Original Research Article

SERUM ELECTROLYTES AND RED BLOOD CELL MEMBRANE POTENTIAL OF HYPERTENSIVE PATIENTS IN OWERRI METROPOLIS

[*1]Nwadike Constance and [2]Winner Kalu;

*****Email of Corresponding Author: nwadikeconstanceimsu@gmail.com

[1]Department Medical Laboratory Science, Imo State University, Owerri, Nigeria.
[2]Department of Chemical Sciences (Biochemistry Unit), Rhema University, Aba, Nigeria.

nwadikeconstnaceimsu@gmail.com

ABSTRACT

Serum electrolyte and red blood cell membrane potential of hypertensive patients in Owerri metropolis was investigated. A total of fifty (50) volunteer subjects were used for the study. Thirty (30) of the volunteer subjects were hypertensive subjects and were used as test subjects; while the remaining twenty (20) subjects were healthy subjects with normal blood pressure used as normentensive subjects (control). Results observed showed increased red blood cell (RBC) K^+ and Cl^- in hypertension subjects against normentensive subjects. Apart from K^+ which reduced significantly ($p<0.05$), other electrolyte ions of the serum increased significantly ($p<0.05$) in hypertensive subjects against normentensive subjects. However, Na^+ and Cl^- membrane potential were not significantly ($p>0.05$) altered in hypertensive subjects against normotensive subjects while K^+ was significantly ($p<0.05$) altered. The observed alterations in the parameters investigated in hypertensive subjects in the present study could be as a result of host of derangements involving electrolyte metabolism, altered membrane transport and a possible increase in membrane fragility. This study has shown the serum electrolyte and red blood cell membrane potential of hypertensive patients in Owerri metropolis.

Keywords: Electrolyte, hypertensive patients, membrane potential, red blood cell

INTRODUCTION

According to the World Health Organization, hypertension is defined as blood pressure persistently equal to or higher than 140 (systolic) /90 (diastolic) mmHg at rest [1]. It is a common chronic and a major global public health problem with a prevalence of 44% in Western Europe and 28% in North America [2-3]. Hypertension could be of primary or secondary types [3-4]. About 90% of patients with hypertension belong to the category of primary type with no definite cause but has been attributed to ageing, hereditary, eating habit, smoking, alcoholism, stress, fatigue, lack of exercise and obesity; while 10% of hypertensive patients suffer from the secondary type and such has been associated with diseases such as chronic renal disease, thyroid disease, coarcitation of the aorta, amongst others [5-10]. Pressure easily returns to normal in secondary hypertensive patients when the underlaying causes are treated [10]. Hypertension has also been recognized as a threat to the health of people in Africa. Kearney *et al*. [11] noted that by 2025, 75% of the world hypertensive population will be in developing countries.

In Nigeria, hypertension is the number one risk factor for diseases like stroke, heart failure, ischemic heart disease, and kidney failure [12]. In recent time, Nigeria has witnessed rapid increase in hypertensive patients due to rapid increase in adult population exposed to hypertensive risk factors. Diwe *et al*. [13] noted that hypertension is a very common non-communicable disease and of major public health importance in Nigeria, with a prevalence range of 8-64% depending on the study population, type of measurement and cut-off value used for defining hypertensive. However, Ajomuobi [8] reported the prevalence of hypertension at 30-45% in Nigeria. Mensah *et al*. [15] noted that heart, kidney, and brain as target organs in hypertension The arterial damage blood vessels are prime target of hypertensive damage [15]. Hypertensive target organ damage (TOD) is common in Nigeria. Because of low awareness of hypertension in the country, hypertensive TOD is often what brings patients to healthcare facilities [15].

A lot of studies associated with hypertension have been carried out in Nigeria [8, 13, 15-19], but not much has been done regarding serum electrolyte and red blood cell membrane potential in hypertensive patients. The present study investigated into this area and used hypertensive subjects in Owerri Municipal of Imo State, Nigeria as a case study.

MATERIALS AND METHODS

Description of Study Area: Owerri Metropolis consists of Owerri Municipal, Owerri North and Owerri West. It lies between coordinates 5°29'1.07" N and 7°01'59.70" E. The city of Owerri in Owerri Mucipality, is assumed to be the headquarters of the metropolis because it is like the heartbeat of the metropolis. Owerri metropolis sits at the intersection of roads from from Port Harcourt, Onitsha, Aba and Umuahia. It is also the trade center for palm products, maize, yams and cassava. The metropolis house major markets such as Eke Ukwu Owerri market, New Markets, Relief markets amongst others. Inhabitants of Owerri municipal indulge in different types of works and business activities to make ends meet.

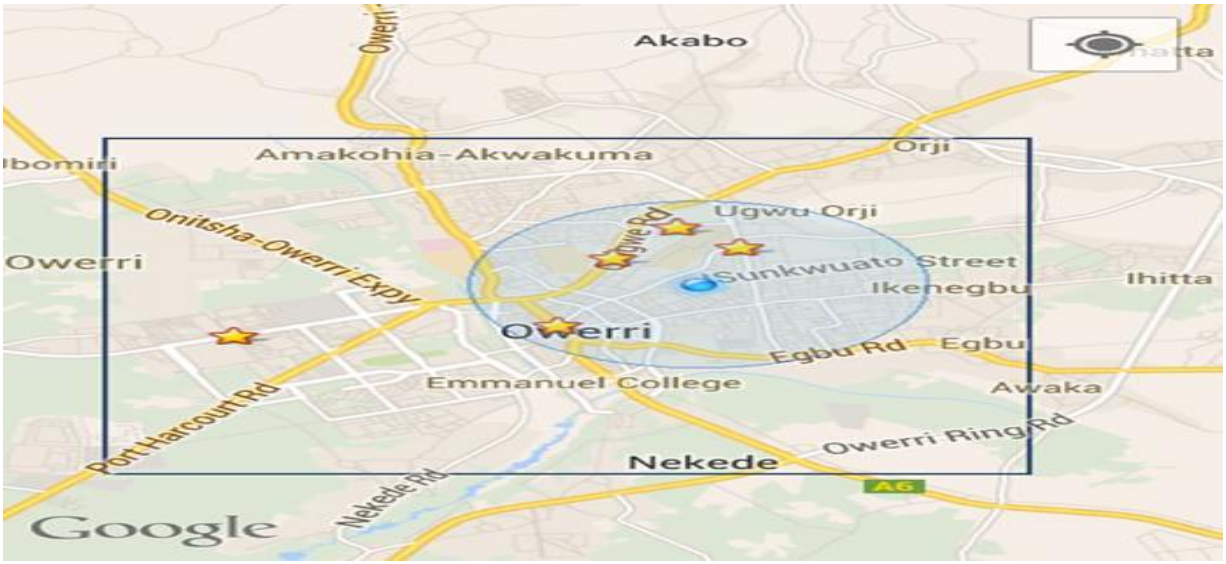

Figure 1: Map showing the location Owerri Metropolis (Accessed from google on 2th March, 2019).

ETHICAL CLEARANCE/CONSENT OF VOLUNTEER SUBJECT

The ethical clearance to conduct this study was appropriately obtained from the ethical and research committee of Imo State University/Imo State hospital management board. All informed consent was sought from the volunteer subjects and adequate verbal information was provided for the subjects, which enabled them to know the essence of collecting their blood samples and the nature of the research work. Anonymity was assured as names were not required at any stage of the study. The participants benefitted from the study by having the knowledge of their blood pressure, electrolyte concentrations and blood components checked.

STUDY POPULATION

The study population was made of fifty (50) volunteer subjects of which twenty (20) hypertensive subjects receiving treatment at Imo State Specialist Hospital, ten (10) hypertensive subjects that were not receiving treatments yet, while twenty (20) healthy subjects with normal blood pressure were used as control. Subjects selected for the present study were hypertensive men and women with systolic blood pressure of 150 mmHg or greater and diastolic blood pressure of 90 mmHg or greater (Bp≥150/90 mmHg). Apparently healthy men and women with normal blood pressure were selected as control. Hypertensive men and women; and healthy men/women whose informed consent was obtained.

Hypertensive subjects with diseases like diabetes, HIV, liver diseases, kidney diseases and sickle cell anemia were excluded to avoid complications in the results. Also, hypertensive subjects whose informed consent could not be obtained because they were skeptical about the research were as well excluded.

BLOOD PRESSURE DETERMINATION

The blood pressure (BP) of the subjects was taken after they had rested for about five minutes with their hands on the table and the feet on the floor. Accoson Mercury sphygmomanometer was the instrument used for the entire subjects and it was ensured that the cuff covered at least 2/3 of the upper arm. Korotkoff phases 1 and 5 were identified as corresponding to systolic and diastolic blood pressures respectively. Two readings were taken at an interval of five minutes. Systolic BP less than 140mmHg and Diastolic BP less than 90 mmHg were taken as normal. Readings above these values were interpreted as elevated BP.

COLLECTION OF BLOOD SAMPLES FROM THE VOLUNTEER SUBJECTS

Blood samples were collected from the subjects with the help of syringes and placed in anticoagulant tubes. The collected blood samples were centrifuged to obtain the sera used for electrolyte estimation. The sedimented red blood cells were lysed with deinoised water for estimation of intracellular electrolytes.

DETERMINATION OF TEST PARAMERS

Electrolyte concentrations for both serum and red blood cells of subjects in the present study were estimated following the instructions as directed on their diagnostic kits (Teco diagnostic kits).

COMPUTATION OF MEMBRANE POTENTIAL

This was carried out by using the Nenst equation

$$£x = 60 \log_{10} \frac{[x^+]_0}{[x^+]_i} mv$$

Where £x = membrane potential using x^0

$[x^+]_0$ = Concentration of ion x^+ in plasma.

$[x^+]_I$ = Concentration of ion x^+ ion red blood cell

STATISTICAL ANALYSIS

Results were presented as mean and standard deviations of triplicate determinations. Students t-distribution was used to establish significant difference at 5% significant levels.

RESULTS AND DISCUSSION

Table 1: Mean systolic and diastolic blood pressure of normentensive and hypertensive subjects.

Parameters	Normotensive	Hypertensive	P value
Systolic BP	115.28±6.28	170.60± 10.28	0.001
Diastolic BP	70.70±8.39	93.50± 7.09	0.001

Results are means and standard deviations of triplicate determinations.

Table of mean systolic and diastolic blood pressure of normentensive and hypertensive subjects (Table 1) shows that mean systolic and diastolic blood pressure (BP) of hypertensive subjects were 170.60± 10.28 and 115.28±6.28 respectively while systolic and diastolic blood pressure (BP) of normotensive subjects were 70.70±8.39 and 93.50± 7.09 respectively. The systolic and diastolic blood pressure of hypertensive subjects significant increased ($p<0.05$) against those of normotensive subjects.

Table 2: Mean RBC K^+, Na^+, and Cl^-concentrations of normotensive and hypertensive subjects.

Parameters	Normotensive	Hypertensive	P value
RBC K^+(mEq/L)	94.51±5.11	92.68± 4.02	0.05
RBC Na^+(mEq/L)	16.61±1.53	16.97± 1.81	0.28
RBC Cl^- (mEq/L)	50.00±4.59	52.11±3.48	0.01

Results are means and standard deviations of triplicate determinations.
RBC=Red Blood Cell

Table 2 shows the mean RBC K^+, Na^+, and Cl^- concentration of normotensive and hypertensive subjects. RBC K^+, Na^+, and Cl^- concentrations for hypertensive subjects were 92.68± 4.02 mEq/L, 16.97± 1.81 mEq/L, and 52.11±3.48 mEq/L respectively against 94.51±5.11 mEq/L, 16.61±1.53 mEq/L, and 50.00±4.59 mEq/L respectively for normotensive subjects. According to Mordecai [20], since many of the Na^+ transport mechanisms that are present in kidney cell membranes (such as $Na^+ + K^+$ co-transport and Na^+ pumps) are also present in RBC and WBC membranes, much attention has recently been devoted to the study of Na^+ transport in RBCs and WBCs. In previous studies, some hypertensive patients were found to have an unusually high RBC $[Na^+]$m level, even in studies in which the mean $|Na^+]_m$ values for hypertensive patients and normotensive subjects were not significantly different [21]. While many hypertensive patients have RBC $[Na^+]_m$ levels within the normal range, the RBC $(Na^+]_m$ distribution curve for the hypertensive patients appears to be skewed toward higher $|Na^+]_m$ values [21-23]. According to Giasuddin *et al*. [24], there are many conflicting reports about the differences in blood electrolyte levels between normotensive and hypertensive population. RBC Na^+ in hypertensive subjects increased insignificantly ($p>0.05$) against that of normotensive subjects in the present study. RBC K^+ and Cl^- increased significantly ($p<0.05$) in hypertensive subjects when compared to normotensive subjects.

Table 3: Mean serum electrolyte concentration of normentensive and hypertensive subjects.

Parameters	Normotensive	Hypertensive	P value
K^+(mEq/L)	4.42±0.73	3.84± 0.51	0.05
Na^+(mEq/L)	141.12±4.16	142.77± 3.61	0.036
Cl^- (mEq/L)	95.78±5.50	100.44±3.61	0.001
HCO_3^- (mEq/L)	25.73±1.77	27.24±5.50	0.001

Results are means and standard deviations of triplicate determinations.

The mean serum electrolyte concentration of normentensive and hypertensive subjects as presented in Table 3 reveals 4.42±0.73 mEq/L, 141.12±4.16 mEq/L, 95.78±5.50 mEq/L, and 25.73±1.77 mEq/L for K^+, Na^+, Cl^-, and HCO_3^- respectively for normentensive subjects while serum electrolyte concentration of K^+, Na^+, Cl^-, and HCO_3^- were 3.84± 0.51 mEq/L, 142.77± 3.61 mEq/L, 100.44±3.61 mEq/L, and 27.24±5.50 mEq/L respectively for hypertensive subjects. The Framingham Heart Study found that adults with serum potassium ≥ 5.2 mEq/L had increased risk of hypertension [25]. Kesteloot *et al*. [26], Pikilidou, *et al*. [27] and Rinner *et al*. [28] found that serum potassium level was negatively associated with blood pressure. Hu *et al*. [29] suggested that serum potassium level was lower in hypertension group compared with non-hypertension group. Serum K^+ level reduced significantly ($p<0.05$) in hypertensive subjects against normentensive subjects in the present study. The observed reduction in K^+ is in line with the observation of Hu *et al*. [29]. The mechanism behind the observed reduction in hypertensive subjects remains unclear. Potassium and sodium play important roles in the maintenance of cellular functions, and raised or lowered serum potassium level may be harmful to health [30]. Sodium, the main extracellular cation has long been considered as the pivotal environmental factor for hypertension. Changes in serum urea, creatinine, Na^+, and Cl^- are associated with impairment of renal function [31]. Reabsorption of filtered sodium by the renal tubules is increased in primary hypertension because of stimulation of several sodium transporters located at the luminal membrane, as well as the sodium pump which is localized to the basolateral membrane and provides energy for transportation [32]. A pivotal luminal transporter is sodium-

hydrogen exchanger type 3, which resides in the proximal tubule and thickens ascending the limb of the loop of Henle, where the bulk of filtered sodium is reabsorbed. The activity of this exchanger is increased in the kidneys of rats with hypertension [32]. The serum Na^+ increased significantly ($p<0.05$) in hypertensive subjects when compared to normentensive subjects in the present study. The observation is inconsistent with earlier study of Hu *et al.* [29], who reported no significant difference in serum sodium level between hypertension and non-hypertension groups. Serum Cl^-, and HCO_3^- increased significantly ($p<0.05$) in hypertensive subjects when compared to those of normotensive subjects. Large epidemiologic studies curiously show that lower circulating levels of serum Cl^- are associated with higher cardiovascular and all-cause mortality, though the mechanism remains unclear [33]. Reduced Na^+ and increased Cl^- ions observed in hypertensive subjects in this present study are not in line with work of Giasuddin *et al*., [24], who reported normal levels of both ions in hypertensive patients. This observation may be taken as an indication that overall renal handling of Na^+ and Cl^- were abnormal in this set of hypertensive subjects. However, handling of electrolytes is modulated by a variety of substances such as aldosterone, angiotensin II, catecholamines and prostaglandins. Of these, aldosterone is the major determinant of potassium balance.

Table 4: Mean K^+, Na^+, and Cl^- membrane potential of normentensive and hypertensive subjects.

Parameters	Normotensive	Hypertensive	P value
MP K^+	-80.11±4.43	-83.20± 3.68	0.001
MP Na^+	55.86±2.53	55.64±2.73	0.672
MP Cl^-	17.00±2.81	17.14±1.76	0.778

Results are means and standard deviations of triplicate determinations.
MP membrane potential

Table 4 reveals the mean K^+, Na^+, and Cl^- membrane potential of normentensive and hypertensive subjects. From the Table, mean membrane potential (MP) for K^+, Na^+, and Cl^- for normotensive subjects ware -80.11±4.43, 55.86±2.53, and 17.00±2.81 respectively while those of hypertensive subjects were -83.20± 3.68, 55.64±2.73, and 17.14±1.76 respectively for K^+, Na^+, and Cl^-. Alteration in membrane potential is indicative of membrane permeability [34]. This study revealed that K^+ membrane potential increased significantly ($p<0.05$) in hypertensive subjects when compared to normotensive subjects. However, Na^+ and Cl^- ion membrane potential were not significantly ($p>0.05$) altered in hypertensive subjects against normotensive subjects.

CONCLUSION

This present study has shown that hypertension results in a host of derangements involving electrolyte metabolism, altered membrane transport and a possible increase in membrane fragility. Changes in the red cell K^+ and Cl^- concentrations as well as K^+ and Na^+ membrane potential may be used as markers in the assessment of hypertension, monitoring of treatment and diseases prognosis.

REFERENCES

1. World Health Organization (2013): A global brief on hypertension. Silent killer, global public health crisis, 2013. World Health Organization Web site.

http://www.who.int/cardiovascular_ diseases/publications/global_brief_hypertension/en/ (accessed April 2013).
2. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005; 365:217–223.
3. Global Health Observatory (GHO) data: NCD mortality and morbidity.mwww. who.int/gho/ncd/mortality_morbidity/en/. (Accessed 20 September 2018).
4. National Heart Foundation of Australia. Guideline for the diagnosis and management of hypertension in adults–2016. Melbourne: National Herat Foundation of Australia; 2016.
5. Esler M. Sprint, or false start, toward a lower universal treated blood pressure target in hyprtension. Hypertension 2016; 67: 266–267.
6. Liu, L.S. Chinese guidelines for the management of hypertension. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2011; 39: 579–615.
7. Oparil S. Low sodium intake—cardiovascular health benefit or risk? N Engl J Med. 2014; 371: 677–679.
8. Ajumobi, K. Hypertension prevalence in Nigeria is about 30–45% -Experts, 2017. http://www.businessdayonline.com/hypertension-prevalence-nigeria-30-45-experts/ (Accessed on 16/5/2018).
9. Onuoha FM, Egwim J. Hypertension amongst the diabetic patients assessing care in a primary care setting in South-Eastern, Nigeria. Journal of Diabetes and Clinical Studies, 2017; 1(1):1-8.
10. Singer DR, Kite A. Management of hypertension in peripherial arterial disease; does the choice of drugs mater? European Journal of Vascular and Endovascular Surgery. 2008; 35(6): 701-708.
11. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide Data. Lancet. 2005; 365: 217-223.
12. Ogah OS, Okpechi I, Chukwuonye II, Akinyemi JO, Onwubere BJ, Falase AO, Stewart S, Sliwa K. Blood pressure, prevalence of hypertension and hypertension related complications in Nigerian. Africans: A review. World J Cardiol. 2012; 4:327-340
13. Diwe KC, Enwere OO, Uwakwe KA, Duru CB, Chineke HN. Prevalence and awareness of hypertension and associated risk factors among bank workers in Owerri, Nigeria. International Journal of Medicine and Biomedical Research.2015; 4(3):142-148.
14. Mensah GA, Janet BC, Wayne HG. The heart, kidney, and brain as target organs in hypertension. Cardiol Clin. 2002; 20: 225-247.
15. Ulasi II, Ijoma CK, Onwubere BJ, Arodiwe E, Onodugo O, Okafor C. High prevalence and low awareness of hypertension in a market population in Enugu, Nigeria. Int J Hypertens. 2011; 869675
16. Akinkugbe OO. Health behavior monitor among Nigerian adult population: a collaborative work of Nigerian Heart Foundation and Federal Ministry of Health and Social Services, Abuja supported by World Health Organization, Geneva. 2003. Available from: URL: http: //www.who.int/ chp/steps /2003 _STEPS _Report _Nigeria. pdf.
17. Onwuchekwa AC, Chinenye S. Clinical profile of hypertension at a University Teaching Hospital in Nigeria. Vasc Health Risk Manag. 2010; 6: 511-516.
18. Onwuchekwa AC, Asekomeh EG, Iyagba AM, Onung SI. Medical mortality in the Accident and Emergency Unit of the University of Port Harcourt Teaching Hospital. Niger J Med.2008; 17: 182-185.

19. Arodiwe EB, Ike SO, Nwokediuko SC. Case fatality among hypertension-related admissions in Enugu, Nigeria. Niger J Clin Pract.2009; 12: 153-156.
20. Mordecai PB. Hypertension. Editorial Bulletin.1984; 6(4):445-453.
21. Wiley JS,Clarke DA, Bonacquisto LA, Scarlett JD, Harrap SB, Doyle AE. Erythrocyte cation co-transport and counter transport in essential hypertension. Hypertension. 1984; 6:360-368
22. Aderounmu AF, Salako LA Abnormal cation composition and transport in erythrocytes from hypertensive patients. Eur J Clin Invest.1979; 9:369-375.
23. Birks RI, Langlois S. Ouabain-insensitive net sodium influx in erythrocytes of normotensive and essential hypertensive humans. Proc R Soc Lond B. 1982; 216:53-69.
24. Giasuddin ASM, Adesanya CO, Isah HS. Serum electrolytes and calcium status in Nigerian patients with essential hypertension. Journal of Islamic Academy of Sciences. 1991; 4:3: 253-256.
25. Walsh CR, Larson MG, Vasa RS, levy D. Serum potassium is not associated with blood pressure tracking in the Framingham Heart Study. Am J Hypertens.2002; 15: 130–136.
26. Kesteloot H, Joossens JV. Relationship of serum sodium, potassium, calcium, and phosphorus with blood pressure. Belgian Interuniversity Research on Nutrition and Health. Hypertension.1998; 12:589–593.
27. Pikilidou MI, Lasaridis AN, Sarafidis PA, Tziolas IM, Zebekakis PE, Dombros NV, Giannoulis E. Blood pressure and serum potassium levels in hypertensive patients receiving or not receiving antihypertensive treatment. Clin Exp Hypertens.2007; 29: 563–573.
28. Rinner MD, Spliet-van Laar L, Kromhout D. Serum sodium, potassium, calcium and magnesium and blood pressure in a Dutch population. J Hypertens.1989; **7**: 977–981.
29. Hu G, Xu X, Liang X, Yang X, Zhang J, Simayi Z, Chen Y. Associations of plasma atrial natriuretic peptide and electrolyte levels with essential hypertension. Exp. Ther. Med.2013; 5(5):1439-1443.
30. Foringer JR, Norris C, Finkel KW. Evidence-Based Nephrology, Molony DA & Craig JC, Eds.; Blackwell Publishing Ltd. 2008; Chapter 56, 633–641.
31. Ike, SO. Prevalence of hypertension and its complications among medical admissions at the University of Nigeria Teaching Hospital, Enugu (Study 2). Niger J Med.2009*;* **18**: 68-72.
32. Meneton P., Jeunemaitre, X., De Wardener, H. E. and MacGregor, G. A. (2005): Links between dietary salt intake, renal salt handling, blood pressure and cardiovascular diseases. *Physiol Rev.* **85**:679-715.
33. Linsay M, Stefanie L, Sandosh P. The hidden hand of chloride in hypertension. Pflugers Arch-Eur J.Physiol. 2015; 467-595.
34. Stojadinovic *ND et al.* Alteration of erythrocyte membrane Na, K-ATpase in children with boarderline essenteial hypertension. Cell Biochem Fund.1996; 14:79-87.