Electrocardiographic abnormalities in persons with type 2 diabetes in Kaduna, Northern Nigeria

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Abstract
Background and Objective: Diabetes mellitus is the most common endocrine disorder in Nigeria. Type 2 Diabetes Mellitus (T2DM) is associated with increased cardiovascular risk, in part due to accelerated subclinical atherosclerosis. Ischaemic Heart Disease (IHD) is an important chronic complication of diabetes mellitus because it is the most prevalent amongst cardiovascular diseases and a major cause of morbidity and mortality. This study sets out to determine the most frequent electrocardiographic (ECG) abnormalities in persons with T2DM in Kaduna (a sub-urban environment). **Subjects, Materials and Methods:** 150 consecutive persons with T2DM and 150 normal controls were recruited from the Diabetes Clinic of Ahmadu Bello Teaching Hospital, Kaduna for the study. Relevant history and physical examination findings were recorded in a protocol. The variables studied were: gender, age, smoking habit, physical activity, and waist circumference, body mass index (BMI) and blood pressure. Resting ECG was recorded and abnormalities grouped according to the classification: ST-T segment changes, left ventricular hypertrophy (LVH) and conduction defects. Serum lipids were also compared. **Results:** The mean age of the diabetics and controls were not significantly different (50.5 ± 9.9yrs vs. 51.1 ± 10.3yrs), respectively. Fifty percent were females. BMI and waist circumference were significantly ($p<0.05$) higher in diabetics (BMI 27.89 ± 1.78 kg/M^2, WC 96 ± 10.2 cm) compared to control (BMI 24.22 ± 1.51 Kg/M^2, WC 86 ± 6.5cm). Sixty two percent of diabetics were hypertensive and 20% of diabetics and 1.5% of control subjects had ECG evidence of IHD, and 7% of diabetics had LVH. Seventy one percent of persons with T2DM had dyslipidaemia, a significant ($p<0.05$) increase compared to control. **Conclusion:** The various resting 12-lead ECG findings among persons with T2DM in this study reflect non-specific features of cardiovascular diseases in general. The most frequent ECG abnormalities T2DM are ST-T segment depression, and left ventricular hypertrophy. Ischaemic heart disease is emerging fast, in a developing, poverty-stricken environment like Nigeria and should be routinely examined. Hypercholesterolaemia and female gender are the strongest and most frequent factors associated with IHD.

Key Word: Diabetes mellitus, electrocardiogram, ischaemic heart disease

Introduction
Diabetes mellitus is a group of metabolic disorders characterized by hyperglycaemia resulting from variable interactions of hereditary and environmental factors due to defects in insulin secretion, insulin action or both.[1] Type 2 diabetes mellitus (T2DM) is the most common type of diabetes, contributing more than ninety percent of diabetes mellitus worldwide.[2] The prevalence rate is rising rapidly particularly in the developing world. The prevalence of diabetes is between 0.6-7.2 percent in Nigeria.[3] Patients with T2DM have insulin resistance and have relative, rather than absolute insulin deficiency.[4] T2DM is associated with increased cardiovascular risk, in part due to accelerated sub-clinical atherosclerosis.[5] Ischaemic heart disease is a common complication of diabetes mellitus because it is the most prevalent among cardiovascular diseases and a major cause of morbidity and mortality.[6] DM is also associated a

greater electrocardiographic left ventricular hypertrophy.[7] Most persons with T2DM are obese, and obesity itself causes some degree of insulin resistance[8]. Those who are not obese by conventional body mass index (BMI) of ≥30kg/M^2 may have central obesity.[9] By nature, Nigerians are not obese with the average BMI of 22 Kg/M^2.[10] The result of a study conducted in Zaria showed that central obesity, however, is prominent (95%) in T2DM patients.[11] This study is undertaken to characterize the electrocardiographic abnormalities in persons with T2DM in Kaduna, a semi-urban environment in Northern Nigeria.

Subjects, Materials and Methods
This is a cross-sectional study carried out at the Diabetes Clinic of the Department of Medicine, Ahmadu Bello University Teaching Hospital, Kaduna, Nigeria. The study population comprised one hundred and fifty (150) consecutive persons with T2DM, and equal number of controls, matched by age, sex (aged 30-70years). Diabetes mellitus was diagnosed using the World Health Organization (WHO) diagnostic criteria of fasting plasma glucose (FPG) of ≥7.0mmol/l and/or 2-h postprandial plasma glucose (2-HPPG) of ≥11.1mmol/l. Precise date of

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diagnosis of diabetes was obtained verbally and confirmed from hospital records to arrive at the duration of diagnosis of diabetes. Information on age, sex and anthropometric measures were obtained from all patients and controls.

Weights (Kg) were taken with only undergarments to the nearest 0.5Kg. Heights (M) were taken to the nearest 0.5cm with subjects standing erect without shoes or headgear. Body mass index (BMI) was derived by dividing the weight by the square of the height. BMI of ≥ 25 to $29.99Kg/M^2$ was used to define overweight while a value $\geq 30Kg/M^2$ was used to define obesity. Waist circumference (WC) was measured at the level of the umbilicus with subjects in the supine position. WC of $\geq 102cm$ and $\geq 80cm$ in males and females, respectively were taken as central obesity. Past or current history of chest pain/discomfort, location, radiation, time, and relieving and aggravating factors were noted.

Social history such as cigarette smoking was considered significant if the subject smoked 10 or more sticks of cigarette per day. Alcohol consumption was considered significant if subject ingests more than 60-80g of alcohol per day for over 5 years.

Family history of diabetes, hypertension, IHD, stroke, and sudden cardiac death were obtained.

A 12-lead resting ECG reading was recorded on all subjects using the ECG machine (Schiller, Baar Switzerland). Significant ECG findings like ST-segment elevation or depression, T-wave inversion, bundle branch block, chamber enlargement, arrhythmias and other changes were noted.

The diagnosis of ischaemic heart disease was made based on the American Heart Association criteria. These criteria include ECG features of significant ST- segment depression defined as an ST-segment depression of more than 1mm in more than one lead, and T-wave inversion. Myocardial infarction was defined as an ST-segment elevation (convex upwards) of more than 0.08sec, associated with T-wave inversion in multiple leads, and reciprocal ST-segment depression in opposite leads.

Statistical Analysis
All data were entered into already prepared proforma and statistically analyzed using EPI-INFO version 6.04. The result is expressed as mean ± 2-standard deviation, with 95% confidence interval. Prevalent rates were calculated as percentages and comparison by chi- square test. The data was considered statistically significant when P < 0.05.

Results
A total of 150 persons with T2DM and 150 control individuals participated in the study. They were aged between 30-70years. The mean age among persons with and without T2DM is 50.5 ± 9.9 and 51.1 ± 10.3yrs, respectively. There was no significant difference in the age and sex distribution between the two groups. There were 72 males and 78 females with diabetes, with mean age 50.0 ± 2.99 and 50.9 ± 2.64, respectively (p > 0.05).

Only 6% among persons with T2DM agreed to

cigarette smoking, four of which are currently smoking. Sixteen percent of the diabetic patients consume alcoholic beverages though mild on occasions only. Twenty percent of diabetics and 1.5% of control subjects had ECG evidence of IHD, and LVH, respectively. Seventy five percent of diabetics had a significantly (p<0.05) high level of dyslipidaemia compared to control (Tables 1-5).

Table 1: The Comparison of clinical characteristics of diabetic and control subjects

Variables	Diabetics Mean (± sem) [Range]	Control Mean (± sem) [Range]	P value
Age (yrs)			
M	50.00 (3.0) [30-70]	49.82 (2.7) [30-69]	>0.05
F	50.90 (2.6) [30-70]	52.39 (3.1) [30-70]	>0.05
BMI (kg/M^2)			
M	27.3 (6.2) [13.6-41.5]	24.3 (5.5) [16.2-60.0]	<0.05
F	29.5 (1.84) [18.0-48.8]	26.9 (0.17) [18.5-40.0]	<0.05
WC (cm)			
M	94.5 (3.01) [87-102]	89.3 (2.34) [67-90]	>0.05
F	96.0 (11.5) [87-114]	81.2 (10.4) [65-86]	<0.05
SBP (mmHg)			
M	139.8 (7.9) [100-200]	122.4 (3.6) [100-140]	<0.05
F	144.7 (5.88) [100-190]	124.4 (3.7) [100-140]	<0.05
DBP (mmHg)			
M	90.1 (4.29) [70-140]	80.7 (2.3) [60-90]	<0.05
F	91.7 (3.2) [60-110]	81.2 (2.2) [60-90]	<0.05

M=males, F=Females, BMI=body mass index, WC=waist circumference, SBP and DBP=systolic and diastolic blood pressures. sem=standard error of mean.

Table 2: Shows comparison of the distribution of ECG abnormalities in controls and persons with T2DM in percentage.

Abnormality	Diab.	Cont	Total	P values
IHD	20	1.5	21.5	<0.05
LVH	7	1	8	<0.05
VE	1	1	2	>0.05
LBBB	1	-	1	>0.05
Peaked T-waves	1	0.35	1.35	>0.05
Sinus tachycardia	1	0.35	1.35	>0.05
RBBB	1	0.5	1.5	>0.05

*IHD=Ischaemic heart disease, LVH= left ventricular hypertrophy, VE=ventricular ectopics, LBBB = left bundle branch block, RBBB =rightt bundle branch block..Diab=Diabetics, Cont=Control.

Discussion
Diabetes has a profound impact on life expectancy, and a person diagnosed with T2DM in middle age (40-60yrs) stands to lose as much as 10 years of life expectancy.[12]

Table 3: Comparison of some biochemical characteristics in all subjects

Variables		Controls n=150 Mean (± sem) [Range]	Diabetics n=150 Mean(± sem) [Range]
FBG (mmol/L)	M	4.63(0.34) [3.00-4.60]	9.77(1.01)* [4.00-20.4]
	F	4.74(0.48) [2.80-6.00]	10.18(0.93)* [3.4-18.0]
2HPPG (mmol/L)	M	7.10(0.40) [4.10-10.0]	13.67(1.11)* [6.90-25.5]
	F	7.77 (0.33) [5.60-9.80]	14.38 (0.99)* [4.4-22.0]
TC (mmol/L)	M	4.43 (0.30) [2.40-8.30]	5.10 (0.37)* [3.2-10.3]
	F	4.49 (0.27) [2.80-7.30]	5.39 (0.34)* [3.1-9.60]
TG (mmol/L)	M	1.08(0.29) [0.30-7.40]	1.49(0.62)* [0.30-15.6]
	F	0.86(0.09) [0.30-1.70]	1.54(0.25)* [0.3-5.52]
LDL-c(mmol/L)	M	2.69(0.19) [1.50-5.41]	3.17(0.31)* [1.50-8.54]
	F	2.65(0.19) [1.60-5.59]	3.15(0.24)* [1.36-5.0]
HDL-c (mmol/L)	M	1.14(0.07) [0.70-1.71]	0.99(0.08)* [0.48-1.70]
	F	1.18(0.08) [0.65-1.76]	1.15(0.10) [0.50-2.30]
TC:HDL ratio:	M	4.01(0.36) [2.40-7.80]	5.47(0.54)* [2.50-10.0]
	F	3.97(0.30) [2.48-6.44]	5.72(0.63)* [1.9-12.0]

*= P value <0.05. FBG=fasting blood glucose, 2-HPPG=2hour postprandial blood glucose, TC=total cholesterol, TG= Triglyceride level, LDL-c= Low-density lipoprotein cholesterol, HDL-c= High-density lipoprotein cholesterol, TC: HDL ratio= total cholesterol- HDL ratio, n= number of subjects

Table 4: Comparison of some clinical and biochemical characteristics in persons with diabetes and IHD, and those without IHD

Variables	Diabetes +IHD Mean (±sem) [Range]	Diabetes -IHD Mean (±sem) [Range]	P value
Age (yrs)	52.4 (9.8) [38-70]	48.03 (9.8) [30-65]	<0.05
BMI (Kg/M^2)	27.99 (3.6) [18.6-41.5]	24.99 (3.5) [13.0-35.6]	<0.05
WC (cm)	113 (6.2) [70 -130]	110 (5.2) [60-115]	<0.05
TC (mmol/L)	5.88 (1.2) [3.2-10]	3.49 (1.10) [2.3-8.10]	<0.05
TG (mmol/L)	4.54 (2.91) [3.3-15.6]	3.99 (1.33) [2.8-13.5]	>0.05
LDL-c (mmol/l)	3.92 (1.2) [2.3-8.54]	3.0 (0.96) [1.99-7.12]	>0.05
HDL-c(mmol/L)	0.96 (0.19) [0.45-1.40]	0.99 (0.17) [0.51-1.80]	>0.05

*BMI= body mass index, WC= waist circumference, TC=total cholesterol, TG= Triglyceride level, LDL-c= Low-density. +IHD= lipoprotein cholesterol, HDL-c= High-density lipoprotein cholesterol. Sem = standard error of the mean

The mean age of presentation in diabetic subjects is 50.5 ± 9.9 with an age range of 30-70 yrs. Similar age ranges were reported by Fasanmade et al,[13] and Qureshi et al[14] in their series. This trend of younger patients presenting with type 2 diabetes in the developing world, is documented in United States, Pacific islands, Hong Kong, and the United Kingdom.[12, 13] The male to female ratio in this study was found to be 1:1.1. The slight female preponderance was also reported by earlier workers in Nigeria.[13]

Type 2 diabetic patients in this study had significantly higher mean body mass index and waist circumference. This is similar to observations in reported from Lagos, Nigeria.[13]

Sixty one percent of persons with T2DM had BMI of >25Kg/M.[2] This is less than the rates reported in industrialized countries, where more than seventy five percent of newly diagnosed T2DM patients are obese.[15, 16] Obesity rates in persons with T2DM in developing countries like Africa and Asia are generally much lower than those from industrialized countries.[3] In a prospective descriptive study by Fasanmade et al, in Lagos among persons with diabetes, obesity was the predominant co-morbidity with frequency much higher in the pre-diabetic states (gestational diabetes mellitus, impaired glucose tolerance) than in type 2 diabetes mellitus.[13]

However, using the waist circumference which is more sensitive for the prediction for risk of cardiovascular disease, the obesity rate is markedly high in this study. The obesity rate was significantly higher in females than males, as was also noted previously in diabetic, and non- diabetic Nigerians.[17,18] BMI correlated well with hypertension among diabetics, this could be explained by the fact that both increased body weight and increase in blood pressure are associated with insulin resistance.[19]

Sixty two percent of persons with T2DM in this study were hypertensive. This is similar to previous observations in Zaria.[18] The Framingham study group has shown that mean systolic blood pressure are higher in diabetics than in age-sex matched controls, similar to the experience in this study.

Some studies comparing persons with type 2 diabetes and those without, showed significantly higher blood pressures among those with type 2 diabetes.

Autonomic function is also influenced by glycaemia and exerts a crucial role in the control of blood pressure and cardiac function. The disruption of this physiological mechanism impacts deeply on cardiovascular mortality in diabetes.[20]

The various resting 12-lead ECG findings amongst persons with type 2 diabetes in this study reflects non-specific features of cardiovascular diseases in persons with type 2 diabetes in general.

The prevalence of IHD by ECG criteria in persons with type 2 diabetes in this study was 20%. Previous reports from this part of the world described IHD as a rarity.[21, 22] None of the patients with suggestive ECG findings of IHD presented with typical angina pain. This may be due to autonomic

Table 5: Clinical Correlations of Risk Factors among Persons with Diabetes and IHD

	Age	BMI	TC	TG	LDL-c	HDL-c	SBP	DBP
Age	1.00	-0.09	0.04	-0.37	-0.07	0.33	0.25	0.09
BMI	-0.09	1.00	-0.13	0.11	-0.18	-0.31	0.04	0.11
TC	0.04	-0.13	1.00	-0.10	0.72*	0.20	0.00#	0.02
TG	-0.37	0.11	-0.10	1.00	0.11	-0.18	-0.03	0.15
LDL-c	-0.07	-0.18	0.72*	0.11	1.00	0.22	0.12	0.19
HDL-c	0.33	-0.31"	0.20	-0.18	0.22	1.00	0.50	0.43
SBP	0.25	0.04	0.00#	-0.03	0.12	0.50	1.00	0.88*
DBP	0.09	0.11	0.02	0.15	0.19	0.43	0.88*	1.00

*=Positive relationship. " = Negative relationship, # = No relationship
SBP, and DBP=systolic and diastolic blood pressures, TG=triglyceride, TC =total cholesterol, LDL-c=low- density lipoprotein cholesterol, HDL-c= high-density lipoprotein cholesterol, BMI= body mass index.

neuropathy in the subjects following chronic non-enzymatic glycation of the vasa nervorum, endothelial dysfunction and inflammation involving the endothelia vascular wall.[23]

Resting 12-lead ECG may be normal in the presence of chronic stable coronary artery disease, thus exercise ECG would have been much more predictive of IHD and future cardiac events.[24] A normal tracing on resting ECG only suggests the presence of normal resting left ventricular function. A normal test does not, however, exclude IHD.[25]

Left ventricular hypertrophy was found in 7% of the diabetic subjects. The frequency of severe and prognostically, unfavourable arrhythmias and LVH was higher in T2DM than healthy population in a study in Russia.[26] This may be because of high prevalence of hypertension, which in itself contributed to the high rate of IHD by concentric hypertrophy of the ventricle and subsequently constricting the coronary arteries.

Conclusions
The various resting 12-lead ECG findings among persons with type 2 diabetes in this study reflects non-specific features of cardiovascular diseases in general. The most frequent ECG abnormalities in type 2 diabetes in this study are ST-T segment depression, left ventricular hypertrophy. Ischaemic heart disease is emerging fast in developing, poverty-stricken environments and should be routinely examined. Hypercholesterolaemia and female gender are the strongest and most frequent factors associated with IHD.

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