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PREVALENCE OF DYSLIPIDEMIA AND ATHEROGENIC RISK AMONG TYPE 2 DIABETIC OUTPATIENTS IN GHANA

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ABSTRACT

Background: Dyslipidemia is a major risk factor for cardiovascular diseases, which in turn contribute 68% of mortality among type 2 diabetics. The study aimed to determine dyslipidemia and atherogenic index, among Type 2 diabetic outpatients in Ghana.

Methods: A cross sectional study was conducted on 152 participants. Anthropometric and biochemical indices (including glycated hemoglobin and lipid profile) were determined.

Result: Thirty-seven (24.3%) participants were males and 115 (75.7%) were females. Prevalence of hyperglycemia was 74.3%. The prevalence of single dyslipidemia, combined dyslipidemia and mixed dyslipidemia were 63.8%, 15.8%, and 1.3% respectively. Also, 35.3% of the participants had high coronary risk and 5.3% had high atherosclerotic risk. Coronary risk was strongly associated with Total Cholesterol (TC), ($r=0.690$, $p< 0.0001$) and Low density lipoprotein Cholesterol (LDL-C), ($r=0.783$, $p< 0.0001$), while atherosclerotic risk correlated with Triglycerides (TG), ($r=0.817$, $p< 0.0001$) and Very low density lipoprotein Cholesterol (VLDL-C), ($r=0.817$, $p< 0.0001$). Regression analyses revealed that a point increase in TC was associated with 2.6-folds increased odds of coronary disease risk (OR= 2.6, 95% CI=1.9-3.7, $p< 0.0001$), TG was associated with 2-folds higher coronary risk (OR= 2.5, 95% CI= 1.3-4.8, $p=0.004$), and LDL-C was associated with 5- folds higher coronary disease risk (OR= 4.9, 95% CI=2.9-8.1, $p< 0.0001$) among participants.

Conclusion: Uncontrolled blood glucose and atherogenic dyslipidemia was common among these diabetics, were significantly associated with high coronary and atherosclerotic risk. Management of diabetes in Ghana needs a critical look at to increase effectiveness and reduce the burden of the disease.

Keywords: Dyslipidemia, atherogenic index, Type 2 diabetes Mellitus

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1.0 Introduction

Type 2 diabetes mellitus occurs when insulin production is defective or its action on the metabolism of carbohydrates, protein and lipids is defective (Meshram et al., 2016). Dyslipidemia and atherogenic dyslipidemia cause complications and mortality in type 2 diabetic patients, in addition to being strong determinant risks for predicting cardiovascular diseases (Taskinen and Boren, 2015; Niroumand et al., 2015). Dyslipidemia is defined as having one or more disorders in serum lipids (Samdani et al., 2017). Atherogenic Index Plasma (AIP) and coronary risk are well-established surrogate independent lipid ratios markers which can predict occurrence of cardiovascular diseases, especially among diabetics (Sharaye, 2015; Lafta, 2014).

Globally, 415 million people lived with diabetes mellitus in 2015 (IDF, 2015) and about 2 in 20 people with diabetes lived in low and middle income countries (IDF, 2013). Currently, it is estimated that in Africa, 14.2 million people within the ages of 20-79 years have diabetes; with prevalence rate of 3.2% (Oguoma et al., 2017). In Sub-saharan Africa, about 30% of patients admitted in cardiovascular intensive care units have diabetes mellitus, and cardiovascular disease is responsible for mortality in two out of three diabetic patients (Kengne et al., 2005). Furthermore, in Ghana, about 266,200 of the population in the age range aged 20-79 years are living with diabetes mellitus, and the prevalence rate is about 1.9% (IDF, 2015).

In type 2 diabetes mellitus, poor blood glucose control induces insulin resistance and subsequently aggravates serious dyslipidemia, which concurrently increases risk of atherosclerotic events and coronary heart disease (Shrestha and Khanal, 2017).

Consequently, persistent high blood glucose in type 2 diabetic patients may also induce glycosylation of proteins in arterial wall. This eventually damage endothelial cells and eventually led to the atherosclerotic events (Devrajani et al., 2011). Dyslipidemia becomes atherogenic when there is combined elevation of triglycerides (TG) and small dense low density lipoprotein cholesterol (LDL-C), and decreased high density lipoprotein cholesterol (HDL-C) in the blood (Kasabe et al., 2017). According to Sert et al., (2010), different populations may observe varying modification in their lipids profile; for instance, low density lipoprotein is somewhat elevated among non-Africans and lowers in other racial groups of diabetics.

In type 2 diabetes, there is alteration in lipids and lipoprotein parameters which contribute to oxidative stress and development of atherosclerosis (Nimmanapalli et al., 2016). Furthermore, dyslipidemia is a longstanding metabolic disturbance which singularly promotes insulin resistance in adipose and muscle tissues. Insulin resistance can then perpetuate persistent hyperglycemia, which becomes susceptible to protein glycation and formation of sorbitol, advanced glycated end products and free radicals (King and Grant, 2016). The formation of these free radicals and advanced glycated end products can cause oxidative stress which causes damage to endothelial tissues (Rolfes et al., 2009). The dysfunction of endothelial tissue can stimulate atherosclerotic events on blood vessels which can progress to cardiovascular diseases.

Clinical research in Ghana has not focused on lipids abnormalities and lipoprotein disorders in type 2 diabetics. Even as evidence from research elsewhere show prevalence of

dyslipidemia, and high predisposition risk of atherosclerotic vascular diseases among type 2 diabetic patients (Khadke et al., 2015; Kalofoutis et al., 2007), very little has been done and reported among Ghanaian diabetics, and the extent to which these observations are true in the Ghanaian context is unknown. Additionally, lipid profile has not been part of the parameters measured and monitored among diabetics in Ghana's health delivery system but a better insight into dyslipidemia and associated issues among diabetics in Ghana will enable such recommendation or otherwise. The study therefore aimed at determining the prevalence of dyslipidemia and atherogenic dyslipidemia among type 2 diabetic outpatients in Ghana.

2.0 Materials and Methods

2.1 Study design and population

This is a cross-sectional study was carried out on type 2 diabetic outpatients within age ranges 35-80 years, attending Komfo Anokye Teaching Hospital, Diabetic Clinic. Komfo Anokye Teaching Hospital is one of the largest teaching hospitals in Ghana. The hospital managed about 9000 cases of diabetic patients across Ghana in 2011. Using the cochrane formular, a sample size of 152 diabetics was determined, and simple random sampling approach was used to select and collect data from the consented participants. Gestational diabetics and Type 1 diabetic patients were excluded from the study.

2.2 Sociodemographic data

A questionnaire was used to collect data on demographics and health status of participants. Data collected included information on health, smoking, alcohol, family history of diabetes knowledge of cardiovascular diseases and medical history of hypertension.

2.3 Anthropometric data

Participants' heights were taken using a stadiometer (SECA 213), while body weight and BMI were taken using the body composition analyser (OMRON). Waist circumference was taken by placing the measuring tape around the waist (midway between the lower rib and iliac crest) while participants stood straight.

2.4 Assessment of Biochemical Parameters

Blood samples used for fasting blood glucose, HbA1c and serum lipid profile were collected from participants after 9–12 hours of overnight fasting. Five ml of blood sample was taken from each participant and placed into gel and clot activator vacuum and fluoride tubes. The collected blood samples stood for about 10 minutes and centrifuged at 4000 rpm for 5 minutes. An Automated Integra 400 plus machine (Roche Diagnostics GmbH, Germany) was used to determine fasting blood glucose using the glucose oxidase method (Fortress Diagnostics, United Kingdom). HbA1c was also determined on 96 participants using cation exchange method as described by (Travelli et al., 1971; Gonen et al., 1978; Gabbay et al., 1977 and Bates, 1978). The supernatant serum of centrifuged blood was analysed for total HDL-cholesterol, total cholesterol and triglycerides containing cholesterol reagents manufactured by Fortress Diagnostic Limited, United Kingdom. The concentration of LDL-cholesterol in all samples was calculated using Friedewald formula; LDL-c = TC − [HDL-c+($\frac{TG}{2.2}$)] (mmol/l); where ($\frac{TG}{2.2}$) = VLDL-c (Fortress Diagnostics, United Kingdom).

Each of the biochemical parameter was defined using internationally accepted cut-offs. The American Diabetes Association cut off for fasting blood glucose < 126 mg/dL (< 7.0 mmol/L) - normoglycemia and ≥ 126 mg/dL as hyperglycemia (≥ 7.0 mmol/L) was used to determine high blood glucose among study participants. In addition, HbA1c < 6.5% was referred to as normoglycemia and HbA1c ≥ 6.5% was termed hyperglycemia (ADA, 2013). The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) cut off values for lipids profile parameters was used to determine the various dyslipidemia. The cut off for log TG/HDL-C ≤ 0.21 – normal atherogenic index of plasma and > 0.21 as high atherogenic index of plasma used by Lima et al., 2011 was used to determine risk of atherogenic. TC/HDL-C values below 3.5 were termed low coronary risk, while values 3.5 and above was categorised as high coronary risk (Shen et al., 2016).

2.5 Data Analysis

Data was analyzed using SPSS version 23 (SPSS Inc Chicago, IL). Categorical variables for sociodemographics (gender, age, educational level, family history of cardiovascular diseases, alcohol intakes, past smoking, history of hypertension) were presented as absolute and relative frequencies. Continous variables were presented as means and standard deviations. The mean values of various variables were compared between those with and those without coronary disease risk using Independent t-test for all continuous parameters (age, BMI, waist circumference, fasting blood glucose, glycated hemoglobin and lipid profile). A partial correlational analysis, controlling for age and gender, was performed on biochemical variables against independent cardiovascular risk markers. Logistic regression was done to calculate odds ratio in order to estimate risks. Statistical significance was set at $p<0.05$.

3.0 Result

3.1 Sociodemographic Characteristics of Type 2 Diabetic Outpatients.

A total number of 152 participants participated in the study. Table 1 summarizes sociodemographic characteristics of participants. About 37 (24.3%) participants were males and 115 (75.7%) participants were females, representing 1:3.1 ratio respectively. Majority of participants (65.8%) were within age range 51-65 years. Also, 51 (33.6%) of the participants had history of alcohol intake; 7 (4.6%) still consumed alcohol as at data collection. Seventy six (50.0%) participants had family history of cardiovascular diseases (CVDs). Majority of study participants (126, 82.9%) had lived with diabetes for 5 years and above.

Table 1: Descriptive characteristics of Type 2 diabetic Outpatients.

Sociodemographic data	**Frequency N= 152**	**Percentage**
Gender		
Male	37	24.3
Female	115	75.7
Age Range (years)		
35-50	5	3.3
51-65	100	65.8
66-80	47	30.9

Past Alcohol Intake		
Yes	51	33.6
No	101	66.4
Current Alcohol Intake		
Yes	7	4.6
No	145	95.4
Past Smoking		
Yes	10	6.6
No	142	93.4
Family History of CVD(s)		
Yes	76	50.0
No	64	42.1
I don't know	12	7.9
Duration of DM (Years)		
Less than 5	26	17.1
5-10	55	36.2
11-15	35	23.0
More than 15	36	

3.2 Pattern of hyperglycemia and Atherogenic dyslipidemia among Type 2 diabetic Outpatients.

The results summarized in Table shows 64.6% of type 2 diabetic patients had high HbA1c while 74.3% had high FBG. The prevalence of singular, combined and mixed dyslipidemia were 97 (69.1%), 24 (15.8%) and 2 (1.3%) respectively. In addition, the prevalence of high coronary risk (TC/HDL-C ratio) was 54 (35.5%), and atherogenic index of plasma (log TG/HDL-C) indicated 8 (5.3%) participants were at risk of atherosclerosis.

Table 2: Prevalence of hyperglycemia and Atherogenic dyslipidemia among Type 2 diabetic Outpatients.

CVD risk factors	Total, N	Frequency	Percentage (%)
Dyslipidemia (mmol/L)			
High TC ≥5.18	152	63	41.4
High TG ≥2.26	152	8	5.3
Low HDL-C	152	32	21.1
Women < 1.3	115	27	23.5
Men < 1.03	37	5	13.5
High LDL-C	152	23	15.1
Single dyslipidemia	152	97	63.8
Combined dyslipidemia	152	24	15.8
Mixed dyslipidemia	152	2	1.3
High TC/HDL ratio	152	54	35.5
High LogTG/HDL-C	152	8	5.3
Hyperglycemia			
≥7.0 mmol/L FBG	152	113	74.3
≥6.5% HbA1c, n=96	96	62	64.6

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3.3 Anthropometric and Biochemical Profile of Type 2 Diabetic Patients.

The mean levels of TC, TG, LDL-C, VLDL-C were significantly higher among type 2 diabetics with high coronary risk (TC= 5.9±1.3 mmol/L, TG= 1.3±0.6 mmol/L, LDL-C= 3.8±0.9 mmol/L, VLDL-C= 0.6±0.3 mmol/L) compared to those with low coronary risk (TC= 4.3±1.2 mmol/L, TG= 1.0±0.4 mmol/L, LDL-C= 2.3±0.9 mmol/L, VLDL-C= 0.4±0.2mmol/L) respectively (Table 3). Mean BMI and waist circumference were similar between those with and without coronary risk.

Table 3: Comparing anthropometric and biochemical data of Type 2 diabetic outpatients with and without Coronary risk

Parameter, N=152	**Total**	**Without CR DM Patients N=98**	**With CR DM Patients N=54**	**P value**
Age	55.5±9.2	55.7±9.3	55.1±9.0	0.695
Anthropometric data				
BMI (Kg/m^2)	27.7±4.6	27.6±4.7	27.9±4.5	0.719
WC (cm)	97.4±11.7	96.9±12.1	98.3±11.0	0.498
Biochemical data				
FBG mmol/L	9.43±1.5	9.3±3.6	9.6±3.4	0.559
HbA1c %, N=96	7.2±1.3	7.1±1.3 (59)	7.4±1.2 (37)	0.380
TC mmol/L	4.9±1.5	4.3±1.2	5.9±1.3	0.000
TG mmol/L	1.2±0.5	1.0±0.4	1.3±0.6	0.007
HDL-C mmol/L	1.5±0.5	1.5±0.3	1.5±0.3	0.295
LDL-C mmol/L	2.8±1.2	2.3±0.9	3.8±0.9	0.000
VLDL-C mmol/L	0.5±0.2	0.4±0.2	0.6±0.3	0.004

Coronary risk, CR <3.5 as low, CR ≥3.5 as High, P value ≤ 0.05 as significant. Independent t-test was used to compare trends of significance differences.

3.4 Relationship between Biochemical Parameters and Independent Cardiovascular Risk Factors

As shown in Table 4, strong significant positive correlations existed between TC (r = 0.690, p value < 0.0001) and LDL-C (r = 0.783, p value < 0.0001) with coronary risk. Additionally, TG (r = 0.263, p value= 0.010) and VLDL-C (r = 0.263, p value= 0.011) showed weak but significant positive correlation with coronary risk. Furthermore, TG (r= 0.817, p value < 0.0001) and VLDL-C (r = 0.817, p value < 0.0001) were strongly associated with

atherosclerotic risk; while HDL-C (r = 0.218, p value = 0.034) was weakly but significantly associated with atherogenic risk.

Table 4: Partial correlation between Biochemical parameters and independent CVD risk factors.

Biochemical Parameters	Total	TC/HDL-Ratio (Coronary risk)	Log TG/HDL-C (Atherogenic index)
		r (p value)	r (p value)
FBG mmol/L	152	0.054 (0.605)	0.030 (0.772)
HbA1c %	96	0.124 (0.233)	0.104 (0.320)
TC mmol/L	152	0.690 (0.000)	0.007 (0.943)
TG mmol/L	152	0.263 (0.010)	0.817 (0.000)
HDL-C mmol/L	152	0.094 (0.365)	0.218 (0.0034)
LDL-C mmol/L	152	0.783 (0.000)	0.120 (0.250)
VLDL-C mmol/L	152	0.263 (0.011)	0.817 (0.000)

Adjusting for age and gender. Correlation is significant at 0.05 level (2-tailed). Correlation is significant at 0.01 (2-tailed)

As summarized in Table 5, binary logistic regression showed TC (OR= 2.6, 95% CI= 1.8-3.7, p< 0.0001), TG (OR= 2.5, 95% CI= 1.3-4.8, p=0.004) and LDL-C (OR= 4.8, 95% CI= 2.9-8.1, p< 0.0001) had significant effects on coronary risk among participants.

Table 5: Binary logistic regression showing relationship between biochemical parameters and Coronary risk for cardiovascular disease

	High Coronary Risk				
		95 % CI			
Predictor variables	**OR**	**Lower**	**Upper**	**P value**	**Hosmer and Lemeshow Test**
FBG	1.0	0.9	1.1	0.556	0.615
HbA1c	1.1	0.8	1.5	0.376	0.528
TC	2.6	1.8	3.7	**0.000**	0.132
TG	2.5	1.3	4.8	**0.004**	0.344
HDL-C	1.6	0.6	4.5	0.294	0.573
LDL-C	4.8	2.9	8.1	**0.000**	0.650

4.0 Discussion

This study found more females (75.7%) compared to adult males (24.3%) with type 2 diabetes in the study participants. Generally, more females than males seek healthcare and hence get identified and this study was a hospital-based study. Similar observation was reported by Sarfo-Kantanka et al., (2017) who found about 60% females compared with 40% males

among participants in Kumasi were diabetic, majority of whom were within ages 51-65 years. However, overweight/obesity prevalence in the females was higher than males and it is well known that obesity predisposes to type 2 diabetes. The higher proportion of females may actually be due to a higher prevalence of diabetes in females due to more females being overweight/obese.

People with type 2 diabetes are susceptible to proatherogenic cardiovascular risk factors resulting from complications associated with uncontrolled blood glucose and atherogenic dyslipidemia (Mokta et al., 2017). Chronic hyperglycemia with underlying dyslipidemia induce damage to endothelial tissue, which can subsequently progress to atherosclerosis and may contribute to risk of developing cardiovascular diseases (Bhutto et al., 2017). In this study, 74.3% of the diabetics had high FBG and 64.6% had high HbA1c, implying that close to three quarters of the study participants had uncontrolled blood glucose and persistent hyperglycemia. It it clear that the type 2 diabetics studied were at increased risk of proatherogenicity and ultimately CVD and its complications, due to blood lipid disorders, secondary to persistent hyperglycemia.

The prevalence of single dyslipidemia among the type 2 diabetics studied was 63.8%, and prevalence of each component of lipid disorders was equally high; hypercholesterolemia (41.4%), low HDL-C (21.1%), high LDL-C (15.1%) and hypertriglyceridemia (5.3%). This is not surprising, considering the prevalence of hyperglycaemia observed. A similar finding by Samdani et al., (2017) reported slightly higher prevalence of combined dyslipidemia (22.0%) and mixed dyslipidemia (24.0%) than was observed in this study. Increased blood cholesterol and low HDL-C in type 2 diabetics are two lipid abnormalities which increase coronary risk, leading to development of coronary heart disease. Studies have found prevalence of single dyslipidemia of 64.1% (Yadav et al., 2014) and 67.1%, (Yan et al., 2016) among type 2 diabetic patients.

To fully understand the effects of dyslipidemia on coronary and atherosclerotic risk among the study participants, we assessed the relationship between specific serum lipids and coronary risk using partial correlation. This revealed that total cholesterol (TC), triglyceride (TG), low density lipoprotein-cholesterol (LDL-C) had significant, direct correlation with coronary risk. This implies that an increase in TC, TG and LDL-C levels in participants studied has direct influence on coronary risk, thereby increasing risk of CVDs. Additionally, TG, VLDL-C had a strong, significant direct association on atherogenic index of plasma. This implies an increased concentration of serum triglyceride and very low density lipoproteins were associated with atherosclerotic risk among the type 2 diabetics studied. The regression result further showed TC, TG, LDL-C had significant effects on coronary risk among the participants. The study found that a point increase in total cholesterol was associated with 2.6-folds increase odds of coronary disease risk among the participants (OR= 2.6, 95% CI= 1.9-3.7, $p< 0.0001$). Additionally, a point increase in triglyceride was associated with 2-folds higher coronary disease risk for (OR= 2.5, 95% CI= 1.3-4.8, $p=0.004$), and a point increase in LDL-C was associated with 5- folds higher coronary disease risk (OR= 4.9, 95% CI= 2.9-8.1, $p< 0.0001$) compared to those with low coronary risk. These suggest that managing blood glucose in diabetes would be helpful in preventing heart disease.

The occurrence of more than one dyslipidemia among study participants of this study makes them susceptible to atherosclerosis and risk of developing cardiovascular diseases. Judging by the high dyslipidemia prevalence and its direct link with coronary disease risk among

participants, it is not surprising that close to 4 in 10 of this study participants (35.5%) had high coronary risk and 5.3% had high atherosclerotic risk. In type 2 diabetes, poor insulin action leads to alteration in lipids, leading to oxidative stress, damage to endothelial tissues, which in turn stimulates atherosclerosis. The general observation is that the diabetics studied were on the road to developing cardiovascular disease, and this could be attributed to uncontrolled blood glucose. It will therefore pay well very well if these diabetics manage the disease and reverse the observed dyslipidemia trend.

5.0 Conclusion

The prevalence of uncontrolled blood glucose and dyslipidemia, were high among the type 2 diabetes participants involved in this study and these were associated with increased atherogenic risk. It can be concluded also that these diabetics are not being well managed and are at increased risk of developing complications associated with the disease, including cardiovascular diseases and co-morbidities, which will ultimately burden the health delivery system, families of the diabetics and ultimately mortality from DM-related issues.

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Approval to undertake the study was sought from the Committee on Human Research Publication and Ethics (CHRPE) of the School of Medical Sciences, KNUST, Kumasi. All participants of this study signed informed consents form in accordance to CHRPE regulations before conducting the study.

Declaration

The manuscript is an original work of the authors. All data and tables used in the manuscript are prepared originally by authors. The manuscript has not been published elsewhere or submitted elsewhere for publication.

Authors contribution

Study concept and design: Odeafo Asamoah-Boakye, Charles Apprey. Analysis and interpretation of data: Odeafo Asamoah-Boakye, Charles Apprey, Reginald Adjetey Annan. Drafting of the manuscript: Odeafo Asamoah-Boakye. Critical revision of the manuscript for important intellectual content: Charles Apprey, Reginald Adjetey Annan. Statistical analysis: Odeafo Asamoah-Boakye

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