

Original Article

Identification of calcium, sodium, magnesium and chloride ion levels in hypertensive and non-hypertensive trinidadians

Andanappa Gadad¹, Stephanie Mohammed², Venkatesan Sundaram³, Shivananda B Nayak², Ashmeed Ryan Mohammed¹, Terry Gavaskar Ramnanansingh¹

¹School of Pharmacy, ²Department of Preclinical Sciences, Faculty of Medical Sciences, ³Department of Basic Veterinary Science, School of Veterinary Medicine, The University of The West Indies, Trinidad

Received June 14, 2019; Accepted July 7, 2019; Epub August 15, 2019; Published August 30, 2019

Abstract: Hypertension is a progressive cardiovascular disease with association to risk factors. These risk factors in conjunction with essential elements has become identifiable with the development of the progressive disease. The key purpose of this investigation was to identify the levels of the essential elements, Sodium (Na⁺), Magnesium (Mg²⁺), Chloride (Cl) and Calcium (Ca²⁺) in both hypertensive and non-hypertensive patients in a Trinidadian population. To achieve this objective a case-control investigation was conducted in which both hypertensive and non-hypertensive patients were assessed. Patients were issued a questionnaire with a series of open-ended questions related to the study. Blood was then drawn from each patient once consent was obtained and sent to the lab to be assayed for the elements. Fifty hypertensive (50) patients were compared with 50 non-hypertensive patients. The average levels obtained for Na⁺, Cl, Ca²⁺ and Mg²⁺ were 162.08±4.27 mmol/dL (P=0.53), 120.1±58.31 mmol/dL (P=0.51), 2.78±0.86 mmol/dL (P=0.47) and 0.52±0.31 mmol/dL (P<0.001) respectively for the hypertensive patients. The results in the present study revealed higher levels of Na⁺, Ca²⁺ and Cl and lower levels of Mg²⁺ in the hypertensive patients. The hypertensive patients were also identifiable with having high cholesterol, type 2 diabetes, and cardiovascular conditions. Sixty-two (62%) of the hypertensive patients lived with the condition for more than 10 years. The results obtained for the Trinidadian population revealed in conclusion that hypertensive patients have higher levels of Na⁺, Ca²⁺ and Cl and lower levels of Mg²⁺. These results are similar to the global results with small differences in their average level of each ion identified.

Keywords: Hypertension, calcium, sodium, magnesium, chloride ions

Introduction

Hypertension also known as high blood pressure (HBP) is a widespread public health challenge that affects approximately 1 billion persons worldwide [1]. The recent JNC-7 (National Joint Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure) has simplified the classification of hypertension into 3 categories: prehypertension (SBP 120 to 139 mmHg, DBP 80 to 89 mmHg), stage 1 hypertension (SBP 140 to 159 mmHg, DBP 90 to 99 mmHg), and stage 2 hypertension (SBP 160 mmHg, DBP 100 mmHg) [2]. According to this report, the baseline blood pressure (SBP 120 mmHg, DBP 80 mmHg) is affected by identifiable causes, which stages the condition of HBP. These stages have been

classifiable with the assessment of the presence or absence of the risk factors associated with cardiovascular diseases (CVD).

Risk factors such as increasing age, elevated blood pressure, increased heart rate, increased weight (obesity), dyslipidemia, type 2 diabetes (T2D), chronic kidney disease, smoking, and sedentary lifestyle have been found synergistic with the deficiency of various trace elements, Sodium (Na⁺), Magnesium (Mg²⁺), Chloride (Cl) and Calcium (Ca²⁺) ions [3, 4]. These trace elements are considered to have specific roles in the pathogenesis and progress of the varying stages of hypertension.

The objective for identifying the variations in trace elements of hypertensive patients helps

Identification of essential elements in hypertensive patients

to address and reduce the risk for CVD and the associated morbidity and mortality worldwide. At present, many researchers have identified the fundamental differences in these trace elements individually. Yet no research has been conducted that investigated all four ions together. This is significantly important as all four ions are closely related. Additionally, no research has been conducted on the Trinidadians in relation to these ions.

Understanding the importance of these ions are crucial. Firstly, Na^+ plays a major role in the development of hypertension as an osmolality element by regulating the extracellular fluid volume between the blood and the surrounding cells [5]. This process is critically important because it determines the delicate balance between the Na^+ and K^+ content in the blood. When Na^+ level increases, it causes the retention of water due to an increase of osmotic pressure. This then raises the blood pressure because of unwanted fluid in the blood, thereby placing strain on the kidneys for the removal of water. Both Na^+ and Cl^- have been very efficient in the development of hypertension when consumed in high quantities [6].

Secondly, Ca^{2+} and Mg^{2+} also help to regulate the blood pressure since Mg^{2+} ensures the availability of calcium channels at each site for the contraction and relaxation of smooth muscles [7]. This is important because when Ca^{2+} levels are too high, the blood vessels become narrower, causing an increase in blood pressure.

The high concentrations in Na^+ , Cl^- and Ca^{2+} along with the deficiencies in Mg^{2+} are therefore very relevant to disorders of blood pressure homeostasis such as hypertension globally [4, 8-10].

However, since no research has been conducted in Trinidad on this observance, the aim of this study seeks to assess the levels of trace elements, Na^+ , Cl^- , Ca^{2+} and Mg^{2+} in blood samples of hypertensive and non-hypertensive patients in Trinidadians and compare these levels to the global levels.

Material and methods

This study was a case-control investigation conducted from September 2017-March 2018.

Ethical approval was obtained from the campus ethics committee at The University of the West Indies (UWI) for patients to be recruited from the cardiovascular clinics of the North Central Regional Health Authority (NCRHA). This study was supported by grant number CRP.3. NOV16.12 obtained from the School of Graduate Studies, grant committee at the UWI. Patients of interest who presented for regular screening were informed of the research and asked to give consent. The inclusion criteria consisted of patients in the range of 30-75 years, both male and female, hypertensive and non-hypertensive, and patients that had T2D, high cholesterol, and CVD. The exclusion criteria consisted of patients less than 30 and greater than 75 years, pregnant women, mentally ill patients and patients with any other chronic condition that may affect the results.

Patients were issued a questionnaire upon consent that assessed their demographics, medical condition, medication is taken, regularity for checking their blood pressure and possession of blood pressure machine.

One hundred and sixty (160) patients were interviewed and 100 patients were selected based on the inclusion criteria. Fifty (50) hypertensive and fifty (50) non-hypertensive patients were used for this study. Venepuncture was performed on patients by a certified phlebotomist to obtain a maximum of 5 mL of blood. Blood samples were sent to the medical laboratory for centrifugation, separation, and storage at -20°C prior to analysis.

Analysis of blood serum samples

The serum samples were assayed for Na^+ , Ca^{2+} , Cl^- and Mg^{2+} by using a Spectrophotometer (Thermo Scientific Multiscan Go). Human Diagnostic Liquicolor Kits for Calcium (907-100 1), Magnesium (907-10010), Sodium (907-10113) and Chloride (907-10115) from Human Gesellschaft fur Biochemical und Diagnostic mbH Max-Planck-Ring 21, 65205 Wiesbaden Germany were used for this analysis.

Statistical analysis

All data were analyzed by using IBM SPSS Statistics 21.0 software. Descriptive statistics were applied to all patients. Data was assessed for normality before performing parametric

Identification of essential elements in hypertensive patients

Table 1. Showing basic demographics of both study groups

Characteristics	Non-Hypertensive N=50	Hypertensive N=50	P
Age (years)	38.6±18.3	59.6±12.8	<0.001*
T2D (%)			<0.001*
Diabetic	8	28	
Non-diabetic	42	22	
Ethnicity (%)			0.82
Indian	32	29	
African	9	11	
Mixed	9	10	

*P<0.05 is statistically significant at the 95% confidence interval.

Table 2. Showing the levels of Na⁺, Cl⁻, Ca²⁺ and Mg²⁺ in both study groups

Ion	Non-Hypertensive N=50	Hypertensive N=50	P
Sodium (mmol/dL)	155.82±56.31	162.08±41.27	0.53
Chloride (mmol/dL)	112.55±56.95	120.09±58.31	0.51
Calcium (mmol/dL)	2.64±1.07	2.78±0.86	0.47
Magnesium (mmol/dL)	0.91±0.61	0.52±0.31	<0.001*

*P<0.05 is statistically significant at the 95% confidence interval.

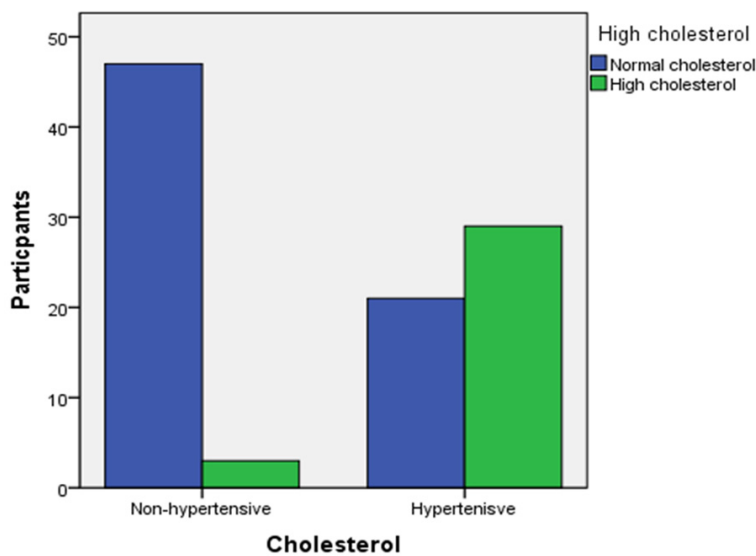


Figure 1. Showing a representation of the patients with cholesterol in both study groups.

tests. Chi-square test was used to compare the association among categorical groups. Independent t-test was used to compare the differences in means of parameters between the hypertensive and non-hypertensive groups. The statistical significance was set at P<0.05

for the study. Categorical data was also represented with the use of bar graphs.

Results

Basic demographics

The study group comprised of 50 non-hypertensive and 50 hypertensive patients chosen at random. There was a significant difference (P<0.05) in the age among both study groups. The hypertensive patients were 59.6±12.8 when compared with the non-hypertensive patients of age 38.6±18.3 years as displayed in **Table 1**. The study group consisted of various ethnicities (Indian, African and Mixed) with Indians being the most prominent among both groups as seen in **Table 1**.

A significantly (P<0.05) higher number of Type II Diabetics was observed to be hypertensive when compared with the higher number of non-diabetics for the non-hypertensive patients as seen in **Table 1**.

Essential elements level found in blood serum

All element ion levels were displayed in **Table 2**. The Sodium ion levels were lower for non-hypertensive patients (155.82±56.31 mmol/dL) when compared to 162.08±41.27 mmol/dL for hypertensive patients but not significantly different.

The Chloride ion levels were lower for non-hypertensive patients (112.55±56.95 mmol/dL) when compared to 120.09±58.31 mmol/dL for hypertensive patients but not significantly different.

The Calcium ion levels were lower for non-hypertensive patients 2.64±1.07 mmol/dL when

Identification of essential elements in hypertensive patients

Table 3. Showing the response of patients from both study groups

Patients Response	Non-Hypertensive N=50	Hypertensive N=50	p
Do you have an HBP machine?			0.01*
Yes	23	37	
No	27	13	
Do you take vitamins?			<0.001*
Yes	9	26	
No	41	24	
Do you feel stressed regularly?			<0.001*
Yes	11	31	
No	39	19	

*P<0.05 is statistically significant at the 95% confidence interval.

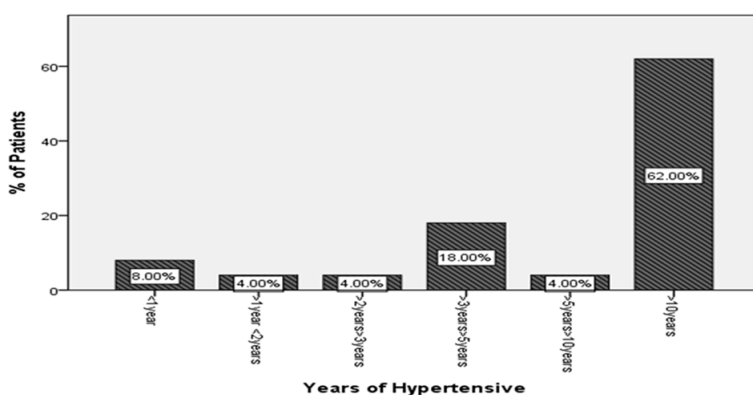


Figure 2. Showing the period of time for which patients have been hypertensive.

compared to 2.78 ± 0.86 mmol/dL for hypertensive patients but not significantly different.

The Magnesium ion levels (0.91 ± 0.61 mmol/dL) were significantly higher in the non-hypertensive patients when compared to the hypertensive patients 0.52 ± 0.31 mmol/dL at $P < 0.001$ significant level.

Chronic conditions

The major chronic condition observed among the hypertension group revealed a greater number of the patients had high cholesterol as seen in **Figure 1**.

Sixty-two percent of the 50 hypertension patients reported to have the condition, HBP for more than 10 years. Four percent reported they had it for more than 5 years while 18% reported more than 3 years as seen in **Figure 2**.

Chronic health condition prevention

Table 3 shows the highlighted responses to the chronic health prevention patients considered most important. Thirty-one of the patients with HBP considered themselves to undergo stress. Twenty-three non-hypertensive patients invested in a high blood pressure machines and at present 37 of the hypertensive had blood pressure machines to monitor their HBP levels. Approximately of the patients with HBP were taking vitamins while the other half were not.

Discussion

On average globally, the values for Na^+ , Cl^- , Ca^{2+} and Mg^{2+} levels fall in the range 137-142 mmol/dL, 96-106 mmol/dL, 2.2-2.7 mmol/dL and 0.85 mmol/dL respectively [4, 5, 10, 11]. The modified lifestyle factors such as diet and exercise would allow for these values to vary with change in geographical location. In this study, we were able to identify that the various ion levels for both groups in Trinidad were significantly higher when compared to the literature values globally as the hypertensive group displayed higher Na^+ , Cl^- and Ca^{2+} levels and lower Mg^{2+} levels when compared to the non-hypertensive patients [3, 7, 8, 12].

The association among these ions individually has been clearly defined in medical literature whereby the action potential is a coordinated sequence of ion movements. Initially, Na^+ enters the cell, followed by a Ca^{2+} influx and finally a K^+ efflux that refers the cell to its resting state. Several antiarrhythmic agents exert their effects by altering these ion fluxes as well.

In general, the association of Na^+ with hypertension has been well documented [6] for inducing high blood pressure. Yet recent research disapproved this by showing that Na^+

alone showed no significant association [13]. Our research was not able to support this as we conducted retrospective research in Trinidad. Additionally, the levels for Na^+ , Ca^{2+} , and Cl^- did not differ significantly in our research as our patients were taking medications for the control of their BP and other chronic conditions associated that they developed. Yet, the levels were still higher for hypertensive patients.

The hypertensive patients showed clear associations with having T2D and high cholesterol which are risk factors for CVD and have been evidently defined in research [14-16]. Management of these risk factors is very important as controlling lipids aids in the prevention of HBP as observed in a previous study among the elderly in Trinidad [17].

Another significant observation was the age differences among both groups, as the hypertensive patients on average had a higher age category. Hypertension and the risk for CVD increase inevitably in the elderly [2, 18]. The rate at which blood flow is produced by the heart and the resistance of the blood vessels to this flow determines blood pressure. As a person ages, their elastic arteries tend to dilate and stiffen which decrease the capacitance of the cardiac cycle which overall increases the systolic blood pressure.

The adoption of a healthy lifestyle is therefore very essential for longevity. Fortunately, the patients in this study started adopting a preventative measure for controlling their HBP by ensuring they have HBP machines to monitor themselves.

Conclusion

The main purpose of this investigation was to identify the level of the trace elements, Na^+ , Cl^- , Ca^{2+} and Mg^{2+} in both the hypertensive and non-hypertensive patients among the Trinidadians. This research was carried out by selecting patients based on an inclusion and exclusion criteria in which patients were assessed by a survey questionnaire and blood samples drawn. The main results obtained showed the average levels for Na^+ , Cl^- , Ca^{2+} and Mg^{2+} were 162.08 ± 4.27 mmol/dL ($P=0.53$), 120.1 ± 58.31 mmol/dL ($P=0.51$), 2.78 ± 0.86 mmol/dL ($P=0.47$) and 0.52 ± 0.31 mmol/dL ($P<0.001$) respectively for the hypertensive patients.

These results in the present study revealed higher levels of Na^+ , Ca^{2+} and Cl^- and lower levels of Mg^{2+} in the hypertensive Trinidadian patients and therefore supported the results obtained globally for hypertensive patients when compared with the non-hypertensive.

Acknowledgements

Authors wish to thank all the patients that participated in this research. We also wish to thank the School of Graduates Studies, UWI, grant number CRP.3. NOV16.12.

Disclosure of conflict of interest

None.

Authors' contribution

Dr. A. Gadad, Ms. S. Mohammed and Dr. V. Sundaram were responsible for the design, writing, review and final approval of the manuscript. Dr. S. Nayak was responsible for analyzing the blood samples. Mr. A. Mohammed and Mr. T. Ramnanansingh were responsible for the collection of data, blood samples and final approval of the paper for submission.

Address correspondence to: Stephanie Mohammed, Department of Preclinical Sciences, Faculty of Medical Sciences, The University of The West Indies, Trinidad. Tel: 1868795-5950; E-mail: Stephanie.Mohammed@sta.uwi.edu; Venkatesan Sundaram, Department of Basic Veterinary Science, School of Veterinary Medicine, The University of The West Indies, Trinidad. Tel: 18687274802; E-mail: dr.venkat1971@gmail.com; Andanappa Gadad, School of Pharmacy, The University of the West Indies, Trinidad. Tel: 18683041187; E-mail: Andanappa.gadad@sta.uwi.edu

References

- [1] Israeli ZH, Hernandez-Hernandez R, Valasco M. The future of antihypertensive treatment. *AM J Ther* 2007; 14: 121-134.
- [2] Chobanian AV, Barkis GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The seventh report of joint national committee on preven-

Identification of essential elements in hypertensive patients

- tion, detection, evaluation and treatment of high blood pressure: the JNC 7 report. *JAMA* 2003; 289: 2560-72.
- [3] Panhwar AH, Kazi TG, Afridi HI, Talpur FN, Arain S, Kazi N. Distribution of potassium, calcium, magnesium and sodium levels in biological samples of Pakistani hypertensive patients and control subjects. *Clin Lab* 2014; 60: 463-74.
- [4] Ackerman GL, Serum Sodium. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical methods: the history, physical and laboratory examinations*. 3rd Edition. Boston: Butterworths; 1990. 194.
- [5] Morrison G, Serum Chloride. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical methods: the history, physical and laboratory examinations*. 3rd Edition. Boston: Butterworths; 1990. 197.
- [6] Boegehold MA and Kotchen TA. Importance of dietary chloride for salt sensitivity of blood pressure. *Hypertension* 1991; 17 Suppl: I158-61.
- [7] Paolisso G, Barbagallo M. Hypertension, diabetes mellitus and insulin resistance. The role of intracellular magnesium. *Am J Hypertens* 1997; 10: 346-355.
- [8] Abbasi IU, Salim-ul-Haque, Kausar MW, Karira KA and Zubaris NA. Correlation of divalent cations (Ca⁺⁺, Mg⁺⁺) and serum renin inpatients of essential hypertension. *J Pak Med Assoc* 2012; 62: 134-8.
- [9] Houston MC and Harper KJ. Potassium, magnesium, and calcium: their role in both cause and treatment of hypertension. *J Clin Hypertens (Greenwich)* 2008; 10 Suppl 2: 3-11.
- [10] Guerrero Romero F and Rodriguez-Moran M. Low serum magnesium levels and metabolic syndrome. *Acta Diabetol* 2002; 39: 209-213.
- [11] Goldstein D, Serum Calcium. In: Walker HK, Hall WD, Hurst JW, editors. *Clinical methods: the history, physical and laboratory examinations*. 3rd Edition. Boston: Butterworths; 1990. 143.
- [12] Asha G and Mohanty S. A study of serum calcium, magnesium and copper levels in patients of essential hypertension. *World Journal of Pharmacy and Pharmaceutical Sciences* 2015; 4: 521-530.
- [13] Xi L, Hao YC, Liu J, Wan W, Wang M, Li GQ, Qi Y, Zhao F, Xie WX, Li Y, Sun JY, Liu J, Qin LP and Zhao D. Associations between serum potassium and sodium levels and risk of hypertension: a community-based cohort study. *J Geriatr Cardiol* 2015; 12: 119-126.
- [14] American Diabetes Association, "Standards of medical care in diabetes 2009". *Diabetes Care* 2009; 32 Suppl 1: S13-S61.
- [15] Scheffel RS, Bortolanza D, Weber CS, Costa LA, Canani LH, Santos KG, Crispim D, Roisenberg I, Lisboa HR, Tres GS, Tschiedel B, Gross JL. Prevalence of micro and macroangiopathic chronic conditions and their risk factors in the care of outpatients with type 2 diabetes mellitus. *Rev Assoc Med Bras (1992)* 2004; 50: 263-7.
- [16] Mohammed SB, Gadad A, Nayak BS, Beharry V. Prognosis of the midlife elderly from ECG testing to gastroesophageal reflux disease and coronary artery disease. *J Fam Med Dis Prev* 2016; 2: 29.
- [17] Nayak SB, Mohammed SB, Nayak AS. Controlling lipids aids in the prevention of type 2 diabetes, hypertension, and cardiovascular disease. *Int J Prev Med* 2017; 8: 39.
- [18] Lionakis N, Mendrinou D, Sanidas E, Favatas G, Georgopoulou M. Hypertension in the elderly. *World J Cardiol* 2012; 4: 135-147.