalola, O., J. Anetor, and F. Adeniyi, *Low blood selenium: A probable factor in essential hypertension*. African Journal of Biotechnology, 2007. 6(14).
 39. González, J., et al., *Essential hypertension and oxidative stress: New insights*. World Journal of Cardiology, 2014. 6(6): p. 353-366.
-