

The Risk of Developing Heart Diseases Increases with the Duration of the Diabetic Disease Illness among the Patients with Type 2 Diabetes Mellitus in Yenagoa Bayelsa State, Nigeria.

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Abstract

Background and objective: The prevalence of type 2 diabetes and cardiovascular diseases has been increasing globally. The increase in the CVD risk factors have been associated with patients suffering from diabetes mellitus. This study was designed to assess the prevalence of CVD risk factors among the type 2 diabetes subjects attending the hospitals in Yenagoa, Bayelsa State, Nigeria with respect to the duration of illness. The purpose was to ascertain if the time of living with the diabetic disease increases the risk of developing CVDs. **Study design and methods:** This was a cross-sectional study on patients with type 2 diabetes mellitus. A total of 356 Diabetic subjects were recruited for the study that included 159 males with mean age of 54.3 years and 197 females with mean age of 53.4 years. They were distributed into 135 diabetic subjects that have suffered the disease for less than 10 years, 119 for 11-20 years and 102 for 21 and above years respectively. A questionnaire was used to document the demographics, the age, gender, duration of illness, medical history and nature of drugs for management etc. Enzyme linked immunosorbent assay (ELISA), fluorescence and spectrophotometric methods were used for the biochemical measurement of cardiac markers, lipid profile and glucose for the assessment of the CVDs. The patients that did not indicate interest were excluded from the study. **RESULTS:** The result showed that 54.90% of the diabetic patients with CVD and 26.12% with the risk of developing CVD's were in the group that have suffered the disease for 21 and above years. This was statistically significant ($P=0.015$) when compared with the 0-10 and 11-20 years groups that had 15.67 and 29.41 percent respectively. Highest prevalence of HBP and dyslipidaemia were observed among the patients that have suffered the disease for ≥ 21 years. This is in addition to a significant ($P=0.046$) elevated mean value for LDL-C and Tg and low HDL-C among the patient group for 21 and above years. The diabetic patients that have suffered the disease for less than 10 years had higher significant 52.0% of the subjects with depression ($p=0.025$). Apart from the fasting blood glucose, other assessed CVD risk variables from the study showed significant difference between the different time of living with the diabetes mellitus disease. Statistical analysis showed a strong correlation between the risk of developing CVD'S and the duration of the diabetic diseases.

Conclusion: The study has shown that the risk for developing cardiovascular disease increases with the duration of the diabetic disease and was significantly high among those that have lived with the disease for above 20 years. This is associated with the lifestyles and the intracellular metabolic changes in those living with type 2 Diabetic Mellitus.

Keywords: Diabetes mellitus, Cardiovascular diseases, Risk factors, Bayelsa State, Nigeria.

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I. Introduction

Diabetes Mellitus (DM) is a metabolic disease that is characterized by absolute or relative deficiency in insulin secretion, insulin action or both [1]. The International Diabetes Federation (IDF) estimates that worldwide, 415 million people have diabetes, 91% of whom have Type 2 diabetes mellitus (T2 DM) [2]. In Sub-Saharan Africa, Nigeria has the highest number of people with diabetes with an estimated 3.9 million people (or an extrapolated prevalence of 4.99%) of the adult population aged 20-79 years old [3]

Diabetes mellitus in chronic conditions is a risk factor in developing coronary heart disease (CHD) and other cardiovascular diseases (CVD) [4]. The prevalence of risk factors for cardiovascular disease is on the increase in the developing nations of the world [5]. Worldwide, CVD account for the majority of deaths due to chronic diseases [6], and more than 80% of the global burden of CVD will occur in low and middle-income countries [7].

Diabetics are at increased risk for developing heart disease and are often present at an earlier age than people without diabetes [8]. Furthermore, people with diabetes have a high prevalence of silent myocardial

ischemia [9] and almost one third of myocardial infarctions occur without recognized or typical symptoms. Whether the patient suffers from Type 1 or Type 2 diabetes, along with the patient's age and duration of time living with diabetes will impact the risk for developing cardiovascular disease, as diabetes itself is a powerful risk factor for the future development of CVD [10, 11]. In patients with type 1 diabetes, CVD becomes the leading cause of death after 10 years of duration and accounts for 40% of all deaths after 20 years of duration [12]. Most studies on cardiovascular risk in patients with diabetes have been performed in patients with type 2 diabetes who are typically older at disease onset than those with type 1 diabetes [8, 12, 13].

Given the clinical burden that CVD complications have on type 2 Diabetes Mellitus patients, there has been an increased focus on the joint management of T2DM and CVD [14]. The increased focus on adequately treating patients with both CVD and T2DM requires that there should be updated prevalence rates of CVD among patients suffering from type 2 DM, particularly in chronic conditions. This is required to inform clinical and policy level decision making by healthcare providers, healthcare policy decision-makers and health economic analysts particularly in an environment with low Socio-economic status (SES). Although the assessment of Co-occurrence of risk factors for CVD is largely studied in diabetic patients [15, 16], the extent that these trends affect the seemingly population of diabetes mellitus patients in this environment needs to be documented.

The objective of this study was to assess the prevalence of CVD's in diabetic subjects and ascertain if the duration of the illness impacts on developing the risk of cardiovascular disease in Yenagoa, Bayelsa State of Nigeria.

II. Materials/Methods

2.1 Study area:

The study was conducted on patients suffering from diabetes mellitus disease population attending the Federal Medical Centre Yenagoa, Bayelsa State capital and Niger Delta University Teaching Hospital (NDUTH) Okolobiri and other diabetic clinics in Bayelsa State, Niger Delta Region of Nigeria between the months of June 2014 to May 2018.

2.2. Study Population

The study is a population-based cross sectional research conducted on 356 chronic and non-chronic Diabetes patients that were recruited. This comprised of 197 females (55.34%) and 159 males (44.66%) diabetic patients. A total of 135 of the subjects have suffered the disease for less than 10 years, 119 of them for 10 - 20 years and 102 for 21 and above years. Inclusion criteria were identified type 2 DM patients that attended these hospitals for routine check and for one form of treatment or other. Excluded were type 1 DM and type 2 DM that did not show interest in the study.

2.3. Ethical Consideration

Ethical approval was gotten from the University's institution committee for Human Research and approval from the patients before sample collection. Before sample collection, a talk was given to the patients on the essence and significance of the study. A questionnaire was issued to them concerning the demographics of age, gender, duration of illness, medical symptoms and nature of drugs for management among others with the medical history. The consent from the subjects were gotten from them at this point of filling the questionnaire.

2.4 Anthropometric measurements

The obesity assessment measurement was taken by measuring the waist circumference mid-way between the iliac crest and costal margin. Height and weight readings were used to determine the body mass index (BMI). The height and weight were measured using a wall mounted stadiometer and human weighing scale machine [18]. A BMI of 30kg/m^2 were considered as obese [19]. For hypertension, systolic and diastolic blood pressure readings were taken with a digital blood pressure machine (Omron, Australia). Hypertension was classified as systolic blood pressure reading $\geq 130\text{mmHg}$ and/or diastolic blood pressures of $\geq 80\text{mmHg}$ were considered elevated according to International Diabetes Federation (IDF) [19]. These measurements were taken in addition to the information from their medical file on previous history of blood sugar, lipid profile, blood pressure and weight and the data compared.

Demographic and other questionnaire based variables. A questionnaire form was developed to collect data for demographic characteristics and other previous medical history and/or screenings. This is according to World Health Organisation questionnaire steps for non-communicable diseases surveillance for subjects participating in this kind of study [18]. The demographic characteristics include gender, age, tribe, nature of disease, complications and drugs etc. The interest to participate in this study were acknowledged at this level.

2.5. Sample Collection

About 10.0 ml of venous blood was drawn from the patients using standard vene-puncture technique after overnight fast for at least 10 hours and discharged into a tube. The sample was separated for fasting blood glucose (Fbg), lipid profile and cardiac markers determination. This was allowed to clot for about half an hour and then centrifuged at 1500 rpm for about 10 minutes. The serum was separated into a plain tube and analysis of the different cardiac markers performed within 14 hours of sample collection.

2.6. Blood Test

Fasting Blood glucose (Fbg): The fasting blood glucose levels were performed on all the patients' samples using the glucose oxidase method as modified by Randox Laboratories Limited (United Kingdom) [21]. Glucose values ≥ 7.0 mmol/l were considered diabetic. The measurement of the lipid profile (Total cholesterol, triglyceride and high density lipoprotein cholesterol) followed the IDF criteria [19]. Boundary values ≥ 6.40 mmol/l indicates hypercholesterolemia, values ≥ 1.58 mmol/l for hypertriglyceridemia and ≤ 1.8 mmol/l were considered low for high density lipoprotein cholesterol [19].

2.7. Assay for Troponins and Myoglobin

The serum Troponin I (CTnI) and T (CTnT), and myoglobin (Myo) were determined using the Fluorescence immune technique. It uses a sandwich immunodetection method. The more antigens in samples forms, the more antigen-antibody complex and leads to strong intensity of fluorescence on detector antibody that is measured [22] [23].

2.8. Assay for Creatine Kinase (CK-MB) and Lactate Dehydrogenase (LDH)

The Enzyme Linked Immunosorbent Assay (ELISA) method [24] was used in the quantitation of the serum CK-MB and LDH. Specifically, the Elabscience assay kit (USA) and the Biotechnologies plate reader were the analytical instruments used. It is a high sensitive and specific biochemical test kits applied for the detection of myocardial enzymes.

2.7. Statistical Analysis

The data generated from the study were expressed as mean \pm standard deviation, standard error of mean and normal ranges. Correlation between the groups studied was tested using the regression analysis. The results obtained from this were subjected to statistical analysis using standard computerized analysis tool of ANOVA: two factors without replication and standard t-test: pair two samples for mean. 95% confidence level ($p < 0.05$) were used and considered significant.

II. Results

The 356 diabetic participants that comprised of 197 (56.06%) females and 156 (43.94%) males with an average age of 53.4 and 54.3 years respectively had distribution and characteristics of demographic variables among the three study groups, 0 – 10, 11 -20 and 21 and above years summarized in the tables below.

Table 3.1. Baseline characteristics of the studied Diabetic mellitus subjects in Yenagoa, Bayelsa State.

Characteristics	N	Age (Years)	Height (m)	Weight (Kg)	BMI (kg/m ²)	SBP (mmHg)	DBP (mmHg)	p-value
Male	159	54.3 \pm 18.7	1.62 \pm 0.06	63.7 \pm 19.1	24.7 \pm 5.9	132.6 \pm 33.1	79.8 \pm 19.3	p>0.05
Female	197	53.4 \pm 19.3	1.58 \pm 0.07	65.3 \pm 16.4	25.2 \pm 7.1	130.7 \pm 30.9	75.9 \pm 12.4	p>0.05
Total	356	55.5 \pm 13.8	1.61 \pm 0.08	64.5 \pm 15.5	24.8 \pm 7.3	131.9 \pm 3.2	77.9 \pm 16.1	
DURATION OF ILLNESS								
<10years	135	46.2 \pm 10.3	1.59 \pm 0.06	66.1 \pm 15.5	26.2 \pm 5.3	130.4 \pm 28.5	75.9 \pm 18.4	p>0.05
11-20years	119	53.5 \pm 12.7	1.61 \pm 0.06	62.6 \pm 16.8	24.1 \pm 6.1	130.1 \pm 33.2	76.3 \pm 17.3	p>0.05
21 and above years	102	65.9 \pm 17.6	1.61 \pm 0.09	65.4 \pm 17.3	25.2 \pm 6.8	132.9 \pm 30.6	78.6 \pm 19.1	p>0.05

From the table, the number of female participants was higher than the male group. The mean age \pm SD of 54.3 \pm 18.7 and 53.4 \pm 19.3 for the male and female groups respectively. There was no statistical difference ($P < 0.05$) between the different groups and duration of illness with respect to the baseline characteristics studied.

Table 3.2: Prevalence of DM subjects with CVD in relation to the duration of illness.

Characteristics	N	Mean age (yrs)	Mean Fbs (mMol/l)	Percentage with CVD	P-Value	Tchol (mMol/l)	Tg (mMol/l)	HDL-L (mMol/l)	LDL-C (mMol/l)	P-Value
gender										
Male	159	54.3	10.43±3.15	22 (6.18)	P=0.049	4.49±1.08	1.78±0.76	0.85±0.41	4.52±1.01	NS
Female	197	53.4	11.78±3.33	29 (8.15)	P=0.041	4.38±1.73	2.03±0.59	0.98±0.63	4.17±0.83	NS
Total	356	55.5	11.21±3.51	51 (14.33)		4.46±1.69	1.89±0.33	0.91±0.75	4.43±0.99	NS
Duration of illness (yrs)										
0-10	135	49.2	9.91±3.22	8 (2.25)	P=0.058	4.16±1.83	1.88±0.84	1.15±0.55	3.45±0.67	P=0.053
11-20	119	53.5	11.52±2.96	15 (4.21)	P=0.031	4.27±1.37	1.92±0.93	0.89±0.39	3.98±1.02	P=0.051
21 and above	102	65.9	11.68±3.01	28 (7.87)	P=0.019	5.97±1.98	2.14±1.03	0.83±0.43	4.96±1.19	P=0.046
Total	356	55.5	11.21±3.51	51 (14.33)						
Subjects with CVD										
0-10 yrs	8	50.1	10.41±2.55	8 (15.67)	P=0.052					
11-20 yrs	15	59.9	11.68±2.71	15 (29.41)	P=0.048					
21 and above yrs	28	67.3	12.91±2.35	29 (54.90)	P=0.015					

* Statistically significant, ^{NS} Not statistically significant at 95% confidence level....

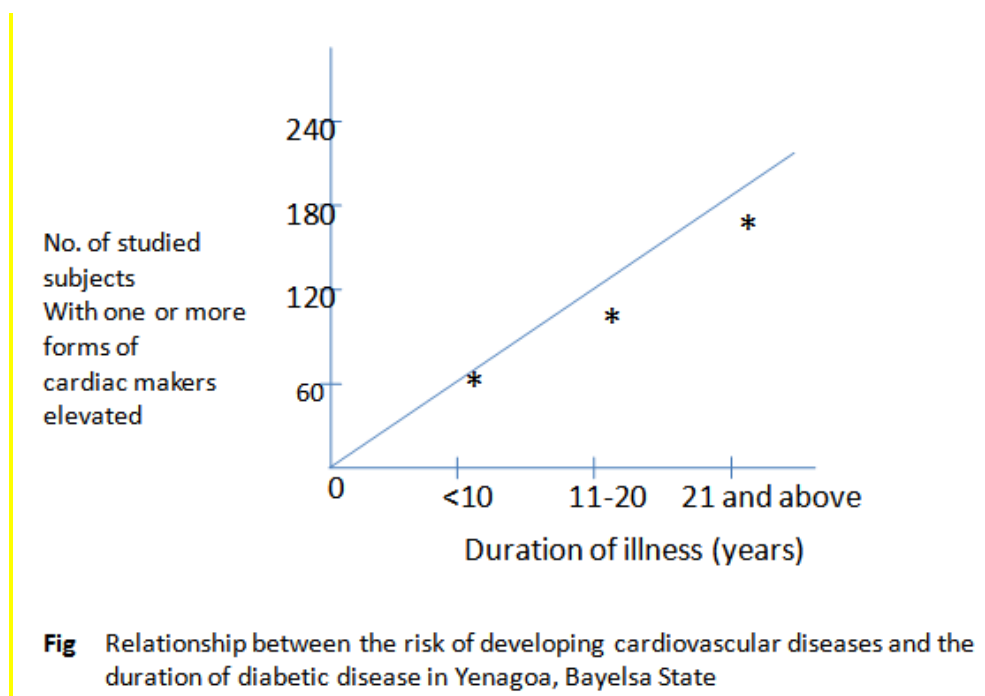
From the table, prevalence of CVD in the entire study was 14.33%. Analysis of the result showed that 8.15% were females and 6.18% were males. The age range of 21 and above years had a significant percentage of 54.90%, with 29.41% and 15.67% respectively for the age range 11-20 and 0-10 years respectively. Results from the study has also shown a statistically significant increased mean value for Tg and LDL-C and low mean value for HDL – C for the age group that have suffered the DM disease for 21 and above years. The mean values for the Fasting blood sugar were not significant (p>0.05) between the age range groups.

Table 3.3: Prevalence of Diabetes with Co-morbidity CVD risk factors

Cardiovascular disease risk factors	No of subjects (n=355)	Prevalence percentage	<10years	11-20 years	>21years	P - value
Obesity	152	42.82	41.45 (63)	33.55 (51)	25.0 (38)	P= 0.023
HBP	102	28.73	17.65(18)	26.47 (27)	55.88 (57)	P=0.026
Dyslipidaemia	73	20.56	20.55 (15)	28.77 (21)	50.68 (37)	P=0.027
Low HDL	22	6.20	18.18 (4)	31.82 (7)	50.0 (11)	P=0.026
High Chol	20	5.63	30.0(6)	25.0 (5)	45.0 (9)	P=0.028
High Tg	31	8.73	16.13(5)	29.03 (9)	54.84 (17)	P=0.022
Stroke	11	3.10	9.10(01)	27.26 (3)	63.04 (7)	P=0.016
Cancer	02	0.56	0.00(0)	0.00 (0)	100.0 (2)	P=0.001
Depression	25	7.04	52.0(13)	24.0 (6)	24.0 (06)	P=0.025
SMOKING	31	8.73	51.61(16)	29.03 (9)	19.36 (6)	P=0.024
Renal Failure	19	5.35	5.26 (1)	21.06 (4)	73.68 (14)	P=0.013
Liver DISEASE	05	1.41	0.00 (0)	20.0 (1)	80.0 (4)	P=0.011
TOTAL			69 (19.38%)	94(26.40%)	180(50.56%)	P=0.025

* Statistically significant

Results from the table have shown that the diabetic subjects that have suffered the disease for <10 years were more obese (41.45%) than those with over weight in the other groups, 33.55% and 25.0% respectively for 11 -20 and 21 and above years. The study found that those that have suffered the disease for ≥21 years had a sizeable prevalence for HBP (55.88%),dyslipidaemia (50.68%), low HDL-C (50.0%), elevated Tg (54.84%), Renal failure (73.68%) and were statistically significant as shown. The diabetic patients that had suffered the disease for less than 10years had higher significant 52.0% of the subjects with depression (p=0.025). The table also showed that 19.38, 26.40 and 50.56 percent of the diabetic subjects studied had one form or other of CVD risk factors in the 0-10, 11-20 and 21 and above year's groups respectively.



The fig1 above showed that 69 (19.38%), 94 (26.40%) and 180 (50.56%) of the diabetic subjects studied had one form or other of CVD risk factors in the 0-10, 11-20 and 21 and above yearsgroups respectively. This has clearly shown from the study that the risk for development of CVD increases with the time of living the disease.

Table 3.4. Mean \pm SEM of Parameters for diagnosis of cardio vascular disease (CVD).

Parameter	N	Mean \pm SEM	p-value
Troponin I [cTnI] (ug/L)			
CVD	53	0.714 \pm 0.026 ^a	<0.0001****
No CVD	303	0.259 \pm 0.009 ^b	
Troponin T [cTnT] (ug/L)			
CVD	51	0.245 \pm 0.012 ^a	<0.0001****
No CVD	305	0.048 \pm 0.004 ^b	
Myoglobin [MYO] (ug/L)			
CVD	65	158.311 \pm 6.388 ^a	<0.0001****
No CVD	291	55.059 \pm 2.109 ^b	
Creatin-Kinase [CK – MB] (u/L)			
CVD	59	34.503 \pm 2.123 ^a	<0.0001****
No CVD	296	7.177 \pm 0.656 ^b	
Total Lactase Dehydrogenase [LDH] (u/L)			
CVD	69	325.897 \pm 9.387 ^a	<0.0001****
No CVD	287	145.524 \pm 3.293 ^b	

SEM: Standard Error of Mean; CVD: Cardio Vascular Disease; within parameter, means \pm SEM with different superscripts are significantly different at $p < 0.05$. Significance Level: **** $p < 0.0001$. Table 3.4 results indicated that 53, 51, 65, 59 and 69 diabetes subjects had elevated levels of cTnI, cTnT, Myo, CK-MB and LDH respectively. The values were statistically significant. 51 DM patients had all the parameters measured elevated, while 93 (26.12%) had either one or more of the parameters elevated.

Table 3.5: The correlation between the risk of developing cardiovascular diseases and the time of living with diabetic disease.

Duration of illness	R-value (+)
< 10years (n=69)	0.237*
11-20years(n=94)	0.396*
>20years (n=180)	0.486*

*P < 0.05, indicate positive correlation (r).

III. Discussion

The Prevalence of Diabetes mellitus is increasing steadily in Nigeria. In the 60's, diabetes was considered to be a rare disease and its prevalence were less than 1.0% [25]. The disease is associated with an increased risk of different heart disease, coronary heart disease (CHD), cardiovascular disease (CVD) and stroke with its connected mortality. The increase in the growing modifiable risk factors for CVD is as a result of increased urban migration that encourages lifestyle changes. The lifestyle changes, together with genetic modifications predisposed individuals to high risk of developing type2 diabetes and subsequent cardiovascular diseases. This is characterised by insulin resistance, beta cell dysfunction, increased lipolysis, inflammation, sub optimal incretin effect and hepatic glucose overproduction [5, 26].

This study showed that greater percentage, 54.90% of the subjects with CVD are in the group that have suffered the disease for 21 years and above (table 3.2). This was statistically significant (P=0.015) when compared with the other groups of 0-10 and 11-20 years with a percentage of 15.67 and 27.41 respectively. This has shown that T2DM increases the risk of developing CVD, particularly at long duration [4, 27]. Adults with diabetes historically have a higher prevalence rate of CVD than adults without diabetes [4] and the risk of CVD increase continuously with rising fasting plasma glucose levels and long duration of the disease [4, 28]. Whether the patient suffers from type1 or type2 diabetes, along with the patient's age and duration of time living with diabetes according to reports, will impact the risk for developing cardiovascular disease, as diabetes itself is a powerful risk factor for the future development of CVD [29, 30]. The assessment of these risk factors and the disease conditions were made possible with the tools of the cardiac markers, that are currently available and that have clinical use as diagnostic, prognostic or predictive biomarkers (table 3.4). In a ten-year incidence of risk of cardiovascular disease study, it was found that the increased risk in individuals with impaired fasting glucose was largely driven by the coexistence of multiple CVD risk factors [31]. This was observed in this study where different risk factors in the studied patients exist. The diabetes subjects with obesity comorbidity CVD were 42.82%, with greater 41.45% in the patients that had suffered the disease for <10years. Obesity and unfavourable lifestyle were associated with higher risk for incident type 2 diabetes regardless of genetic predisposition [32]. This is in contrast to hypertension as a risk factor for developing CVD in diabetic subjects where the patients that have suffered the disease for ≥21 years had a statistical significant percentage of 55.88 as against 17.65% and 26.47% for 0-10 and 11-20 years respectively (table 3.3).

Apart from the fasting blood glucose (Fbg), other assessed CVD risk variables from the study showed significant difference between the different time of living with the diabetes mellitus disease. Highest prevalence of dyslipidaemia (table 3.3), were observed among the patients that have suffered the disease for 21 and above years. This is in addition to a significant (P=0.046) elevated mean value for LDL-C and Tg and low HDL-C among the patients group for 21 and above years (table 3.2 and 3.3), it has been suggested [33] that an association between hyperglycemia and intracellular metabolic changes can result in oxidative stress, low grade inflammation and endothelial dysfunction leading to increased risk of CVD's. From the study 7.04% of the diabetic subjects studied that had CVD were depressed and 52.0% of the depressed diabetic patients were among the non-chronic diabetic sufferers (0-10 years). The percentages for 11-20 and 21 and above years (24.0%) were not significant, suggesting that the patients with the disease at on set are more depressed than the chronic sufferers [34]. The baseline characteristics carried out in this study has shown no statistical significant difference (P>0.05) in the weight, BMI and blood pressure measured (table 3.1) for the different groups with respect to the time the subjects have lived with the disease. From the study 26.12% of the assessed patients showed evidence of developing CVD (table 3.4). This is as a result of elevation in the serum values of the different biomarkers investigated and used for this study. There's a strong positive correlation between the risk of developing CVD's and the duration of the diabetic disease (fig 1) (table 3.5).

In longstanding diabetes mellitus, the extent to which cardiovascular disease and others is an independent comorbidity versus a diabetic complication is not easy to measure because both diseases are quite multivariate and there are likely aspects of both simultaneity and consequence. Many tests attempt to

standardize the weight or value of comorbid conditions whether they are secondary or tertiary illness. Each test attempts to consolidate each individual comorbid conditions into a single predictive variable that measures mortality or other outcomes.

IV. Conclusion

The cardiac markers were used to identify the subjects with CVD and CVD risk in this study. The study has shown that the risk for developing cardiovascular disease increases with the duration of the diabetic disease and was significantly high among those that have lived with the disease for above 20 years. This is associated with the lifestyles and the intracellular metabolic changes in those living with type 2 Diabetic Mellitus.

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Limitations of the Study

- 1) Getting the consent of the identified subjects, as many of them are not literate enough to understand the reasons for the study.
- 2) The cost of the various cardiac markers kit.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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