CORRELATION BETWEEN GLYCATED HEMOGLOBIN AND LIPID PROFILE STATUS AMONG NEWLY-DIAGNOSED TYPE 2 DIABETICS OF INDIVIDUALS OF THREE ETHNIC GROUPS IN SOKOTO, NIGERIA

Authors:
Bunza, F. U.[1]*, Onyenekwe, C.C.[2], Wasagu, I. Z.[1], Ihim, A. C.[2]

Author Affiliations:
[1]Department of Chemical Pathology, School of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto
[2] Department of Clinical Chemistry, Faculty of Medical Laboratory Science, Nnamdi Azikiwe University, Awka

*Corresponding Author:
Bunza, F. U.
fbunza@gmail.com
+2348038301842

ABSTRACT

Background: Glycated haemoglobin (HbA1c) has been suggested to be a better predictor for coronary heart disease and strongly associated with atherosclerosis. Changes in lipid profile is linked with severity of diabetes as adjudged by HbA1c. Lipid abnormalities are common in type 2 diabetics, but the pattern may vary between ethnic groups.

Aim: The current study was undertaken to explore the association of HbA1c and serum lipid profile parameters in type 2 diabetics among persons of three ethnic groups in Sokoto.

Methods: The current study was a cross-sectional case-control study. The Cochran formula was used to determine the number of subjects recruited. Demographic and clinical characteristics were obtained from all the participants. HbA1c and lipid profile parameters were determined using standard laboratory tests. Ranges for TC <200mg/dl, TG <150mg/dl, LDL-c <100mg/dl and ranges between 51-60 for females and 41-60 for males for HDL-c were considered dyslipidaemia. All data were presented using mean and standard deviation, while independent samples t-test and one-way analysis of variance (ANOVA) followed by Bonferroni multiple comparison test to evaluate the

mean differences between the groups at statistical significance of <0.05.

Results: The mean values for serum HbA1c were slightly higher in diabetic groups (7.58±0.87 for Hausa/Fulani, 7.23±0.58 for Igbo and 7.34±0.67 for Yoruba) compared to their corresponding control groups (5.21±0.56 for Hausa/Fulani, 5.15±0.55 for Igbo and 5.21±0.55 for Yoruba) with p<0.0001. Serum levels of total cholesterol, triglyceride and LDL-c in diabetic group (207.99±89.82, 183.16±60.76 and 101.27±52.19 respectively) were higher than the control group (161.68±27.64, 137.14±24.18 and 90.16±28.14 respectively) p<0.0001; whereas, HDL-c was decreased in diabetics (37.26±12.90) than the control group (46.64±11.15) p<0.005. The HbA1c correlated with increased TC, TG and LDL-c (r = 0.483269, 0.623952 and 0.390193 respectively) p=0.0001 and decreased HDL-c level (r= -0.247900) p=0.0001.

Conclusion: It was concluded that HbA1c is positively correlated to dyslipidaemia. HbA1c may be considered as an indirect predictor for dyslipidaemia. The current study therefore, recommend adequate glycaemic control via serum evaluation of HbA1c among type 2 diabetics irrespective of ethnic background.

Keywords: Type 2 diabetics, Glycated haemoglobin, Lipid profile, Sokoto Ethnic Groups

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INTRODUCTION

Diabetes mellitus (DM), a heterogeneous group of metabolic disorders is characterized by persistent hyperglycaemia with interruptions in carbohydrates, fats and protein metabolism due to relatively or absolute lack of insulin secretion, insulin action or both.[1] Type 2 diabetes (T2DM) is considered globally to be one of the most pervasive non-communicable diseases. Long-term damage, dysfunction, and failure of various organs, most especially the eyes, kidneys, nerves, heart, and blood vessels are the consequences of uncontrolled hyperglycaemia.[2] Abnormalities in lipid profile parameters among diabetics are often termed as “diabetic dyslipidaemia” typically characterized by increased serum levels of total cholesterol (TC), triglycerides (TG) and low density lipoprotein cholesterol (LDL-c) as well as decreased serum level of high density lipoprotein cholesterol (HDL-c). Diabetes dyslipidaemia may be a risk factor for macrovascular (stroke, peripheral vascular disease, and coronary artery disease [CAD]) and microvascular (nephropathy, neuropathy, and retinopathy) complications in type 2 diabetics.[1,2]

Glycated haemoglobin (HbA1c), a form of haemoglobin chemically connected to a sugar, is considered a gold-standard measure of chronic glycaemia in diabetes. Glycated haemoglobin (HbA1c) has been a better predictor of coronary heart disease (CHD) than the fasting blood sugar (FBG) or 2-hpp glucose; and also strongly associated with atherosclerosis.[2] Measurement of HbA1c in both type 1 and

2 diabetes was recommended, first to determine the degree of glycaemic control and for continuous diabetes management.[1]

Type 2 diabetics often exhibit an atherogenic lipid profile, which greatly increases the risk of cardiovascular disease (CVD) compared to non-diabetics. About 50% of type 2 diabetics die of CVD (primarily heart disease and stroke).[3] Individuals with T2DM have two- to four-fold increased risk of coronary artery disease (CAD), the leading cause of death in diabetes.[4] Changes in lipid profile is also well related with severity of diabetes as adjudged by HbA1c.[5] Lipid abnormalities are common in T2DM, but the pattern of the different lipids may vary between ethnic groups, economic status as well as health care system.[6] Hence, the current study was undertaken to explore the correlation of serum lipid profile parameters with glycated haemoglobin in type 2 diabetics of three ethnic groups (Hausa/Fulani, Igbo and Yoruba) in Sokoto, North West, Nigeria.

MATERIALS AND METHODS

Site of Study

The study participants were males and females with type 2 diabetes attending diabetic clinics at Specialist Hospital Sokoto, Women and Children Hospital Sokoto and Maryam Abacha Hospital Sokoto and recruited using a purposive sampling technique. Apparently healthy individuals (age-, sex, ethnic- matched) served as controls were also similarly recruited within the metropolis.

Study Population

The study was conducted among the three major ethnic groups: the Hausa/Fulani, Yoruba and Igbo situated in the north, west, and east respectively, together comprising over 70% of the total population. The total of 300 participants recruited comprised of 100 participants each for Hausa, Igbo and Yoruba ethnic groups, aged 18-54 years. The total of 174 were Males and 126 were Females. The participants were divided into six groups (3 groups were type 2 diabetics and 3 groups were healthy control). Of the 174 male participants Hausa/Fulani has 56 male, Igbo has 64 males and Yoruba has 54 males. The remaining 44 participants, 36 participants and 46 participants were female for Hausa/Fulani, Igbo and Yoruba respectively. Ethnic backgrounds were identified through clinical records, informed consent form and questionnaire administered.

Study design

The study design was a cross-sectional case-control study. The diabetic participants were consecutively recruited at the diabetic clinics.

Ethical consideration and clearance

Ethical approvals were duly was sought and obtained Sokoto state ministry of health with reference number SMH/1580/V.IV.

Informed consent

Informed consent for inclusion into the study was duly obtained from each participant using standard protocol prior to recruitment.

Instrument for data collection

Self-structured questionnaire was prepared and administered to all the study participants to obtain their socio-demographic characteristics including, gender, age, tribe, occupation, life style, family history of DM, history of DM, etc.

Sample Size Determination

Calculation of sample size of the study, using Cochran formula (1977).[7]

$n=Z^2P(1-P)/d^2$

Where, n= desired sample size

P= Prevalence rate of diabetes in Nigeria = 7.0% = 0.07 (Michael. *et al.*, 2024).[8]

Z= 95% confidence interval=1.96

W= degree of accuracy= 0.05

Therefore,

n =118, approximated to150, thus we have equal sample size (n=50) for each ethnic groups.

Inclusion Criteria

Newly diagnosed type 2 diabetics (with first diagnosis ≤ 2 years), under good glycemic control (HbAIc = 6.5-7.3%) of both sexes (aged between 18 to 55 years old), non-hypertensive and without any apparent disease condition and who reside in the Sokoto metropolis were included for this study. Age-, sex-, tribe- and BMI-matched healthy individuals who had given their informed consent were included in the study

Exclusion criteria

Patients with other disease conditions such as HIV/AIDS, tuberculosis, thyroid disorder, pregnant women and hypertensive were excluded from the study. Other conditions such as retinopathy, nephropathy, and neuropathy were also excluded from the study.

Sample collection and analytical techniques

Blood pressure was measured using the Belsk digital blood pressure monitor (Northfield, IL 60093 USA). The body height and weight were also measured using appropriate instrument (Mechanical Brecknell HS-200M scale, UK). A systolic blood pressure of ≥ 140 mmHg and diastolic blood pressure of ≥ 90 mmHg were considered hypertensive.[9] Body mass index (BMI) was calculated using the equation: Weight in (Kg)/Height (M^2). Values of 20-25, <30 but > 25, >30 and <20 were considered Normal, overweight, obese and underweight respectively. Blood glucose was tested in capillary blood samples by glucose oxidase and peroxidase methods.[10] Four milliliters of venous blood were collected in a red top tube with a clot activator collected from each participant by venipuncture using a 21G needle. It was then subjected to centrifugation at 3000 rpm for five min and the obtained serum was used to test for HbA1C, TG, TC, and HDL. Humastar 80 Auto Analyzer (Human, Wiesbaden. Germany) was utilized to measure the concentration of TC, TG, and HDL in the sera. Glycated hemoglobin was measured as described by Prosenz *et al.*, 2019.[11]

Data analysis

All data were summarized using mean and standard deviation. One-way analysis of variance (ANOVA), followed by Bonferroni multiple comparison test, and independent t-test to evaluate the mean difference of the data between the groups (control and type 2 diabetics). The correlations were measured using Pearson's coefficient of correlation (r) between study variables. Analysis was done at the 95% confidence level and the statistical significance was considered when p-value <0.05.

RESULTS

Table 1 shows the Socio-demographic and clinical characteristics of the study participants. The mean age of the diabetic participants was 50.04±6.64 compared to that of control subjects 45.97±7.58 (p>0.05). The total of 300 participants recruited for this study comprised of 174 (58%) Males and 126 (42%) Females. Of the 174 male participants, Hausa/Fulani has 56 (56%), Igbo has 64 (64%) and Yoruba has 54(54%); while females were 44(44%), 36(36%) and 46(46%) for Hausa/Fulani, Igbo and Yoruba respectively. Table 1 further presents the body mass index (BMI) of the study participants. The mean average BMI of the diabetics was higher compared to control subjects (F=2.741; p <0.05). No statistically significant difference observed in mean systolic and diastolic blood pressure for diabetics of the ethnic groups compared to their corresponding control (F=0.127; p>0.05).

Table 2a showed the mean fasting blood glucose (FBG), HbA1c and lipid profiles of diabetes mellitus and control participants. The mean concentration of FBS, HbA1c, TC, TG and LDL-c (122.20±17.60, 7.39±0.73, 207.99±89.82 and 101.27±52.19 respectively) in the diabetics were significantly higher than those in the control group (93.26±8.68, 5.19±0.55, 161.68±27.64, 137.14±24.18 and 90.16±28.14 respectively) (p<0.05). However, the mean values for HDL-c in diabetics (37.26±12.90) was significantly lower than the control group (46.64±11.15) (p<0.05).

Table 2b showed the mean FBG, HbA1c and lipid profiles of diabetes mellitus and control Hausa, Igbo and Yoruba participants. Higher TC (mg/dl) levels were observed in diabetics of the different ethnic groups (203.74±89.49 for Hausa/Fulani, 216.51±90.35 for Igbo and 203.71±90.29 for Yoruba) compared to their corresponding control groups (159.71±27.70, 162.60±27.15 and 162.74±28.35 respectively) (F= 17.474; p<0.0001), Table 2b. Higher levels of TG were similarly higher in the diabetics of the different ethnic groups (181.21±59.85 for Hausa/Fulani, 189.41±63.40 for Igbo and 178.87±0.67 for Yoruba) with compared to their corresponding control groups (F= 14.083; p<0.0001). Table 2b further showed higher levels of LDL-c (mg/dl) in diabetics compared to control of the different ethnic groups (100.05±51.46 for Hausa/Fulani, 104.82±53.98 for Igbo and 98.94±51.67 for Yoruba) (F= 9.815; p<0.05). Table 2b further showed that HDL-c (mg/dl) was lower in diabetics of the different ethnic groups (34.92±13.72 for Hausa/Fulani, 39.72±12.37 for Igbo and 37.15±12.68 for Yoruba) compared to their corresponding control groups (F=6.015; p<0.05).

Table 3 showed the correlation between HbAIc and serum lipid profile of the study population, HbAIc was found to be associated with increased TC, TG and LDL-c (r=0.432284, 0.569792 and 0.339701 respectively) (p=0.000001). HbAIc was associated with decrease in serum HDL-c (r= -0.247900) p=0.000001.

Table 1: Socio-demographic and clinical characteristics of the study participants

Groups		Mean age (Years)	Gender Male (%)/Female (%) N N	BMI (Kg/m^2)	SBP (mmHg)	DPB (mm/Hg)	Hypertensive: no N(%)/yes N(%)
All Participants	T2DM (n=150)	50.04±6.64	87(58)/63(42)$^{\&}$	30.71±5.15*†	128.95±9.47	80.80±5.01	150(100)/0(0)
(n=300)	Control(n=150)	45.97±7.58	87(58)/63(42)	24.15±4.18	114.06±7.08	79.24±4.57	150(100)/0(0)
Hausa/Fulani	T2DM(n=50)	55.57±7.39	28(56)/22(44)	27.59±4,90	123.74±9.30	78.17±5.00	50(100)/0(0)
(n=100)	Control(n=50)	42.27±8.11	28(56)/22(44)	23.21±4.62	115.18±7.78	69.78±3.80	50(100)/0(0)
Igbo	T2DM(n=50)	55.04±6.34	32(64)/18(36)	32.6±4.60*†	129.37±8.36	72.64±4.19	50(100)/0(0)
(n=100)	Control(n=50)	46.98±7.48	32(64)/18(36)	25.6±3.71	116.71±6.41	74.48±4.89	50(100)/0(0)
Yoruba	T2DM(n=50)	54.51±6.18	27(54)/23(46)	29.81±5.50	131.74±8.42	78.57±4.60	50(100)/0(0)
(n=100)	Control(n=50)	48.65±7.14	27(54)/23(46)	23.6±2.72	110.30±5.94	71.48±4.18	50(100)/0(0)
	F value	6.015	3.474	2.751	0.122	0.127	4.384
	P value	>0.05	>0.05	<0.05	>0.05	>0.05	>0.05

Values are mean ± Standard Deviation of the mean of age, SBP, DBP and BMI ,n= number of participants, T2DM= type 2 diabetics, %= percentage, Kg/m^2, kilogram per meter square; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP. Blood pressure, n, sample size; †= comparison between patients and control, &= comparison within the group, and *=p≤0.05 was considered significant in the statistical analysis t-test

Table 2a: Mean (+/- SD) fasting blood glucose, HbA1c and lipid profiles of diabetes mellitus and control participants

Groups		FBS (mg/dL)	HbAIc (%)	TC (mg/dL)	TG (mg/dL)	HDL-c (mg/dL)	LDL-c (mg/dL)
All Participants (n=300)	Diabetes mellitus (n=150)	122.20±17.60***†	7.39±0.73*†	207.99±89.82***†	183.16±60.76***†	37.26±12.90*†	101.27±52.19**†
	Control (n=150)	93.26±8.68	5.19±0.55	161.68±27.64	137.14±24.18	46.64±11.15	90.16±28.14
	p-value	0.000001	0.041232	0.000001	0.000001	0.025210	0.000162

Values are mean ± Standard Deviation of the mean of FBS, LP and HbAIc , glycated hemoglobin; n, number of participants; %, percentage,; †= comparison between patients and control, *=p≤0.05, **=p≤0.01 and ***= p≤0.000001 were considered significant in the statistical analysis t-test.

Table 2b: Mean (+/- SD) fasting blood glucose, HbA1c and lipid profiles of diabetes mellitus and control Hausa, Igbo and Yoruba participants

Ethnicity	Groups	FBS (mg/dL)	HbAIc (%)	TC (mg/dL)	TG (mg/dL)	HDL-c (mg/dL)	LDL-c (mg/dL)
Hausa/Fulani (n=100)	Diabetes mellitus (n=50) (A)	127.70±23.48	7.58±0.87	203.74±89.49	181.21±59.85	34.92±13.72	100.05±51.46
	Control(n=50) (B)	92.80±8.95	5.21±0.56	159.71±27.70	132.91±18.89	46.61±11.23	93.51±30.30
Igbo (n=100)	Diabete mellitus (n=50) (C)	118.12±10.62	7.23±0.58	216.51±90.35	189.41±63.40	39.72±12.37	104.82±53.98
	Control(n=50) (D)	91.68±8.94	5.15±0.55	162.60±27.15	139.38±26.00	46.55±11.19	89.10±26.95
Yoruba	Diabetes mellitus (n=50) (E)	120.80±14.98	7.34±0.67	203.71±90.29	178.87±0.67	37.15±12.68	98.94±51.67
(n=100)	Control(n=50) (F)	95.31±7.82	5.21±0.55	162.74±28.35	139.14±26.66	46.75±11.18	87.88±27.13
	F- value	17.384	5.972	17.474	14.083	6.015	9.815
	P-value	0.000001	0.041232	0.000001	0.000001	0.025210	0.000162
	Post hoc						
	A vs Bs	0.000001 S	0.041232 S	0.000001 S	0.000001 S	0.025210S	0.000162 S
	A vs C	0.132128 NS	0.142503 NS	0.534868 NS	0.092128 NS	0.182503 NS	0.734168 NS
	A vs E	0.634868 NS	0.634868 NS	0.634868 NS	0.634868 NS	0.634868 NS	0.634868 NS
	C vs E	0.142503 NS	0.934868 NS	0.132503 NS	0.212503 NS	0.714868 NS	0.142503 NS
	C vs Ds	0.000001 S	0.041232 S	0.000001 S	0.000001 S	0.025210S	0.000162 S
	B vs D	0.225092 NS	0.301503 NS	0.221092 NS	0.234192 NS	0.181503 NS	0.256092 NS
	B vs F	0.412092 NS	0.456868 NS	0.321154 NS	0.191092 NS	0.452868 NS	0.271154 NS

Values are mean ± Standard Deviation of the mean of FBS, LP and HbAIc , glycated hemoglobin; n, number of participants; %, percentage,; †= comparison between patients and control, *=p≤0.05, **=p≤0.01 and ***= p≤0.000001 were considered significant in the statistical analysis t-test., **Key:** S = Significant, NS = Not Significant

Table 3: Correlation between FBG, HbAIc and BMI with serum lipid profiles of the study population

Parameters		TC (mg/dL)	TG (mg/dL)	HDL-c (mg/dL)	LDL-c (mg/dL)
HbAIc (%)	r value	0.432284**	0.569792**	-0.247900**	0.339701**
	P value	0.000001	0.000001	0.000001	0.000001

**** Correlation is significant at the < 0.01 level (2-tailed).**

DISCUSSION

In this study, the mean values of glycated haemoglobin (%) in diabetics were significantly increased compared to controls. The diabetes complications and control trial (DCCT) considered HbA1c as the gold standard of glycaemic control. Similar findings were also observed in a study conducted by Pasupathi *et al.*, (2018).[14] Mean values of serum Total cholesterol, Triglycerides and LDL-c, in diabetics were higher than the mean values observed in non- diabetic healthy controls ($p<0.05$). However, decreased serum levels of HDL-c were observed in diabetics compared to controls. Similar findings were observed in a study by Samatha *et al.*, (2012)[15] with increased levels of mean total cholesterol, triglyceride and LDL-cholesterol diabetics compared to controls. A significant positive correlation was observed between HbAIc and serum total cholesterol, TG, LDL-c (r=0.339701). In contrast, a significant negative correlation was observed between HbAIc and HDL-c (r=-0.247900).

Similarly, Albrki *et al.*, 2017[16] and Idogun *et al.*, 2017,[17] observed a significant positive correlation between HbA1c and serum total cholesterol, serum triglyceride and serum LDL-cholesterol ($r<0.508$); and a significant negative correlation (r=-0.300) between HbA1c and serum HDL-c. Diabetics with elevated HbA1c and serum lipid values are at very high-risk for cardiovascular disease (CVD). Significant correlations between HbA1c and the lipid parameters and a linear relationship between HbA1c and dyslipidemia point towards the usefulness of HbA1c in screening diabetics at higher risk. It has been estimated that reducing HbA1c levels by 0.2% could lower the cardiovascular risk by 10%.[18]

Patients with diabetes have been evidently recognized with arising complications due to the continuous hyperglycaemic episodes through numerous mechanisms like dyslipidaemia, platelet activation, and altered endothelial metabolism.[19] Both lipid profile and diabetes have been shown to be the vital forecasters for metabolic disorders including cardiovascular complications, dyslipidaemia and hypertension.[20] Blood lipid levels are modifiable risk factors for coronary heart diseases (CHDs). Being hydrophobic in nature, cholesterol, cholesterol esters, triglycerides and phospholipids are

transported to the other tissues in the form of lipoproteins such as chylomicrons, LDL and HDL. Elevated plasma levels of non-HDL lipoproteins are major risk factor for CHD. Dyslipidaemia as a metabolic irregularity is recurrently connected with diabetes mellitus.[21]

In the current work, significantly elevated serum levels of total cholesterol, triglycerides and LDL cholesterol were figured out in patients with diabetes, which are well-identified threat causes for cardiovascular diseases. The prevalence rates for high total cholesterol, very high LDL-C and low HDL-C were seen in the diabetic subjects. HbA1c is done to monitor the control of blood glucose in diabetes mellitus. Several studies have shown the positive correlation of HbA1c with duration of diabetes and as a strong risk factor for cardiovascular diseases in diabetes.[22]

According to a study conducted by Palem SP[23] type 2 diabetes patients with high level of Hb1Ac were at a higher risk of developing cardiovascular diseases in future. The results of the study conducted by Hussain *et al*[24] proved that HbA1c can also be used as a predictor of dyslipidaemia and thus early diagnosis of dyslipidaemia can be used as a preventive measure for the development of CVD in patients with type 2 diabetes. In this present study, we found a statistically significant increase in TC, LDL TG and decrease in HDL among the diabetics compared to control group which is in agreement with the study conducted by Ali *et al*.[25] where diabetic group had high level of TC, TG, LDL, and low level of HDL in comparison to non-diabetic subjects.

HbA1c is considered a key and more accurate criterion in diabetes management than fasting blood glucose levels. HbA1c levels offer an index for long-term glycaemic control related to two to three months of average blood glucose concentration.[21] It has been evident that lowering HbA1c is associated with a reduction in microvascular and macrovascular complications in diabetes.[25] The HbA1c value <7.0% reduced the risk of cardiovascular diseases and value >7.0% leads to dyslipidaemia and thus prone to CVD. It is also reported that lower levels of HbA1c in type 2 diabetics decreases the absolute risk of developing CHD by 5-17%, as well as decreasing all-cause mortality by 6-15%.[20]

A number of studies conducted on type 2 diabetes patients showed that a high levels of HbA1c is positively corelated to higher levels of cholesterol, TGs, and LDL-C.[26, 27] However, investigation on Nepal diabetic population suggested that patients with HbA1c >7.0% did not have different HDL-C compared to the patients with HbA1c≤7.0%,[25] Indeed, a number of studies revealed that inappropriate levels of lipid profile might predict high HbA1c value.[23,26,27]

CONCLUSION

It was concluded that type 2 diabetics were more susceptible to dyslipidaemia. HbA1c, a biomarker for glycemic control, may also be considered as an indirect predictor for dyslipidaemia. The current study therefore, recommend adequate glycaemic control via serum evaluation of HbA1c among type 2 diabetics irrespective of ethnic background.

Competing Interest: There is no conflict of interests.

Acknowledgement: The authors acknowledge all the participants particularly the control subjects for availing themselves for the study.

Funding: No fund received for the study from any external organization or persons.

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