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Associations of asymptomatic coronary heart disease in a cohort of stable type 2 diabetic subjects in a tertiary health center in south eastern Nigeria: A cross sectional study

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Abstract

Background: Coronary heart disease (CHD) is a type of heart disease where the lumina of the major arteries of the heart (coronary arteries) are narrowed by a build-up of plaque with a resultant limitation of blood flow to and oxygenation of the heart. Coronary heart disease can pose a diagnostic challenge in diabetic subjects due to the fact that it is often asymptomatic with a resultant lack of overt clinical complaint by the patients. It is an important cause of diabetes-associated morbidity and mortality and also a huge contributor to the cost of diabetes care.

Objective: To determine the association between CHD and age, sex, cigarette smoking, duration of diabetes, central obesity, glycaemic control, hypertension, chronic kidney disease (CKD), stroke, transient ischaemic attack (TIA), dyslipidaemia, lack of exercise and metabolic syndrome in type 2 diabetic subjects attending the diabetes outpatient clinic of Nnamdi Azikiwe University Teaching Hospital, Nnewi in South Eastern Nigeria.

Materials and Methods: This was a cross-sectional, observational study comprising 136 clinically stable T2DM subjects that were asymptomatic of coronary heart disease. The participants had two contacts with the researcher. Firstly, all the participants were evaluated with resting ECG for the diagnosis of CHD, 30 subjects had CHD while 106 had not. Next, the 30 subjects that had CHD and 98 of the 106 that had not, were met a second time on another clinic visit where medical history was extracted and anthropometric measurements were done. Next, biochemical tests, which included fasting blood glucose (FBG), glycated haemoglobin (HbA1c), fasting lipid profile (FLP) and serum creatinine were done and the glomerular filtration rate estimated using the Modification of Diet in Renal Disease (MDRD) calculator. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 25 (Chicago, IL, USA). The level of significance was set at $p < 0.05$.

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Results: A total of 128 subjects completed the study and had their data analyzed. 30 subjects had CHD while 98 had not. There was significant association between CHD and TIA (p = 0.040), but no significant association between CHD and age (p = 0.959), sex (p = 0.679), educational status (p = 0.094), cigarette smoking (p = 1.000), duration of diabetes (p = 0.335), central obesity (p = 0.726), glycaemic control (p = 1.000), hypertension (p = 1.000), CKD (p = 0.570), stroke (p = 0.141), dyslipidaemia (p = 0.290), exercise (p = 0.641) and metabolic syndrome (p = 0.633) respectively among the subjects.

Conclusion: There was a high prevalence of asymptomatic CHD among stable type 2 diabetic subject and with the exception of TIA, there was no significant association between CHD and all the other risk factors for CHD that were studied, although these risk factors were found more among the subjects that had CHD compared with those that had not.

Keywords: Associations; Asymptomatic; Coronary heart disease; Nigeria; Stable; Type 2 diabetes.

1 Introduction

Diabetes mellitus, especially type 2 diabetes mellitus (T2DM) has assumed a pandemic proportion. Current statistics show that 9.3% of adults aged between 20 and 79 years all round the world are living with diabetes[1]. Nigeria as a country has her own big share of the growing global burden of diabetes. A systematic review and meta-analysis done in 2018 placed the overall pooled-prevalence of DM in Nigeria at 5.77%[2]. Similarly, the prevalence rate of coronary heart disease (CHD), also known as coronary artery disease (CAD) or atherosclerotic heart disease (AHD) in the diabetic population is high and still counting[3]. Coronary heart disease is a disease of the heart's major blood vessels (coronary arteries) that results from a build-up of plaque inside the arteries, causing narrowing of the lumina of the arteries and limiting blood flow to the heart. Coronary heart disease can pose a diagnostic challenge in diabetic subjects due to the fact that it is often asymptomatic with a resultant lack of overt clinical complaint by the patients[3]. Coronary heart disease is an important cause of diabetes-associated morbidity and mortality and also a huge contributor to the cost of diabetes management, both direct and indirect.[4] Currently, diabetes is viewed as CHD risk equivalent and this is because it has been found that the risk of CHD, including myocardial infarction (MI) in a diabetic patient without prior history of CHD or MI is similar to the risk of re-infarction in a non-diabetic patient with a previous history of myocardial infarction[5].

Type 2 diabetes subjects have been found to have increased risk of CHD, as well as a faster progression of CHD once it was developed and a greater severity of CHD compared to their non diabetic counterparts[3]. Silent CHD and MI are also more prevalent in the diabetic population and the reason for this is ascribed to the presence of autonomic neuropathy that affects sympathetic innervations of the heart which causes a prolongation of angina perception threshold[6,7]. Additionally, it has been found that diabetic subjects post MI have a twofold increase in a 30-day and 5-year mortality compared with their non diabetic counterparts[8,9].

Various clinical tests exist for diagnosing CHD and they include electrocardiography (ECG), echocardiography (ECHO) and single photon emission computed tomography (SPECT) scan. Of all these tests, ECG is more readily available, affordable and simpler to perform and hence it is more suited for use in resource poor and rural settings, typical of the sub-Saharan Africa.

Resting ECG may not readily diagnose silent CHD, but its interpretation in line with the University of Minnesota code for resting ECG increases its accuracy[10,11]. The prevalence rate of asymptomatic CHD in T2DM subjects diagnosed using ECG as reported by Ezeude CM et al was 16.5%, by Wackers FJ et al and Zellweger MJ et al using SPECT were 22% and 42% respectively and by Scognamiglio R et al using ECHO was 60%[11,7,12,13].

The risk factors for CHD evaluated in T2DM subjects by this study included age, sex, cigarette smoking, duration of diabetes, central obesity, glycaemic control, hypertension, chronic kidney disease (CKD), stroke, transient ischaemic attack (TIA), dyslipidaemia, lack of exercise and metabolic syndrome.

Coronary heart disease is very common in subjects with T2DM and majority of the cases are asymptomatic raising great concerns because of the high possibility of missed diagnosis, more especially early diagnosis and treatment. The risk factors for CHD in the setting of diabetes are many, necessitating the need for routine screening for, prevention of and where established, treatment of these risks. There is a dearth of published studies on the associations of cardiovascular risk factor of CHD in subjects with T2DM, especially the asymptomatic cohorts in the sub-Saharan Africa generally and Nigeria in particular. This study attempted to bridge these gaps and stimulate further studies on this very important topic.

2 Material and methods

This was a cross-sectional observational study carried out at the out-patient diabetes clinic of Nnamdi Azikiwe University Teaching Hospital, (NAUTH) Nnewi in South Eastern Nigeria. The study population comprised clinically stable T2DM subjects who were asymptomatic of coronary heart disease and the study period was between July, 2022 and April, 2023. A total of 136 consenting T2DM subjects who met the inclusion criteria were recruited for the study as they were consulted consecutively at the clinic. Subjects were excluded if they were aged less than 30 years, had T1DM, were pregnant, had clinical symptoms and or signs suggestive CVD or if they were very ill. The study was carried out in two stages and the subjects were met twice, on two separate days. During the first stage, at the first meeting all the participants were evaluated with a resting ECG for the diagnosis of coronary heart disease. This was done using Schiller AT-102 plus 12 lead resting ECG machine. 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 and the ECG recordings were interpreted by a cardiologist using the University of Minnesota Codes for Resting Electrocardiograms[10].

Of the 136 participants, 30 had CHD while 106 had not. All the subjects that had CHD and 98 subjects that did not have CAD proceeded to the second stage of the study, while 8 subjects without CHD voluntarily dropped out from further participation in the study. The 128 subjects that remained were given appointments in batches on subsequent clinic days between 8 a.m and 9 a.m, after they had observed a 10-12 hour fast as they were instructed. At this second meeting a focused medical history was taken; a focused examination, blood pressure and anthropometric measurements were done. These findings and other relevant data were filled in a researcher structured and administered study pro-forma.

Next, biochemical tests, which included fasting blood glucose (FBG), glycated haemoglobin (HbA1c), fasting lipid profile (FLP) and serum creatinine were done. A total of 7ml of blood was collected from each subject for the tests following a venipuncture of the cubital vein, while observing full aseptic procedures, 2ml for FBS, 1ml for HbA1c, 4ml for both FLP and serum creatinine.

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[16]. The samples for FPG were collected in fluoride oxalate bottles and measured by the Trinder glucose oxidase method[17]. The blood samples for FLP and serum creatinine were collected in plain bottles. High density lipoprotein (HDL) level was measured by precipitation technique[18]. Total cholesterol level was determined using the kit employing the enzymatic and the 4-hydroxybenzoate/4-aminophenazone system (BioSystems)[19]. Triglyceride level was determined using a kit employing enzymatic hydrolysis of triglyceride with lipases (Randox) and low-density lipoprotein cholesterol (LDL-C) was measured using a kit employing a precipitation technique[20, 21]. Serum creatinine was measured using Jaffe's reaction[22]. Estimated glomerular filtration rate (eGFR) was estimated from calibrated serum creatinine values using the four-variable Modification of Diet in Renal Disease (MDRD) study equation[23].

Weight and height were measured using Stadiometer (RGZ -120), waist circumference measured with a measuring tape and blood pressure measured using Accoson mercury Sphygmomanometer.

Data were 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 $p < 0.05$.

2.1 Definition of terms and criteria

- 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[24].
- Poor glycaemic control was taken as HbA_{1C} ≥ 7.0%[25].
- Global obesity was defined by body mass index (BMI) >30 (kg/M^2)[25].
- Central obesity (abdominal obesity) was defined as waist circumference (WC) > 102 cm in men and 88 cm in women[26].
- Dyslipidaemia was taken as HDL-C < 40 mg/dl or TG ≥ 150 mg/dl or LDL-C ≥100 mg/dl or total cholesterol (TC) ≥ 200 mg/dl or if the patient is on lipid lowering agents[26].
- 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[25].

- Type 1 DM was defined as subjects with DM who are dependent on insulin for survival and are at risk for ketoacidosis[25].
- 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[25].
- 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[10].
- Metabolic syndrome was defined by the presence of three (3) or more of the following five (5) criteria: WC > 101.6 cm in men and 88.9 cm in women, BP > 130/80 mmHg, fasting TG > 150 mg/dl (1.7 mmol/l), fasting HDL < 40 mg/dl (1.0 mmol/l) for men and 50 mg/dl (1.3 mmol/l) for women and FBS > 100 mg/dl (5.5 mmol/l) or the patient is a known diabetic[26].
- Young age was taken as 18-44 years, middle age as 45-64 years and old age as 65 years and above[27].
- Chronic kidney disease (CKD) was determined by eGFR < 90 ml/min/24 hours or patient had proteinuria[23].

3 Results

Of the 136 participants recruited for this study, 128 subjects completed the study: 30 (23.4%) had CHD while 98 (76.6%) had not.

3.1 Descriptive statistics of the subject with CHD

The mean age of the T2DM subjects with CHD was 57.87 ± 15.08 years, mean WC was 97.27 ± 10.99 cm, mean BMI was 27.69 ± 5.59 kg/m^2, mean HbA1c was 8.36 ± 1.90 %, mean FBS was 9.48 ± 5.01mmol/L, mean SBP was 133.70 ± 19.69 mmHg, mean DBP was 78.17 ± 11.18 mmHg, mean creatinine was 93.40 ± 33.14 μmol/L, mean eGFR was 88.13 ± 34.91 ml/min, mean TC was 4.39 ± 1.30 mmol/L, mean TG was 1.29 ± 0.64 mmol/L, mean HDL was 1.08 ± 0.31 mmol/L and mean LDL was 2.86 ± 1.05 mmol/L (details in Table 1).

3.2 Socio-demographic statistics of the subjects

Among the ~~subjects~~ 30 subjects with CHD, 16 (53.3%) were males, 14 (46.7%) were females, 5 (16.7%) were young, 14 (46.7%) were middle aged and 11 (36.7%) were elderly. 25 (83.3%) subjects were married, 1 (3.3%) was single and 4 (13.3%) were widowed. 12 (40.0%) subjects had tertiary education, 3 (10.0%) had secondary education, 15 (50.0%) had primary education and none had no formal education. Also 8 (26.7%) subjects smoked previously while only 1 (3.3%) subject was still smoking as of the time of the study, 6 (20.0%) subjects had regular physical exercise (details in Table 2).

3.3 Clinical characteristics of the study subjects

Also 18 (60.0%) subjects had hypertension and all but one of the hypertensive subjects were on antihypertensive medications, 8 (47.0%) were on angiotensin converting enzyme inhibitors (ACEIs), 7 (41.2%) were on angiotensin 2 receptor blockers (ARBs) while 2 (11.8%) were on other antihypertensive medications. 17 (56.7%) subjects were on lipid lowering medications, 17 (56.7%) subjects had various degrees of CKD, 12 (40.0%) had global obesity while 23 (76.7%) had central obesity. All the subjects were on anti-diabetic medications, 20 (66.7%) were on oral anti-diabetic drugs (OADs) alone, 2 (6.7%) on insulin alone while 8 (26.7%) were combining both insulin and oral anti-diabetic medications.

Equally, 26 (86.7%) subjects had dyslipidaemia, 22 (73.3%) had metabolic syndrome, 3 (10.0%) had TIA while 3 (10.0%) has stroke. 16 (53.3%) had CKD and lastly, 13 (43.3%) subjects had DM for less than 5 years (short duration), while 17 (56.7%) had DM for a minimum of 5 years (long duration) (details in Tables 3 & 4).

3.4 Control to recommended targets of the clinical and biochemical risk factors among the subjects with CHD

Among the subjects with CHD, 7 (23.3%) had good long term glycaemic control, 11 (36.7%) had good immediate (fasting) blood glucose control, 14 (46.6.%) had good SBP control, 20 (66.7%) had good DBP control, while 19 (63.3%), 20 (66.7%), 13 (43.3%) and 14 (46.7%) subjects had their TC, TG, HDL-C and LDL-C adequately controlled respectively (details in Table 5).

3.5 Associations between CHD and the cardiovascular risk factors among the subjects

There was significant association between CHD and TIA in the subjects (p = 0.040), but there was no significant association between CHD and the rest of the risk factors studied that included age (p = 0.959), sex (p = 0.679), educational status (p = 0.094), cigarette smoking (p = 1.000), duration of diabetes (p = 0.335), central obesity (p = 0.726), glycaemic control (p = 1.000), hypertension (p = 1.000), CKD (p = 0.570), stroke (p = 0.141), dyslipidaemia (p = 0.290), exercise (p = 0.641) and metabolic syndrome (p = 0.633) among the subjects, although CHD was more frequent among, males subjects, those with primary education. longer duration of DM, central obesity, poor glycaemic control, CKD, dyslipidaemia, metabolic syndrome and those with hypertension (details in Table 6).

3.6 Comparison of the mean values of risk factors based on the occurrence of CHD

There was no significant difference in the mean values of some of the risk factors for CHD among the subjects with CHD compared to those without CHD that included age, WC, W/H ratio, BMI, HbA1c, FBS, blood pressure, serum creatinine, eGFR, TC, TG, HDL and LDL. Although mean HbA1c, FBS, SBP, DBP, serum creatinine, eGFR, were higher among subjects with CHD compared with those without (details in Table 7).

Table 1 Descriptive characteristics of subjects with CHD

Variable	Minimum	Maximum	Mean ± SD
Age (years)	32.00	93.00	57.87 ± 15.08
Waist circumference (cm)	70.00	112.00	97.27 ± 10.99
Waist-hip ratio	0.72	1.07	0.94 ± 0.09
BMI (kg/m^2)	19.22	44.30	27.69 ± 5.59
HbA1c	5.00	14.07	8.36 ± 1.90
FBS (mmol/L)	5.00	28.40	9.48 ± 5.01
Heart rate (bpm)	58.00	112.00	86.00 ± 16.29
SBP (mm Hg)	100.00	180.00	133.70 ± 19.69
DBP (mm Hg)	60.00	110.00	78.17 ± 11.18
Serum creatinine (µmol/L)	53.00	188.00	93.40 ± 33.14
eGFR	33.70	168.5	88.13 ± 34.91
TC	1.10	7.40	4.39 ± 1.30
TG	0.19	3.13	1.29 ± 0.64
HDL	0.54	2.04	1.08 ± 0.31
LDL	0.74	6.10	2.86 ± 1.05

BMI = body mass index; FBS = fasting blood sugar; SBP = systolic blood pressure; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; TC = total cholesterol; TG = Triglyceride; HDL = high density lipoprotein; LDL = low density lipoprotein.

Table 2 Socio-demographic statistics of the subjects with CHD

Variable	Options	Frequency	Percentage (%)
Age (years)	<45	5	16.7
	45-64	14	46.7
	>64	11	36.7
Sex	Male	16	53.3
	Female	14	46.7
Marital status	Single	1	3.3
	Married	25	83.3
	Widowed	4	13.3
Level of education	No formal	0	0
	Primary	15	50.0
	Secondary	3	10.0
	Tertiary	12	40.0
Previous smoking	Yes	8	26.7
	No	22	73.3
Current smoking	Yes	1	3.3
	No	29	96.7
Exercise	Yes	6	20.0
	No	24	80.0

Table 3 Clinical characteristics of the subjects with CHD

Variable	Options	Frequency	Percentage (%)
Treatment for DM	OADs	20	66.7
	Insulin	2	6.7
	Both	8	26.7
Duration of DM	Short duration	13	43.3
	Long duration	17	56.7
Central obesity	Yes	23	76.7
	No	7	23.3
Body mass index	Normal	12	40.0
	Overweight	6	20.0
	Global obesity	12	40.0
Global obesity class	Class I	11	91.7
	Class II	0	0
	Class III	1	8.3

Stage of CKD	Stage I	2	11.8
	Stage II	6	35.3
	Stage III	9	52.9
Hypertensive	Yes	18	60.0
	No	12	40.0
On antihypertensive Medications	Yes	17	56.7
	No	13	43.3
Antihypertensive medications used	ACEI	8	47.0
	ARB	7	41.2
	Others	2	11.8
On lipid lowering Medications	Yes	17	56.7
	No	13	43.3

DM = diabetes mellitus; OADs = oral antidiabetic drugs; CKD = chronic kidney disease; ACEI = angiotensin converting enzyme inhibitors; ARB = angiotensin 2 receptor blocker.

Table 4 Presence of certain co-morbidities that are also risk factors for CHD among the subjects

Condition	**Present**		**Absent**	
	Frequency	**%**	**Frequency**	**Percentage (%)**
CKD	16	53.3	14	46.7
Stroke	3	10.0	27	90.0
TIA	3	10.0	27	90.0
Hypertension	18	60.0	12	40.0
Dyslipidaemia	26	86.7	4	13.3
Metabolic syndrome	22	73.3	8	26.7

CKD = chronic kidney disease; TIA = transient ischaemic attack

Table 5 Control to desired target of clinical & biochemical cardiovascular risk factors among the subjects

Parameter	**Good control**		**Poor control**	
	Frequency	**%**	**Frequency**	**Percentage (%)**
HbA1c	7	23.3	23	76.7
FBS	11	36.7	19	63.3
SBP	14	46.6	16	53.3
DBP	20	66.7	10	33.3
TC	19	63.3	11	36.7
TG	20	66.7	10	33.3
HDL	13	43.3	17	56.7
LDL	14	46.7	16	53.3

HbA1c = glycated haemoglobin; FBS = fasting blood sugar; SBP = systolic blood pressure; DBP = diastolic blood pressure; TC = total cholesterol; TG = Triglyceride; HDL = high density lipoprotein; LDL = low density lipoprotein.

Table 6 Association of CHD with perceived cardiovascular risk factors among the study subjects

Variables	Options	CAD n (%)		X^2	p-value
		Present	Absent		
Age (years)	<45	5 (26.3)	14 (73.7)	0.113	0.959
	45-64	14 (22.6)	48 (77.4)		
	>64	11 (23.4)	36 (76.6)		
Sex	Male	16 (25.4)	47 (74.6)	0.265	0.679
	Female	14 (21.5)	51 (78.5)		
Educational Level	No formal	0	2 (100)	6.792	0.094
	Primary	15 (35.7)	27 (64.3)		
	Secondary	3 (10.7)	25 (89.3)		
	Tertiary	12 (21.4)	44 (78.6)		
Smoking	Yes	1 (25.0)	3 (75.0)	0.006	1.000
	No	29 (23.4)	95 (76.6)		
Duration of DM	Long	17 (20.7)	65 (79.3)	0.931	0.335
	Short	13 (28.3)	33 (71.7)		
Central obesity	Yes	23 (24.2)	72 (75.8)	0.123	0.726
	No	7 (21.2)	26 (78.8)		
HbA1c control	Good	7 (22.6)	24 (77.4)	0.017	1.000
	Poor	23 (23.7)	74 (76.3)		
Hypertension	Present	18 (23.7)	58 (76.3)	0.006	1.000
	Absent	12 (23.1)	40 (76.9)		
CKD	Present	16 (21.6)	58 (78.4)	0.322	0.570
	Absent	14 (25.9)	40 (74.1)		
Stroke	Present	3 (50.0)	3 (50.0)	2.475	0.141
	Absent	27 (22.1)	95 (77.9)		
TIA	Present	3 (75.0)	1 (25.0)	6.118	0.040
	Absent	27 (21.8)	97 (78.2)		
Dyslipidaemia	Present	26 (22.2)	91 (77.8)	1.121	0.290
	Absent	4 (36.4)	7 (63.6)		
Routine exercise	Yes	6 (27.3)	16 (72.7)	0.218	0.641
	No	24 (22.6)	82 (77.4)		
Metabolic syndrome	Present	22 (22.4)	76 (77.6)	0.228	0.633
	Absent	8 (26.7)	22 (73.3)		

HbA1c = glycated haemoglobin; DM = diabetes mellitus; CKD = chronic kidney disease; TIA = transient ischaemic attack.

Table 7 Comparison of mean values of CVD risk factors based on occurrence of CHD

Parameter	CAD		T	p-value
	Present	Absent		
Age (years)	57.86 ± 15.08	59.78 ± 17.48	0.542	0.589
WC (cm)	97.27 ± 10.99	99.20 ± 12.99	0.741	0.460
Waist-hip ratio	0.94 ± 0.09	0.94 ± 0.10	0.033	0.974
BMI (kg/m^2)	27.69 ± 5.58	28.04 ± 5.65	0.294	0.769
HbA1c (%)	8.36 ± 1.90	8.25 ± 2.17	0.245	0.807
FBS (mmol/L)	9.49 ± 5.01	8.25 ± 2.17	0.848	0.398
Heart rate (bpm)	86.00 ± 16.29	85.12 ± 14.11	0.287	0.775
SBP (mm Hg)	133.7 ± 19.70	130.64 ± 22.14	0.678	0.499
DBP (mm Hg)	78.16 ± 11.17	77.01 ± 12.75	0.447	0.656
Serum creatinine (μmol/L)	93.40 ± 33.14	87.89 ± 21.38	1.073	0.285
eGFR (ml/min)	88.13 ± 34.91	85.07 ± 24.34	0.541	0.590
TC	4.39 ± 1.30	4.61 ± 1.32	0.787	0.433
TG	1.29 ± 0.63	1.39 ± 0.90	0.571	0.569
HDL	1.08 ± 0.31	1.04 ± 0.27	0.641	0.523
LDL	2.86 ± 1.05	2.89 ± 1.21	0.152	0.880

WC = waist circumference; BMI = body mass index; HbA1c = glycated haemoglobin; FBS = fasting blood sugar; SBP = systolic blood pressure; DBP = diastolic blood pressure; eGFR = estimated glomerular filtration rate; TC = total cholesterol; TG = Triglyceride; HDL = high density lipoprotein; LDL = low density lipoprotein.

4 Discussion

A total of 128 subjects completed this study out of the 136 T2DM participants recruited. 30 (22.4%) of these subjects had CHD. Comparably, Wang C et al found a prevalence rate of CHD of 23.5% in a large cohort of 30,693 T2DM patients[26]. A multicenter study in South Eastern Nigeria found the prevalence rate of asymptomatic CHD of 16.5% among clinically stable T2DM subjects[11]. In that study, the sample size of type 2 diabetic cohort evaluated using ECG was smaller (79), compared to 128 in this index study. Also similar to our finding was the prevalence rate of asymptomatic CHD diagnosed using ECG of 18.6% found in Thane, India[27]. Contrastingly, the prevalence rate of asymptomatic CHD detected with ECG in Yaounde, Cameroon, was 58.4%[28]. In Japan the prevalence rate of asymptomatic CHD was 53% among T2DM subjects with vascular complications[29]. This study utilized stress SPECT for the diagnosis of CHD as different from the resting ECG utilized by this index study[29]. A land mark study found that the prevalence of silent myocardial ischaemia diagnosed with stress myocardial perfusion imaging among asymptomatic patients with T2DM was 22%[7]. Another study reported 42% abnormal SPECT scan in asymptomatic T2DM patients[12]. In Padua, Italy, the prevalence rate of asymptomatic CHD was 60% among T2DM patients, this study deployed ECHO as the diagnostic tool[13]. Valensi P et al found that the prevalence rate of silent myocardial infarction (MI) detected using SPECT among diabetic subjects was 35.4% and this was more among patients older than 60 years of age[30]. Lastly, a study found the prevalence of asymptomatic CHD of 6.4% among TDM subjects, using ECG as the diagnostic tool[31].

The wide variations in the ranges of prevalence rates of asymptomatic CHD among type 2 diabetic subjects reported by these studies could be explained in parts by the differences in the methodology adopted, and these included subjects' selection and evaluation criteria and the screening and diagnostic modalities deployed.

4.1 Associations of CHD with the cardiovascular risk factors ~~studied~~ among the subjects

With the exception of TIA, this study did not find significant association between CHD and the cardiovascular risk factors studied which included age, sex, educational status, cigarette smoking, duration of diabetes, central obesity, glycaemic control, hypertension, CKD, stroke, dyslipidaemia, exercise and metabolic syndrome among the subjects. Another local

study equally, did not find any association between all the risk factors studied and CHD among clinically stable T2DM subjects with asymptomatic CHD[11].

Tsujimoto T et al, found that male sex was the only significant predictor of CHD in T2DM subjects with vascular complications[29]. Mfeukeu-Kuate L et al found that abdominal obesity and female sex were independently associated with CHD[28]. The UKPDS and another land mark study on Finnish type 2 diabetic cohorts reported that poor glycaemic control weakly predicted CHD while the classic risk factors of CHD, particularly dyslipidaemia (high total cholesterol, LDL-C, triglyceride and low HDL-C) were strong predictors[32,33].

Wang C et al observed an additive interaction between hypertension and BMI as CHD risks[26]. Srinivasan MP et al found no significant association between fasting lipid profile, HbA1c, FBS, BMI, waist hip ratio, hip circumference and CHD among subjects that had T2DM for more than 10 years[34]. Microalbuminuria was significantly more among the subjects without CHD[34]. This report is similar to that of this study: although this study found that CHD was more prevalent among subjects with longer duration of diabetes, central obesity, poor glycaemic control, CKD and dyslipidaemia compared with those without, this was not significantly ~~so~~.

The strength of this study lies in the fact that there is a dearth of published data on the associations of CHD in type 2 diabetic subjects in sub-Saharan Africa, especially the stable asymptomatic subjects. This work will add to the existing literature and stimulate further studies on this very important topic.

This study has a number of limitations. This study was hospital based and may not reflect the true prevalence and associations of CHD among type 2 diabetic subjects in the rural settings. The population of the subjects with CHD studied was small compared to those without CHD. Lastly, the cross-sectional nature of the study did not allow the researchers make inference on the cause and effect of the risk factors for CHD in the type 2 diabetic subjects studied.

5 Conclusion

In conclusion, there was a high prevalence of asymptomatic CHD among stable type 2 diabetic subjects. With the exception TIA, there was no significant association between CHD and all the other risk factors for CHD that were studied, although these risk factors were found more among the subjects that had CHD compared with those that did not have CHD. Transient ischaemic attack and some of the other classical risk factors could easily be treatable and even preventable thus underscoring the need for a regular and timely screening for and treatment of CHD and its risk factors in T2DM subjects, including the asymptomatic cohorts.

Recommendations

The authors recommend further hospital and community-based studies involving larger population of type 2 diabetic subjects with CHD. Prospective studies that allow the subjects to be followed up over some periods of time are highly advocated.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that no competing interests exist.

Statement of ethical approval

Ethical clearance for the study was obtained from the ethics committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi.

Statement of informed consent

Informed consent was obtained from each of the study participants before their recruitment into the study. They were also allowed to withdraw their participation voluntarily at any point in the study by simply indicating so orally.

Author's contributions

- CM Ezeude – conception, design of research and manuscript writing
- AM Ezeude – data collection/cleaning, data analysis and manuscript editing
- MC Abonyi – Literature search
- MO Nkpozi – design of research and manuscript writing
- CV Ugwueze – manuscript writing and editing
- K Akhidue – literature search and manuscript writing/editing
- AA Onwuegbuna – data collection and interpretation
- OB Anyim – proposal design, literature review and manuscript editing.
- UC Okechukwu – literature search and manuscript writing/editing
- HE Ikeabbah – literature search and editing of the manuscript
- GU Eleje – Final review and certification of the manuscript

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