ORIGINAL ARTICLE

PREVALENCE AND PATTERN OF ABNORMAL GLUCOSE TOLERANCE IN ADULT NIGERIANS WITH PRIMARY HYPERTENSION

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ABSTRACT

Background: *Hypertension and diabetes mellitus relate to one another aetiologically and prognostically. Studies show that hypertension occurs frequently in diabetics than non-diabetics. Data on the prevalence of abnormal glucose tolerance in hypertensive Nigerians are scanty. This study assesses the magnitude of this problem in adult Nigerians with primary hypertension.*

Method: *Oral glucose tolerance test was performed on 124 adult Nigerians (64hypertensives, 60normotensives) to determine the prevalence of abnormal glucose tolerance. Body mass index and waist circumference were measured. Plasma glucose was analyzed by the glucose oxidase method.*

Results: *The hypertensive(32 males,32females) and normotensive (30males, 30females) had mean ages of 47.6+/-10.1years and 44.2+/-7.6years.The mean body mass index and waist circumference of hypertensives and normotensives were 30.2+/-80kg/m,100.8+/-17.2cm and28.5kg/m,88.5+/-14.1cm. The mean plasma glucose in mmols/l, during oral glucose tolerance test of hypertensives and normotensives, at 0hr, 1hr and 2hrs were,4.79+/-0.99,6.94+/-1.5,5.96+/-1.82 and4.42+/-0.90,6.25+/-1.02,5.05++/-1.8 respectively. The response to glucose load was significantly higher in the hypertensives than normotensives particularly at 2hours p<0.001. 62.5% of hypertensives responded normally to glucose load.32.8% had impaired glucose tolerance. All controls responded normally. 6.25% of hypertensives had impaired fasting glucose. 4.6% of hypertensives had diabetes. No control had diabetes. The hypertensives with abnormal glucose tolerance had higher body mass index and waist circumference, than hypertensives with normal glucose tolerance, and controls.*

Conclusion: *Mean venous plasma glucose levels are higher in hypertensive adult Nigerians, than their normotensive counterparts. Impaired glucose tolerance is more prevalent than impaired fasting glucose and diabetes mellitus.*

Keywords: Abnormal Glucose Tolerance; Primary Hypertension; Adult Nigerians.

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Introduction

Abnormal glucose tolerance- (Impaired glucose tolerance IGT, Impaired fasting glucose IFG, Diabetes mellitus DM), and primary systemic hypertension (HT) are prevalent in the general population. Both disorders may occur together. HT may antedate the development of DM and vice versa. Either may predispose to cardiovascular disease and death.[4]

The effect of their combination is additive[5]. It therefore seems reasonable to detect the early addition of glucose intolerance on hypertension and vice versa, as treatment may alter the outcome.[6]

A number of population based studies have revealed a positive association between hypertension and abnormal glucose tolerance.[7,8]In contrast, there are scanty reports of IGT and DM in hypertensive subjects[9]. The reports are even scantier in indigenous Africans. Obasohan *et. al*[10] reports that glucose intolerance is common in hypertensive subjects, in Benin, Nigeria.

The treatment of hypertension has variable outcomes, indicating involvement of factor or factors other than hypertension in the prognosis, and impaired glucose metabolism is one of such factors.[11,12] Berglund *et al* has demonstrated a positive correlation between systolic blood pressure and blood glucose levels[13]. It has been hypothesized, that blood glucose concentrations lower than those necessary to diagnose IGT and DM are associated with increased risk of cardiovascular disease[14].

Emerging evidence suggests that abnormal glucose tolerance and hypertension may be aetiologically related through insulin resistance and hyperinsulinemia. The insulin resistance syndrome is a cluster of well known atherogenic cardiovascular risk

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factors which predict type 2DM and ischemic heart disease.[15, 16]

Most of the studies of prevalence of abnormal glucose in primary hypertension have been in Caucasians. Therefore, there is need to further assess the magnitude of the problem in Black Africans, particularly hypertensive Nigerians. This study examines the prevalence and pattern of abnormal glucose tolerance in hypertensive Nigerians with or without drug treatment, in comparison with normotensive controls.

Subjects, Materials and Methods

Hypertensives that were above the age of 35 years with systolic BP > 160mmhg and diastolic BP > 95 mmHg or lower if on medication (calcium channel blockers or ACE inhibitors) were selected.

Hypertensive subjects who had the following features were excluded:

i. Hypertensive subjects who had an identifiable cause for hypertension;

ii. Evidence of target organ damage such as hypertensive heart disease or heart failure, renal disease or failure or proteinuria, retinopathy or stroke.

iii. Use of thiazide diuretics and or B-blockers.

iv. Smokers

v. Usually non-residents in Calabar.

The normotensive control subjects were drawn from a pool of hospital staff that was known to have normal blood pressure after the routine pre-employment medical examination. They were free of the above exclusion criteria and had no history of medical illness. A total number of 200 hypertensive subjects were screened over the study period and 64 who met the criteria were selected. Similarly, 60 non- hypertensive (control) subjects out of a total of 150 screened who met the study criteria were also selected. A total of 124 subjects and controls (64 subjects and 60 controls) were studied. The subjects were made up of 32 males and 32 females. The controls were made up of 30 males and 30 females. The study was explained to them and informed consent obtained from the subjects and controls. An approval for the study by the University of Calabar Teaching Hospital Ethical Committee was also obtained. The relevant personal data and history including age, sex, family history of hypertension and diabetes or both, and drug history were obtained. A thorough general physical examination to confirm criteria was carried out. The physical examination included blood pressure, weight, height and waist circumference (WCR) measurements. The blood pressure was measured with a standard adult size mercury glass sphygmomanometer (Accouson England). The cuff size was selected to cover approximately two thirds (2/3) of the upper arm with edge about 2.5 cm above the ante cubital fossa. All pressures were taken on the right arm, at the level of the heart, with the subject sitting and after 15 min rest. An average of two readings taken at the beginning and end of interview was recorded as the systemic arterial pressure.

The systolic pressure was determined by Korotkoff sound phase 1, while the diastolic blood pressure was taken at the point of disappearance, Korotkoff phase V. The weight was measured with a weighing beam (way master made by Precision Weighing, Reading England). Each measurement was done with subject in light clothing (under clothes), no shoes or headgear, to the nearest O.1kg. The weighing beam had Standiometer graduated scale for measuring height (Seca made in Germany). Height was in the erect position to the nearest 0.5cm, without shoes or headgear.

The body mass index is calculated from the formula, BM1 = Weight (Kg)/Height (M^2).

The waist circumference (WCR) was measured following the procedure recommended by the Airlies conference. Various blood samples were drawn from all the study subjects, after an overnight fast following a one week usual Nigerian diet which is usually (about 90%) carbohydrate.[18] This blood sample is for the fasting blood glucose at 0 hrs.

Then they were given 75g of anhydrous glucose dissolved in 250 mls of water to drink over 5 minutes. A second and third venous blood samples were drawn at 1 hour and 2 hours. Urine samples were also collected at 0 hr, 1 hr and 2 hrs and analyzed for glucose using the Bayer diagnostic dipstick and result recorded as positive or negative. The three samples of venous blood were analyzed for glucose using the glucose-oxidase method according to Trinder[19] All samples were assayed immediately. Analysis of the OGTT was as recommended by the WHO expert committee on Diabetes Mellitus.[20] Data were presented as means ± standard deviation (SD). The venous blood glucose levels of each time point of OGTT were compared between the groups by the unpaired student t-test. A p-

value < 0.05, was considered significant. Each subroutine of the statistical package Epi info 2000 was used for analysis of data.

Results

The hypertensive subjects (32 males/32 females) and normotensive controls (30 males/30 females) had mean ages of 47.6±10.1yr and 44.2±7.6 yrs respectively. The mean BMI and WCR of subjects and controls differed significantly, table 1.

Table I

Comparison of baseline data of hypertensive subjects with those of Normotensive Controls

	Hypertensive Subjects n = 64	SD	Normotensive controls n = 60	SD	P. value
Age (years)	47.6	10.0	44.2	7.6	0.079
Weight (kg)	78.8	21.2	72.7	16.2	0.087
Body mass index (BMI) kg/m^2	30.2	8.0	28.5	5.3	0.013
Waist Circumference (cm)	100.8	17.2	88.5	14.1	0.0001
Systolic BP (mmHg)	169.5	22.3	129.3	14.1	0.0001
Diastolic BP (mmHg)	109.5	13.9	84.4	6.4	0.0001

Values as means = SD
P-values <0.05 significant

The hypertensive subjects had a higher mean fasting blood glucose level than controls, P<0.05. Similarly, the response of the subjects to glucose load was significantly higher than controls, particularly at 2 hours P = 0.001, table 2. About 43% of subjects had one form of abnormal glucose tolerance. There were 4 cases of IFG (6.25%) amongst the subjects. One male control had IFG (1%). Twenty-one hypertensive subjects 32.8% (9 males and 12 females) had IGT. No control had IGT. Forty (62.5%) subjects responded normally to OGTT. There were 3 cases (4.25%) of DM amongst the hypertensive subjects, all males. No control had DM. Two of the four hypertensive subjects with IFG had diabetic response to OGTT. However, gender wise, the mean plasma glucose levels of the male subjects in response to glucose load were significantly higher at 1hour and 2hours time points, than those of controls, though the mean plasma glucose levels at 0 hour did not vary significantly, fig 1.The females had significantly higher mean fasting plasma glucose level, and more so in response to glucose load 1hour and 2hours, fig 2.

Table II

Blood glucose values of hypertensive subjects and Normotensive controls in response to Oral glucose Tolerance Test

Oral glucose Tolerance Test	subjects n = 64	controls n = 60	P -value
Fasting (Ohr)	4.79 ± 99	4.42 ± 0.90	0.03
1 hour post load	6.94 ± 1.55	6.25 ± 1.02	0.005
2 hours post Load	5.96 ± 1.82	5.05 ± 1.18	0.001

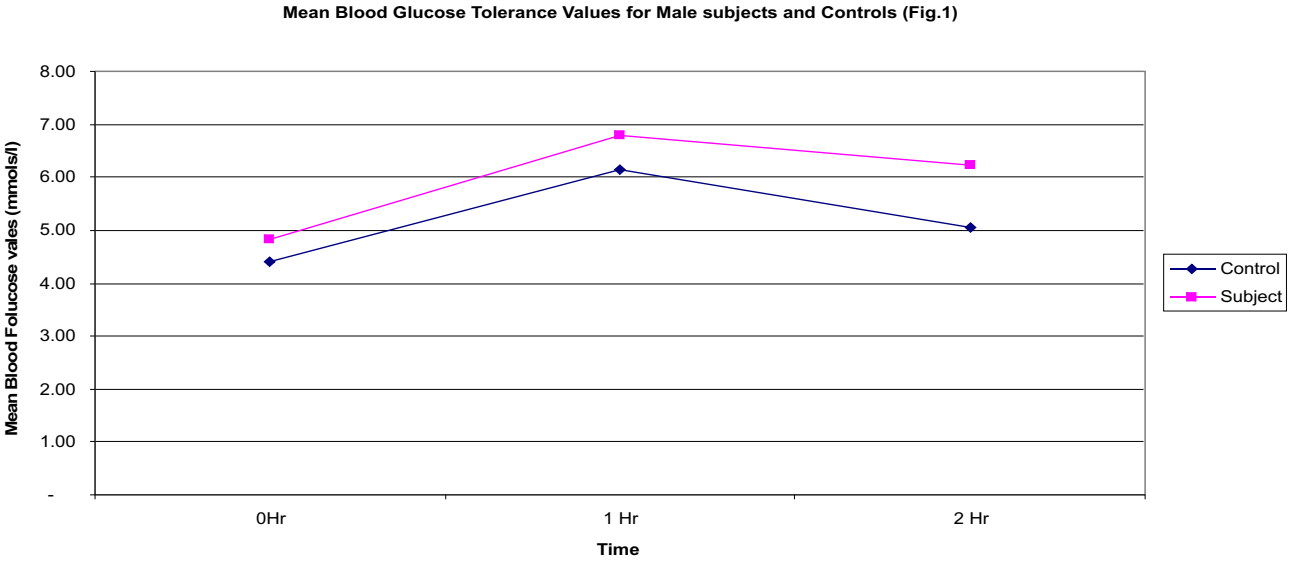
Values as means ± SD
P-values <0.05 significant

LEGEND TO FIGURE 1

MEAN BLOOD GLUCOSE VALUES FOR MALE SUBJECTS AND CONTROLS.

LEGEND TO FIGURE 2

MEAN BLOOD GLUCOSE VALUES FOR FEMALE SUBJECTS AND CONTROLS.



The hypertensive subjects with abnormal glucose tolerance had a higher mean BMI and WCR than those hypertensive subjects with normal glucose tolerance and normotensive controls, table 3.

Table III

Mean values BMI and WCR of groups of Hypertensive Subjects and Normotensive Controls with respect to response to Oral glucose tolerance test

Anthropometric Features	Group 1 (60)	Group 2 (40)	Group 3 (24)
BMI (kg/m^2)	28.5 ± 5.3	28.82 ± 7.76	32.55 ± 8.09
WCR (cm)	88.5 ± 14.1	94.71 ± 22.7	105.44 ± 15.63

Mean value ± SD

Group 1 -Normotensive controls with normal glucose tolerance

Group 2 -Hypertensive subjects with normal glucose tolerance

Group 3 -Hypertensive subjects with abnormal glucose tolerance

Discussion

This study shows that abnormal glucose tolerance, particularly IGT, is prevalent in adult Nigerians with primary hypertension, even when they are not taking thiazide diuretics and B -adrenergic blockers, the first and second line antihypertensive agents known to affect glucose metabolism. The patients in this study that were on drug treatment were either on calcium channel blockers (Nifedipine, amlodipine) or angiotensin converting enzymes inhibitors (captopril or lisinopril) and alpha - methyldopa. These classes of drugs have been shown not to adversely affect glucose metabolism. The hypertensive subjects had a higher mean fasting blood glucose than controls. They also responded to the oral glucose load with higher blood glucose levels than the normotensive controls.

Abnormal glucose tolerance (AGT) was present in 43% of the hypertensive subjects and IGT was the more prevalent present in 32%. The frequency of IFG and DM were 6.25%, 4.60% respectively. The finding of this study are consistent with a previous Nigerian study which had shown that some adult hypertensive Nigerian responded to glucose load with higher blood glucose levels, than matched controls[10]. The IGT rate in hypertensive Nigerians are lower than the rates in middle aged Japanese [23] and caucasians[16], but is considered high enough to contribute to the prevalence of cardiovascular disease[14].

The exact mechanism that links IGT and hypertension are not known, but there are abundant evidences that suggest that both might be aetiologically related through hyperinsulinemia and insulin resistance.[9,15,16,24-,26]Hence, hyperinsulinemia and or resistance to the action of insulin in glucose metabolism, is considered a common underlying mechanism linking glucose intolerance, obesity, and hypertension. Insulin stimulates the sympathoadrenal system and kidney, by increasing nerve function and by promoting sodium reabsorbtion in the renal tubules[25]. These mechanisms cause vasoconstriction and increase peripheral resistance, and cause expansion of plasma volume on a chronic basis with increased cardiac output.

This may represent the role insulin plays in elevating and sustaining elevated blood pressure in subjects with hypertension. However, insulin resistance and hyperinsulinemia are not found in every subject with hypertension. Neither is hypertension present in every patient with hyperinsulinemia. This is as expected since isolated changes in the physiologic mechanisms that regulate blood pressure, are seldom sufficient to cause hypertension. The hypertensive subjects in this study were significantly more obese, than controls. Their obesity was distributed centrally. The hypertensive subjects with abnormal glucose tolerance were even more obese than controls, table 3. Obesity is frequently encountered in persons with a clustering of risk factors such as hypertension ,IGT, hyperinsulinemia and type 2 DM. Reaven had emphasized the underlying feature common to these conditions as insulin resistance[16]. He named the complex syndrome X. It has been hypothesized that in obesity ,the hyperinsulinemia that is a consequence of insulin resistance stimulates the sympathetic nervous system, increasing sympathetically mediated thermogenesis and re-

establishing energy balance[25]. We did not measure insulin levels because of lack of facilities to do so, but because IGT (an intermediate stage known to relate to insulin resistance) was more prevalent than DM (more related to B-cell failure) insulin resistance and hyperinsulinemia might play a part. These observations may explain the high blood glucose levels seen in the hypertensive subjects compared to the controls in this study. Though, the glucose levels were higher at all stages of the OGTT in the HT, the differences were only marginally significant in the females HT and not in male HT at the fasting level, but became progressively significant at 1 hour and 2 hours post-test in the delayed phase of the OGTT which is the more important part of the test (Figs. 1 & 2).

Gender did not affect the response to glucose load. It is note worthy that only 1% of the normotensive subjects had any form of AGT i.e. IFG. This may be due to the small number studied, but it further suggests that AGT is relatively uncommon in normotensive Nigerians.

This study has shown that adult hypertensive Nigerians have a higher prevalence of abnormal glucose tolerance than their normotensive counterparts. IGT is more prevalent than IFG and DM. They also have a higher mean blood glucose level at fasting and in response to glucose load. This finding further supports the aetiologic relationship of hypertension and DM. Moreover, it also supports the principle that treatment of hypertension particularly in DM, should go beyond blood pressure values alone in order to reduce the risk of developing cardiovascular complications.

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