



SJMLS-2(2)-2017-013

Thyroid Profile in Nigerians with Essential Hypertension in Benin City, South-South Nigeria

Igharo Osaretin Godwin¹, Osadolor, Humphrey Benedo¹ and Okosun Romanus Erimwingbovo²

Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, P.M.B. 1154, Benin City, Nigeria¹, Department of Chemical Pathology, University of Benin Teaching Hospital, Benin City, Nigeria²

Author for Correspondence: osaretin.igharo@uniben.edu / +234-803-866-4896

Abstract

Endocrine-related studies have been gaining more relevance in the investigation of the causes of hypertension. Hypothyroidism has been listed as a reversible cause of hypertension. In this study, thyroid hormones and body mass index (BMI) were determined in hypertensive Nigerian adults (n=104) attending the outpatient clinic in the University of Benin Teaching Hospital, Benin City, Nigeria. Age – and gender- matched normotensive (n=80) from similar socio-economic background were monitored as controls. The study aimed to determine if the Nigerian subjects enlisted were predisposed to hypertension due to thyroid dysfunction and to find out the possibility of thyroid-induced reversible hypertension. Thyroid-Stimulating Hormones (TSH), Triiodothyronine (T₃) and thyroxine (T₄) were determined using enzyme immunoassay on microtiter plate format and the Body Mass Index (BMI) values were obtained from height and weight values taken with standard height and weight scale. The results obtained showed that the blood pressures (mmHg) in hypertensives (155.89 ± 25.65/93.09 ± 12.26) while that of as significantly higher than that of normotensive controls (121.81 ± 7.17/80.18 ± 6.03) (p < 0.05). TSH level was (2.99 ± 2.16 µIU/mL) r in hypertensives compared to normotensive controls (3.25 ± 1.87 µIU/mL). T₃ and T₄ levels among hypertensives was (1.13 ± 0.28 ng/mL) and (7.04 ± 1.84 µg/dL) respectively compared to normotensive controls (1.06 ± 0.24 and 6.56 ± 1.36). The mean BMI among hypertensives was (27.40 ± 6.2) compared to normotensive controls (24.91 ± 3.45). These differences however were not statistically significant. BMI in hypertensives was negatively correlated with TSH (r = -0.10, p = < 0.05) and T₄ (r = -0.13, p = < 0.05), while in normotensives, there was a weak positive correlation between BMI

and T₄ (r = 0.10, p < 0.05). Additionally, BMI showed weaker positive linear correlation with T₃ in hypertensives (r = 0.21, p > 0.05), compared with normotensive controls (r = 0.39, p < 0.05). The study suggests that there appears to be subclinical thyroid dysfunction in hypertensive Nigerians, which tends to underscore the usefulness of occasional thyroid assessment in the management of hypertension.

Keywords: Hypertensives, Normotensives, Thyroid stimulating hormones, Thyroxine, Triiodothyronine, Body mass index.

Introduction

The world Health Organization/ International Society of Hypertension Joint Committee defined hypertension as blood pressure consistently above 140/90mmHg (Ayodeji and Makanjuola, 1998). Over 95% of cases of hypertension has unknown etiology, while chronic renal disease accounts for 2.5% or more of cases. Endocrine disorders are responsible for a fraction of cases of hypertension (Endocrine Society, 2001; Bing *et al.*, 1980).

A majority of cases of hypertension are without exact cause. The risk factors for this condition are only known but not the aetiological factors. This type is known as primary (essential) hypertension. A second type of hypertension exist in which a specific cause can be identified. This is called secondary hypertension (Adams and Anthony, 1993; Brendam, 1993 and Pickering, 1981) This is also called treatable hypertension.

Since the past decades and up till now, endocrine – related studies keeps gaining more and more relevance in the investigation of the causes of hypertension, of which the influences of thyroid hormones are also being considered (Ayodeji and Makanjuola, 1998; Ifeanyi and Joson, 1997).

The Endocrine Society has also stated that endocrinology plays a role in hypertension because the major known causative factors are hormonal. It is likely that all hypertension has endocrine – related causes. Therefore, major progress in hypertension knowledge will come from endocrine research that defines the genetic factors that change hormonal functions and predispose a person to hypertension (Endocrine Society, 2001; Ayodeji and Makanjuola, 1998).

Recent research has already produced several advances. For the first time, research has identified an abnormal gene that cause abnormal production of a hormone aldosterone, resulting in increased blood pressure. This abnormality is called glucocorticoid remediable aldosteronism. Thyrotoxicosis, hyperthyroidism and hypothyroidism have all been listed among factors predisposing to high blood pressure (Koch and Chrousos, 2016; Endocrine Society, 2001).

Again, it has been stated that treatment of hypothyroidism alone resulted in restoration of blood pressure to normal in a substantiated number of patients. Bing et al. (1980) in the summary of research work, presented the case of six patients with hypothyroidism and hypertension whose blood pressure fell to normal when treated with thyroxine.

Mean blood pressure of the six patients $\frac{172 \pm 7.2}{112 \pm 2.1}$ was restored to $\frac{140 \pm 3.2}{84 \pm 1.6}$. They concluded that hypothyroidism is a reversible cause of hypertension.

There is paucity of data of the role of hypothyroidism on hypertension in Nigerian. This study was therefore designed to investigate if hypothyroidism predisposes to hypertension.

Materials and Methods

Participants and specimen collection

Venous blood samples were collected into plain containers using acceptable medical techniques from

104 hypertensives subjects visiting the Outpatient Department of University of Benin Teaching Hospital. Patients were diagnosed hypertensive based on clinical signs and symptoms as well as blood pressure values repeatedly taken by a Consultant Clinician. The blood samples were allowed to clot, and were centrifuged at 3000 revolutions per minute for 5 minutes and the serum obtained where frozen united analyzed. Patients' heights and weight were taken using standard scales. Gender and age were also recorded.

Similarly, blood samples were obtained from 25 apparently health normotensives for use as controls. These samples were treated as for clinical (test) samples. Due informed verbal consent was sought and ethical procedures were adhered with. Blood pressures, weights and heights were also taken by standard clinical methods.

Anthropometric and Basic Health Indices

Standing Height

This was measured against a pre-graduated scale at vertical surface with the subjects standing barefooted as upright as possible on a firm level ground. The weight of the subjects was ensured to be evenly distributed on both feet. The heels of the feet were placed together with both heels touching the base of the vertical board. The feet while together were placed pointed slightly outward at 60 degree angle. The buttocks scapulae and head were positioned in contact with the vertical backboard and the arms hanging freely by the side of the trunk with the palms facing the thighs. The subject was requested to inhale deeply while the measurement was taken. The measurement taken was recorded on the nearest 0.1cm.

Weight

This was taken with a standard weight measurement scale placed on a flat surface. The subjects while on light clothing and without shoes stood on the pre-zeroed scale and the readings were recorded in kilograms. Body Mass Index (BMI) was calculated from height and weight using the formula: $BMI = \frac{Weight (kg)}{Height^2 (m^2)}$ as previously described by Romero-Corral *et al.*, (2008).

Blood Pressure (BP)

This was taken with the use of a stethoscope and a mercury column sphygmomanometer with blood



pressure cuff. Subject was made to relax for about five minutes before the reading. Each subject was made to sit upright with the upper arm positioned in a way that it was level with the heart and feet flat on the floor. Talking was avoided during the process. The pressure cuff was wrapped snugly around the subject's arm. The arm palpated at the antecubital fossa (crease of the arm) to locate the strongest pulse sound and the bell of the stethoscope placed over the brachial artery at this location. Cuff bulb was pumped while listening to hear the pulse sounds. The cuff was inflated to between 160 and 180 mmHg and at this level no sound was heard through the stethoscope. Then the process of deflation began, allowing the pressure to fall 2 to 3 mmHg. The first occurrence of rhythmic sounds heard as blood begins to flow through the artery was recorded as the subject's systolic pressure. The BP cuff pressure continued dropping and the sound fade. The gauge reading at the point at which the rhythmic sound stopped was recorded as the diastolic pressure. A second reading was taken again following the same procedure. At the end, the average reading was calculated and documented as the subject's BP.

Methods of Assay

Enzyme Immunoassay methods (EIA), (Uotila et al., 1981) on microtiter plate format were used for the Quantitative determination of the triiodothyronine, thyroxine and thyroid Stimulating hormone in human serum using Enzyme Immunoassay test kits as marketed by Immuno Biosystems were used (Log numbers: BC-1001, 1005 and 1007) for TSH, T₃, and T₄ respectively.

Statistical Analysis

Data collected were analyzed using the Statistical Package for Social Sciences (SPSS) version 16.0 (IBM Inc., USA). The unpaired Student's t-test was computed to find out whether significant differences exist between Thyroid hormone levels in hypertensives and normotensive controls. Correlation analysis was computed to find out whether any relationship exist between BMI and thyroid hormone levels and between blood pressure and thyroid hormone levels. Interrelationship among the parameters were determined using Pearson's Correlation Coefficient analysis. A p-value of less than 0.05 ($p < 0.05$) was considered significant.

Results

The mean \pm S.D values of Systolic and Diastolic pressures of hypertensives ($155.89 \pm 25.68/93.09 \pm 12.25$ mmHg), as expected, were higher than those of the normotensive controls ($121.82 \pm 7.17/80.18 \pm 6.03$ mmHg) (table 1). The differences of which are statistically significant ($p < 0.05$).

Thyroid hormones levels were lower in hypertensives than in the normotensive controls; but the differences are not statistically significant; ($p > 0.05$). As shown in table 2, levels of TSH (μ IU/mL), T₃ (ng/mL) and T₄ (ug/dL) of hypertensives were 2.99 ± 2.16 ; 1.13 ± 0.28 and 7.04 ± 1.84 respectively; while those of normotensives were 3.25 ± 1.87 ; 1.06 ± 0.24 and 6.56 ± 1.36 respectively. BMI (kg/m^2) for hypertensives (27.40 ± 6.02) was higher but not significantly different from normotensives (24.91 ± 3.45) (Table 3).

Table 1: Comparison of Blood Pressure (mmHg) of Hypertensives (Test) and Normotensives (Control)

| Study Group | Systolic B.P. | Diastolic B.P |
|-----------------------|--------------------|-------------------|
| Hypertensives n = 104 | 155.89 ± 28.68 | 93.09 ± 12.26 |
| Normotensives n = 80 | 121.82 ± 7.17 | 80.18 ± 6.03 |
| p – value | < 0.05 | < 0.05 |

Table 2: Comparison of TSH, T₃ and T₄ levels in Hypertensives (Test) and Normotensives (Control)

| Study Group | TSH (μ IU/mL) | T ₃ (ng/mL) | T ₄ (ug/dL) |
|-----------------------|--------------------|------------------------|------------------------|
| Hypertensives n = 104 | 2.99 ± 2.16 | 1.13 ± 0.28 | 7.04 ± 1.84 |
| Normotensives n = 80 | 3.25 ± 1.87 | 1.06 ± 0.24 | 6.56 ± 1.36 |
| p – value | > 0.05 | > 0.05 | > 0.05 |

Table 3: Comparison of BMI (kg/m²) in Hypertensives and Normotensives

| Study Group | Mean ± S.D. |
|-----------------------|--------------|
| Hypertensives n = 104 | 27.40± 6.02 |
| Normotensives n = 80 | 24.91 ± 3.45 |
| p- value | > 0.05 |

Table 4: Correlation of Thyroid Hormones with BMI in Hypertensives and Normotensives

| Correlated pair | Hypertensives | | Normotensives | |
|------------------------|---------------|---------|---------------|---------|
| | r value | p value | r value | p value |
| TSH vs. BMI | -0.10 | <0.05 | 0.10 | >0.05 |
| T ₃ vs. BMI | 0.21 | >0.05 | 0.39 | <0.05 |
| T ₄ vs BMI | -0.13 | <0.05 | 0.10 | <0.05 |

Table 5: Correlation of Thyroid Hormones with Blood Pressure in Hypertensives and Normotensives

| Correlated pairs | Hypertensives | | Normotensives | |
|---|---------------|---------|---------------|---------|
| | r value | p value | r value | p value |
| TSH vs. Systolic Blood Pressure | 0.03 | >0.05 | 0.10 | <0.05 |
| TSH vs. Diastolic Blood Pressure | 0.13 | <0.05 | 0.23 | >0.05 |
| T ₃ vs. Systolic Blood Pressure | 0.004 | <0.05 | -0.27 | <0.05 |
| T ₃ vs. Diastolic Blood Pressure | 0.04 | <0.05 | -0.31 | >0.05 |
| T ₄ vs. Systolic Blood Pressure | 0.10 | >0.05 | 0.14 | <0.05 |
| T ₄ vs. Diastolic Blood Pressure | 0.17 | <0.05 | 0.20 | <0.05 |

Discussion

Endocrine related studies have been gaining more relevance in the investigation of the causes of hypertension (Koch and Chrousos, 2016; Endocrine Society, 2001; Ayodeji and Makanjuola, 1998 and Bing et al., 1980). Hypothyroidism has been listed as a reversible cause of hypertension. Findings from the present study have shown that the blood pressure in hypertensives was expectedly higher than that of normotensive controls and the observed difference was significant (p< 0.05). It is noteworthy also that in these patients, the blood pressures were clinically controlled.

Though levels of T₃ and T₄ in hypertensives were higher than those of normotensive controls coupled with the observed lower TSH in hypertensives compared with normotensive controls, these differences were not statistically significant (p > 0.05). These observations appear to suggest that the

hypertensives enrolled in this study were having no considerable thyroid dysfunction. These findings corroborate with the report of Ayodeji and Makanjuola (1998) that hypertensives cases caused by endocrine disorders (thyroid dysfunction included) are very rare. Though hyperthyroidism and hypothyroidism may be found as predisposing factors in hypertension, but this occurs in very scanty cases, as both conditions have been grouped under minor or miscellaneous predisposing factors in hypertension. Being et al, (1980) found that six (6) hypothyroid hypertensive patients had their blood pressures restored to normal by thyroxine replacement. The fact that the six (6) patients were earlier diagnosed and confirmed to have primary hypothyroidism makes the experimental settings different from that of this study. In this study, lest subjects were neither showing symptoms of thyroid dysfunction nor diagnosed of any. However, the fall in blood pressure in Bing's observation was also partly



attributed to the considerable fall in body weights of all the patient during the time of the study.

Correlation analysis shows that rather weak significant relationships exist between hormones levels and the BMI of hypertensives in the present study. For TSH, ($r = -0.1$); this indicates that in the Nigerian hypertensives studied, as BMI increases, TSM level reduces; though this was more or less a weak correlation. The same was observed for T₄; ($r = -0.13$). For T₃, ($r = 0.21$) indicating that the BMI has positive linear correlation with T₃ levels in hypertensives; as BMI increases, T₃ level also increases. This is possibly linked with the metabolic function of T₃ as the main active hormone (Lazarus, 1997). As body size increases, 'more metabolic activities would be required and therefore need for T₃ becomes greater. The picture was somewhat different from observation seen among the normotensive controls. Though TSH, T₃ and T₄ showed positive correlations with BMI (r value; ~ 0.1 , 0.4 and 0.1 respectively), T₃ showed a strong positive correlation, this agrees also with the fact that more metabolic functions are needed in increasing BMI, and these functions are mediated by T₃ (Gerald and Thomas, 2002 and Whitley, 2001).

Also in the present study, the observed higher BMI in hypertensives compared with control observed in this study agrees with a previous report (Oladipo, 1998) who found a strong correlation between BMI and the prevalence of hypertension. It was also reported that increased BMI (obesity) as well as hypertension, is a risk factor in cardiovascular disorder (Obasohan, 1995).

The fact that results obtained in this study shows no statistical significance as regards BMI of hypertensives and normotensives might have been due to weight shedding which the obese hypertensives embark on as part of the management of their cases. This is based on the understanding that weight reduction enhances the antihypertensive effects of drugs (Kadiri, 2001).

The correlation analysis done in this study between thyroid hormones and blood pressure have shown that weak positive correlation exists between TSH and blood pressure, T₄ and blood pressure. In the case of T₃, a weak negative correlation was found. It suggests that increase in blood pressure may predispose to low level of T₃ or vice versa.

In the Nigerian hypertensives enrolled in the present study, a significant thyroid dysfunction was not observed and this may suggest that they could not have been possibly predisposed to hypertension due to abnormality of thyroid function. However, T₃ and T₄ levels were found higher in hypertensives than in normotensive controls. This observation may indicate that a trend of either increase (as seen in this study) or decrease as observed by Bing *et al.* (1980), could set in with increasing severity of hypertension. It is therefore concluded that thyroid assessment should be an adjunct occasional investigation in the management of hypertension.

References

- Adams, D., Anthony, W. (1993): Essentials of Cardiology, 2nd Edition, Blackwell Scientific Publication, New York: 30-551.
- Ayodeji, A.O. and Makanjuola, A.D. (1998): Endocrine Hypertension. *Archives of Ibadan Medicine*; **1(1)**:1- 11.
- Bing, R.F., Briggs, R.S.J., Burden, A.C., *et al.* (1980): Reversible Hypertension and Hypothyroidism. *Clinical Endocrinology*; **13**:339-342.
- Brendan, P. (1997): The Human Heart, 2nd Edition. Lippincott-Raven Publishers, New York: 30-51.
- Gerald, L. and Thomas J.S. (2002): Biochemistry of Hormones 1: Polypeptide Hormones; In Textbook of Biochemistry with Clinical Correlations, 5th Edition. Devlin T.M (ed). John Wiley and Sons Publication, New York: 905 - 935.
- Ifeanyi, O., Joson, W. (1999). Gene/Environmental/Behavioural Influences on Hypertension in Blacks of African Descent. *Dateline Health (Nigeria) Dec.*: 1 - 2.
- Kadiri, S. (2001): Management of Hypertension with Special Emphasis on Nigeria. *Nigerian Clinical Review*; May/June, 5-8. 677.
- Koch, C.A. and Chrousos, G.P. (2016): An overview of Endocrine Hypertension. *Endotext*. Available at www.endotext.org. Assessed 15/06/2017.
- Lazarus J.U. (1997). Hyperthyroidism. *Lancet*; **34(2)**:339 - 343.
- Obasohan, A.O. (1995): Body Weight and Heart Failure in Hypertensives: A Nigerian Experience. *Tropical Cardiology*; **21(82)**: 47 - 50.
- Oladipo, O.A. (1998); Current Epidemiology of Hypertension in Nigeria. *Archives of Ibadan Medicine*; **1 (1)**: 7 - 11.



- Pickering, G. (1981): Hypertension. Definition, Histories and Consequences: In Leraph Manual of Hypertension, Jeldin, J.H. (ed). Philadelphia: 3-7.
- Romero-Corral, A., Somers, V., Sierra-Johnson, J., *et al.* (2009) Accuracy of body mass index in diagnosing obesity in the adult general population. *International Journal of Obesity*; **32**: 959-966.
- The Endocrine Society (2001). Endocrinology and Hypertension. *Endocrine Society Manual: 1-2*.
- Uotila, M.L., Ruoslahti, E. and Engvall, E. (1981): Enzyme Immunoassays. *Journal of Immunology Methods*; **42**: 11-15.
- Whitley, R.J. (2001); Thyroid Function; In Tietz Fundamentals of Clinical Chemistry, 5th Edition. Carl, A.B and Edward R.A. (eds). W.B Saunders, Philadelphia: 839 - 865.