Pattern of Electrocardiographic Abnormalities in Asymptomatic Type 2 Diabetes Mellitus Out-patients at Nnamdi Azikiwe University Teaching Hospital, Nigeria

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ABSTRACT

Background: Cardiovascular diseases rank among the major causes of diabetes-associated morbidity and mortality and are early markers of type 2 diabetes mellitus (T2DM). Electrocardiogram (ECG) remains a relevant diagnostic tool for cardiac abnormalities. **Objective:** To determine the prevalence and pattern of electrocardiographic abnormalities in asymptomatic T2DM out-patients at NAUTH, Nigeria. **Materials and Methods:** This was a cross-sectional descriptive study that evaluated 136 T2DM out-patients seen at diabetes clinic. Relevant data was extracted with a researcher-structured questionnaire and anthropometric measurements were done. A 12-lead non-stress ECG and laboratory tests were done. ECG was interpreted based on the Minnesota Codes for Resting Electrocardiograms. Data was analyzed using SPSS version 25. Categorical data were analyzed and compared using Chi-square test: results presented in frequencies and percentages. The mean values of continuous variables were calculated and compared between groups using Students t-test and analysis of variance (ANOVA). The level of significance was set at $p<0.05$. **Results:** 128 T2DM subjects with complete data were analyzed: 63 (49.2%) males and 65 (50.8%) females. The mean age was 58.43 ± 12.85. Q-wave abnormality occurred in 4.7%, QRS abnormality in 21.9%, left ventricular hypertrophy in 10.2%, T-wave abnormality in 21.9%, ST segment abnormality in 3.9%, atrioventricular (AV) block in 0.8%, bundle branch block (BBB) in 4.7%, sinus rhythm abnormality in 22.7%, atrial enlargement in 21.1% and coronary artery disease was seen in 23.4% of the participants. **Conclusion:** There was high prevalence of abnormal ECG findings that depicted a high prevalence of cardiac abnormalities in T2DM subjects.

Keywords: Cardiovascular; Electrocardiographic; South East; Type 2 Diabetes.

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INTRODUCTION

Cardiovascular diseases (CVDs) are common in patients with type 2 diabetes mellitus (T2DM) and rank among the most prevalent causes of diabetes-associated morbidity and mortality.[1] This occurs through DM induced micro-vascular and macro-vascular complications.[2,3] In addition to coronary artery diseases (CAD), CVDs include cerebrovascular disease and peripheral artery disease. Cardiovascular changes are an early marker of and can even ante-date the diagnosis of type 2 diabetes mellitus. Type 2 diabetes subjects have 2-4-fold higher risk for CVD morbidity and mortality compared with healthy non-diabetics.[2] Additionally CVDs are responsible for 24-30% of hospitalization and about one-third of deaths in subjects with DM, from which CAD accounts for 75-90% of deaths.[4,5] Studies have reported worse outcomes from CVDs in subjects with DM compared with non-diabetic subjects.[6]

Electrocardiogram (ECG) remains a simple, non-invasive, cost effective and important diagnostic tool for cardiac abnormalities. Electrocardiographic changes are common and appear early in the course of DM including sinus tachycardia, heart rate variability, ST-T changes, left ventricular hypertrophy (LVH) and others.[7,8]

Globally, about 30% of asymptomatic T2DM patients showed ECG abnormalities.[8] More advanced diagnostic tools like computerized tomography (CT) angiography and echocardiography could be deployed in the evaluation of cardiac abnormalities in the setting of DM, but in resource-constrained settings, their routine availability and affordability may not be guaranteed. Resting ECG assessment may not be sufficient to diagnose some cardiovascular abnormalities, including silent cardiovascular disease. However, the use of coding system such as the Minnesota coding system may improve its utility.[9]

ECG abnormalities are common in T2DM patients. In Nigeria, features of ischemic heart disease (IHD) were seen in 20%, while those of LVH were seen in 7% of T2DM subjects in the North, in the West the prevalence of prolonged QTc was 25.5%, T-wave changes was 22%, LVH 18.5%, sinus tachycardia 15.5%, IHD 9%, conductive defects 7% and ectopic beats was 4% among type 2 diabetic subjects [10,11]. In the East, CAD was detected in 16.5%, ST-T changes in 53.3%, arrhythmias in 23.1% and chamber hypertrophy in 38.5% of stable T2DM subjects.[12]

In Ethiopia, Bedane et al found that 61% of asymptomatic T2DM subjects they studied had ECG abnormalities while Sinamaw *et al* found the prevalence rate of ECG abnormalities of 45% among T2DM subjects; 21% had T-wave abnormality, 14% left axis deviation (LAD) while 9.3% sinus tachycardia. [13,14] Electrocardiographic abnormalities were also found in 20% of Senegalese with type 2 diabetes mellitus. [15].

In India, Gupta et al found that among their T2DM cohort, 6 had left atrial enlargement (LAE), 4 had LVH, 2 had right bundle branch block (RBBB), 2 had left bundle branch block (LBBB,) while 12 had ST depression and T-wave abnormality. [16]. Kittner et al similarly found that 52% of T2DM subjects in India had ECG abnormalities. [17] Kikuko et al found that the prevalence rate of arrythmia in the T2DM subjects in Indonesia was 14.2%. [18]

Electrocardiographic abnormalities were also seen in 60% of African Americans and 22% of Canadians with type 2 diabetes mellitus.[19, 20]

In the management of patients with DM routine screening for cardiovascular diseases can easily be missed in asymptomatic patients.[12]

There is a paucity of studies on ECG abnormalities in T2DM subjects in the sub-Saharan Africa and South Eastern Nigeria in particular. This study sets out to determine the prevalence and pattern of ECG abnormalities in stable T2DM outpatients at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nigeria.

MATERIALS AND METHODS

This was a cross-sectional observational study among asymptomatic T2DM subjects who were evaluated for ECG abnormalities at the out-patient diabetes clinic of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi in South Eastern Nigeria. This study was carried out between July, 2022 and April, 2023. A total of 136 T2DM subjects were recruited for the study, 128 subjects had complete results and were analyzed. Diabetes

clinic runs every Wednesday of the week and an average of about 12 new patients are seen per clinic day. A convenient sampling method was used for subjects' recruitment whereby all consenting consecutive patients with T2DM that presented to the diabetes clinic and who met the inclusion criteria were recruited for the study. Participation in the study was entirely voluntary and data handled with confidentiality.

Inclusion criteria were: consenting T2DM subjects aged 30 years and above who had no symptoms suggestive of cardiovascular disease(s) and who were not on antiarrhythmic drugs. Subjects were excluded if they were aged less than 30 years, had T1DM, were pregnant, had clinical symptoms suggestive of CVDs or were very ill. The study participants were met twice. At the first meeting, a focused medical history was taken and examination done. Also, blood pressure and anthropometric measurements that included height, weight, waist and hip circumference were done. Other relevant data were extracted using a researcher structured and administered study protocol. Next, a resting electrocardiogram was done using Schiller AT-102 plus 12-lead resting ECG. Ten electrodes were placed in the specific anatomic positions to obtain quality tracings. The four limb leads were applied to the four limbs: the right and the left legs and the right and left arms. The six chest leads were applied at the pre-cordial locations (V1-V6). The recording was done over a period of about 10 seconds after the connections were made.

The interpretation of the ECG recordings was done by a cardiologist using the University of Minnesota Codes for Resting Electrocardiograms.[9] The second meeting with the participants was a week later at the next clinic appointment between 8 a.m and 9 a.m. This was to enable the subjects fast for about 10-12 hours before sample collection that included fasting blood sample and to avoid any possible effects the fear of or the trauma of venipuncture might have on the ECG findings of the subjects.

3ml of blood sample was taken via venipuncture from each subject following strict aseptic procedure, for fasting blood glucose (FBG) and glycated haemoglobin (HbA1c).

The samples for HbA1c were collected in EDTA bottles and measured with automated CLOVER A1c Analyzer (Infopia, Korea) and CLOVER A1c Self-Test Cartridge using the boronate affinity method.[21] The samples for FPG were collected in fluoride oxalate bottles and measured by the Trinder glucose oxidase method.[22] Weight and height were measured using Stadiometer (RGZ -120), waist circumference measured with a measuring tape and blood pressure measured using Accoson mercury Sphygmomanometer.

Statistical Analysis of Data

Data was analyzed using SPSS version 25 (Chicago, IL, USA). Categorical data were analyzed and compared using Chi-square test: results presented in frequencies and percentages. The mean values of continuous variables were calculated and compared among groups using student's t-test and analysis of variance (ANOVA). The level of significance was set at $p < 0.05$.

Definition of Terms and Criteria

1. Hypertension was defined as systolic BP ≥ 140mmHg and or diastolic BP ≥ 90 mmHg measured on at least 2 separate occasions or if a patient is already on anti-hypertensive medications.[23]
2. Poor glycaemic control was taken as HbA_{1C} ≥ 7.0%.[24]
3. Global obesity was defined by body mass index (BMI) >30 (kg/M^2). [24]
4. Central obesity (abdominal obesity) was defined as waist circumference (WC) > 102 cm in men and 88 cm in women.[25]
5. Diabetes mellitus was defined by fasting plasma glucose of ≥ 7.0 mmol/l (126 mg/dl) measured on at least 2 separate occasions or the patient is already on glucose lowering agents.[24]
6. Type 1 DM was defined as subjects with DM who are dependent on insulin for survival and are at risk for ketoacidosis.[24]
7. Type 2 DM was defined as patients with DM on diet therapy either alone or in combination with oral glucose lowering agent(s) for glycaemic control.[24].
8. Major ECG abnormality was defined as pathological Q waves (codes 1-1 and 1-2),

marked ST depression ST depression (codes 4-1 and 4-2) and/or T wave inversion (codes 5-1 and 5-2), bundle branch block (codes 7-1 and 7-2) or some significant arrhythmias. Minor ECG abnormalities were defined as high voltage, axis deviation and lesser degrees of ST-T wave abnormality (4-3,5-3). "Ischaemic ECG" was defined as pathological Q waves (any code 1), ST and or T wave inversion of any degree (any code 4 or 5) or left bundle branch block (code 7, 1-1). Left ventricular hypertrophy was defined as a combination of high voltage and either ST depression or T wave inversion on the basis of appropriate Minnesota code.[9]

RESULTS

A total of 128 T2DM subjects had complete results and were analyzed. They were made up of 63 (49.2%) males and 65 (50.8%) females.

Descriptive characteristics of the study subjects

The mean age of the subjects was 58.43 ± 12.85, mean duration of DM was 9.03 ± 7.36 years, mean BMI was 27.96 ± 5.61 kg/m^2, mean WC (males) was 97.80 ± 12.40 cm, mean WC (females) was 99.59 ± 12.70 cm, mean HbA1c was 8.28 ± 2.11 %, mean FBS was 8.97 ± 3.84 mmol/L, mean SBP was 131.28 ± 21.26 mmHg, mean DBP was 77.05 ± 12.41 mmHg and mean HR was 85.33 ± 14.60 bpm (details in Table 1).

Socio demographic characteristics of the study subjects

Among the participants 63 (49.2%) were males and 65 (50.8%) were females, 106 (82.8%) subjects were married, 4 (3.2%) were single and 18 (14.1%) were widowed. 2 (1.6%) had no formal education, 45 (35.1%) had primary, 28 (21.9%) secondary and 54 (41.1%) had tertiary education (details in Table 2).

Also 63.5% and 55.4% of the male and female subjects had their blood pressure within the hypertensive range respectively. Equally 20.0%, 63.3% and 70.8% of the young, middle and elderly subjects had their blood pressure in the hypertensive range while 58.5% of the married and 77.8% 0f the widowed population similarly had their blood pressure within the hypertensive range (details in Table 3).

Additionally, majority of the subjects, 74 (57.8%) were on anti-hypertensive medications. Of these, 39 (52.7%) were on angiotensin converting enzyme inhibitors (ACEIs), 34 (45.9%) were on angiotensin 11 receptor blockers (ARBs), while 1 subject (1.4%) was taking other medication for blood pressure control. Similarly, 91 (71.1%) subjects were on OADs for DM control, 11 (8.6%) were on insulin alone, 23 (18.0%) were on both OADs and insulin, while 3 (2.3%) were on dieting alone for their glycaemic control. 87 (68.0%) subjects were on statins for dyslipidaemia (details on Table 4).

Prevalence and pattern of Electrocardiographic abnormalities among the subjects

Among the subjects studied, 45.3% had abnormal ECG findings: Q-wave abnormality occurred in 4.7%, QRS abnormality occurred in 21.9%, LVH in 10.2%, T-wave abnormality in 21.9%, ST segment abnormality in 3.9%, AV block in 0.8%, BBB in 4.7%, sinus rhythm abnormality in 22.7%, atrial enlargement in 21.1% and CAD in 23.4% of the participants (details in Table 5).

Table 1: Descriptive statistics of the study population

Variable	Minimum	Maximum	Mean ± SD
Age (years)	32.00	93.00	58.43 ± 12.85
Duration of DM (years)	0.25	40	9.03 ± 7.36
WC males (cm)	72.5	131.00	97.80 ± 12.40
WC females (cm)	70.00	127.00	99.59 ± 12.70
BMI (kg/m^2)	18.28	45.18	27.96 ± 5.61
HbA1c (%)	3.37	14.80	8.28 ± 2.11
FBS (mmol/L)	4.00	28.40	8.97 ± 3.84
HR (bpm)	54.00	122.00	85.33 ± 14.60
SBP (mm Hg)	100.00	190.00	131.38 ± 12.37
DBP (mm Hg)	60.00	110.00	77.26 ± 10.89

DM = diabetes mellitus; WC = waist circumference; BMI = body mass index; HbA1c = glycated haemoglobin; FBS= fasting blood sugar; HR = heart rate; bpm = beats per minute, SBP = systolic blood pressure; DBP = diastolic blood pressure

Table 2: Socio-demographic characteristics of the study population

Variable	Options	Frequency n (%)
Sex	Male	63 (49.2)
	Female	65 (50.8)
Marital status	Single	4 (3.2)
	Married	106 (82.8)
	Widowed	18 (14.1)
Level of education	No formal	2 (1.6)
	Primary	45 (35.1)
	Secondary	28 (21.9)
	Tertiary	53 (41.4)

Table 3: Prevalence rate of Hypertension among the study subjects

	Hypertension n (%)	
	Present	Absent
Sex		
Male	40 (63.5)	23 (36.5)
Female	36 (55.4)	29 (44.6)
Age (years)		
<45	4 (20.0)	16 (80.0)
45-64	38 (63.3)	22 (36.7)
>64	34 (70.8)	14 (29.2)
Marital status		
Single	0	4 (100)
Married	62 (58.5)	44 (41.5)
Widowed	14 (77.8)	4 (22.2)
Level of education		
No formal	1 (50.0)	1 (50.0)
Primary	28 (66.7)	14 (33.3)
Secondary	19 (65.5)	10 (34.5)
Tertiary	28 (50.9)	27 (49.1)

Table 4: Clinical characteristics of the study subjects

Variable	Options	Frequency n (%)
DM treatment	Diet alone	3 (2.3)
	OADs	91 (71.1)
	Insulin	11 (8.6)
	Both OADs & Insulin	23 (18.0)
On anti-hypertensive medication(s)	Yes	74 (57.8)
	No	54 (42.2)
Antihypertensive medication used	ACEIs	39 (52.7)
	ARBs	34 (45.9)
	Others	1 (1.4)
On Statins	Yes	87 (68.0)
	No	41 (32.0)

DM = diabetes mellitus; OADs = oral anti diabetic drugs; ACEIs = angiotensin converting enzyme inhibitors; ARBs = angiotensin receptor blocker

Table 5: The overall ECG abnormalities among study population

ECG parameters	Frequency n (%)	
	Present	Absent
Q-wave pathology	6 (4.7)	122 (95.3)
QRS axis abnormality	28 (21.9)	100 (78.1)
LVH	13 (10.2)	115 (89.8)
T-wave abnormality	28 (21.9)	100 (78.1)
ST segment abnormality	5 (3.9)	123 (96.1)
AV block	1 (0.8)	127 (99.2)
BBB	6 (4.7)	122 (95.3)
Sinus rhythm abnormality	29 (22.7)	99 (77.3)
Atrial enlargement	27 (21.1)	101 (78.9)
CAD	30 (23.4)	98 (76.6)

AV = atrioventricular; LVH = left ventricular hypertrophy; BBB = bundle branch block; CAD = coronary artery disease

DISCUSSION

This study evaluated the prevalence and pattern of electrocardiographic abnormalities in apparently asymptomatic T2DM subjects and this is in keeping with previous research works.[10,14] This study subjects were younger with a mean age of 58.43 ± 12.85 years and had a shorter duration of DM with a mean duration of 9.03 ± 7.36 years compared with that of Olamoyegun et al with a mean age of 66.8 years and mean duration of DM of 20 years in Western Nigeria.[10] The rate of major ECG abnormalities was found to be significantly higher in older age in both genders. [26] The prevalence rate of ECG abnormalities from this study was 45.3% and is similar to 45% found by Sinamaw et al but lower than the 61% by Bedane et al, all in Ethiopia.[13,14] Khanal et al found that the prevalence rate of ECG abnormalities was 6.1% in T2DM subjects in Nepal.[27] Gupta et al found a prevalence rate of ECG abnormalities of 26% among asymptomatic T2DM subjects in India and the mean age of their subjects was 50.1 ± 11.90 years and is comparable with that of this study.[16] It has been found that the odd of having major ECG abnormalities surged with an increasing age. [26] Seller et al in North America found a prevalence rate of ECG abnormality of 60% among African Americans with T2DM. [19] The mean age of their subjects was 56 years and is lower than that of this study (58.3%). [19] Geographical and life style differences between the different settings could explain the high prevalence found in North America. These include consumption of highly atherogenic diets, life style practices like smoking and sedentary living and the attendant obesity that are very common in the Western World. The prevalence rate of major ECG abnormalities was 2.9% and that minor abnormalities 25.9% among the general population in Iran.[26] In Indonesia the prevalence rate of arrythmia was 14.2% among hypertensive and diabetic subjects. [18]

The pattern of ECG abnormalities in the subjects

According to this study, Q-wave abnormality occurred in 4.7%, QRS abnormality in 21.9%, LVH in 10.2% and T-wave abnormality in 21.9% of the study subjects. This study also found 3.9% of ST segment abnormality, 0.8% of AV block, 4.7% of bundle branch block (BBB), 22.7% of sinus rhythm abnormality, 21.1% of atrial enlargement and 23.4% of CAD among the subjects.

Bello-Sani et al similarly found that 7% of T2DM subjects had LVH in Northern, Nigeria.[11] The prevalence rate of LVH of 10.2% found by the index study is very close to 7% found in Northern Nigeria. Both studies were conducted in Nigeria and among subjects with high prevalence rate of hypertension: 59.3% in this study and 62% in the other. Hypertension has a strong and graded relationship with CVDs and is an independent risk factor for LVH. [28] It is viewed as a precursor for CVD especially in the elderly. [29] Also found by Bello-Sani et al was a 20% prevalence rate of IHD, 1% of ventricular ectopic beats, left bundle branch block (LBBB), peaked T-waves and right bundle branch block (RBBB) respectively among their subjects.[11] Ezeude et al in Eastern Nigeria similarly found 22% of T-wave changes and 15.5% of sinus tachycardia among their T2DM subjects, while Olamoyegun et al in Western Nigeria found prolonged QTc in 25.5%, LVH in 18.5%, IHD in 9%, conduction defects in 7% and ectopic beats in 4% of their T2DM subjects.[12,10] Olamoyegun et al studied a much older population with a longer duration of diabetes. Their study equally did not deploy the University of Minnesota codes for resting ECG in their ECG interpretation.[10] These peculiarities regarding their study and also the higher mean age (66.8 years) and longer duration of DM (20 years) among their subjects could explain some of the differences in the results of both works.

Sinamaw et al found 21.1% of T-waves abnormality among their T2DM subjects.[14] This was very close to the 21.9% found from this study. Other findings from their study included 14% of left axis deviation and 9.3% of sinus tachycardia.[14] Harms et al found a prevalence rate of 16.0% of “minor” and 13.1% of “major” ECG abnormalities among their T2DM subjects.[30] Most of these other works unlike this index work studied both symptomatic and asymptomatic T2DM patients and expectedly most of them recorded higher prevalence rates of abnormal ECG findings. Gupta et al found that the most common ECG abnormality observed among their T2DM cohort was ST-T changes, followed by left atrial enlargement (LAE), LVH, LBBB and right bundle branch block.[16] Rai et al contrastingly

found a lower prevalence rate of ECG abnormalities of 28.61% among T2DM subjects that were also hypertensive compared with this study.[31] Equally their ECG interpretation was not based on the Minnesota code for ECG interpretation for DM subjects.

There is a dearth of published data on prevalence and pattern of electrocardiographic abnormalities in type 2 DM subjects, especially the apparently asymptomatic cohorts in the sub-Saharan Africa. This group of patients could easily be missed during routine investigations for cardiovascular diseases. Some existing data on this very important topic were generated decades ago, while some studies did not deploy the University of Minnesota code for resting ECG interpretation for DM subjects, hence the need for an updated study and the rationale for this study. This work in addition to adding to the existing literature will also stimulate further studies on this very important topic locally and globally. Being a hospital-based study the findings from this work may not reflect the true prevalence and pattern of ECG abnormalities in the communities. Also, the ECG interpretation was done by a cardiologist and may not have been completely flawless.

CONCLUSION

The burden of CVDs shown by the prevalence of ECG abnormalities in asymptomatic subjects with T2DM in this study was very high.

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Author's Contributions:

CME – conception, design of the research and manuscript writing; MON– design of research and manuscript review; MCA – literature search; AAO– data collection and interpretation; ACA - manuscript writing/editing; HEI – literature search and editing of the manuscript; AME – data collection, cleaning and analysis; IOA– data analysis; OCO– critical review of manuscript; The authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Data Availability

The data used to support the findings of this study would be made available by the corresponding author upon reasonable request.

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Conflict of interests

None declared

Ethical Approval

Ethical clearance was obtained from the Research Ethics Committee of the Nnamdi Azikiwe University Teaching Hospital, Nnewi before commencement of the study. A written informed consent was gotten from the study subjects before they were enrolled to participate in the study.

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