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GLYCOSYLATED HAEMOGLOBIN: A SURROGATE MARKER FOR DYSLIPIDEMIA AND GLYCEMIC INDEX IN TYPE 2 DIABETES MELLITUS SUBJECTS

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ABSTRACT

Glycosylated haemoglobin is the substance formed when glucose chemically combine with haemoglobin molecule. This study examined glycosylated haemoglobin as a possible surrogate marker for dyslipidemia and glycemic index in type 2 diabetes mellitus subjects. A cross- sectional study was carried out in Warri, Delta State with a total of four hundred (400) volunteers recruited comprising of three hundred and twenty (320) diabetes mellitus subjects and eighty (80) apparently healthy subjects. Standard methods were used for anthropometric measurement and biochemical assays. Data were analyzed using statistical package for social sciences (SPSS). Parameters including Blood pressure, body mass index, fasting blood glucose, glycosylated haemoglobin, total cholesterol, triglycerides, LDL-C were significantly higher in diabetic subjects than non- diabetics while HDL-C was significantly lower in diabetics. Glycosylated haemoglobin is positively correlated with blood glucose, cholesterol, triglycerides, and LDL-C but inversely associated with HDL-C. Based on this study, glycosylated haemoglobin has the potential to serve as surrogate marker of dyslipidemia.

Keywords: *Body mass index, Blood pressure, Diabetes mellitus, dyslipidemia, glycosylated haemoglobin.*

INTRODUCTION

Diabetes mellitus is an endocrine and metabolic disorder that stem from insufficiency of insulin or non-response of cells to insulin. It has been considered a global problem due to its high prevalence in both advanced and low – medium income countries coupled with a high incidence of cardiovascular disease (CVD) in these subjects (Berry *et al*., 2007). Although there is high prevalence of type 1 diabetes mellitus, however, type 2 diabetes mellitus accounts for over 90% of all cases (Babakhanian *et al*., 2022)

Glycemic indices can be defined as biomarkers used as index of glycemic control in an individual to access therapeutic compliance (Rodbard, 2015). Glycated hemoglobin (HbA1c) is a commonly used biomarker in the determination of effective glycemic control and also in risk assessment for development of diabetic complications. Evidence has shown that, increase level of HbA1c is a sole risk factor for cardiovascular disease even in the absence of diabetes mellitus (Selvin *et al*., 2004). A study in the United States, reported HbA1c as the gold standard in glycemic control. They opined that values less than or equal to 7.0% are good for effective glycemic control and are good for risk reduction of cardiovascular complications. Evidence from earlier studies have shown that HbA1c is directly proportional to degree of coronary artery disease (CAD) in diabetic individuals and observed that any one percent increase in absolute value of HbA1c will result in 18% propensity in estimated risk of coronary artery disease diabetic subjects (Selvin *et al*., 2004).

Alteration in two or more lipid profile components of an individual is regarded as dyslipidemia. Raven *et al*. (1976) identified chronic hyperglycemia, dyslipidemia as well as insulin resistance as common abnormalities of diabetes mellitus. This alteration may be high triglycerides, high low-density lipoprotein cholesterol and low high-density lipoprotein cholesterol (Cleeman, 2001). Evidence has shown that lipid alteration is a usual characteristic in diabetes mellitus which may either be a result of insulin insufficiency or insulin resistance that affects enzymes as well as lipid metabolism pathways (Adu, 2014). Eschwe'ge (2003) reported that premature atherosclerosis from dyslipidemia have resulted in the death of about 78% of type 2 diabetes mellitus individuals. Adu *et al*. (2015), in their study, opined that diabetes mellitus subjects have a greater propensity to cardiovascular diseases.

HbA1c is a known traditional biomarker for glycemic control and it is the mean glucose concentration of the proceeding 8 to 12 weeks when compared to other Diabetes diagnostic tests. However, dyslipidemia is implicated as a determinant in diabetes mellitus complexity such as cardiovascular diseases (Khaw and Wareham, 2006). Arising from the fact that diabetes mellitus give rise to dyslipidemia and glycemic control can be assess accurately with HbA1c, It is therefore imperative to evaluate the association between dyslipidemia and HbA1c in diabetes mellitus subjects. Hence this study sought to examine the association of HbA1c with lipid profile components and if possible be used as a surrogate biomarker of diabetic or atherogenic dyslipidemia and can considered as dual biomarker (as glycemic control and dyslipidemia biomarker) in type 2 diabetes mellitus.

MATERIALS AND METHODS

Study subjects

This study was undertaken in Warri, the commerce epicentre of Delta State, with a total of four hundred (400) individuals comprising, three hundred and twenty (320) type 2 diabetes mellitus subjects and eighty (80) control healthy individuals volunteered in this study. Participants' informed consent was obtained while ethical clearance was

approved by the ethics committee of the state ministry of health with number MOH/ECC Vol. 280. Sample size was calculated to be one hundred and thirty-one (131) according to Araoye (2004) with a prevalence of 8.5% as reported by Essiet and Osadolor (2019).

Collection of samples

Blood sample was collected from the cubital vein and dispensed into fluoride oxalate for glucose estimation, ethylene diamine tetraacetic acid (EDTA) for HbA1c estimation and plain container for lipid profile estimation. The non-anticoagulated blood sample was left to clot and spun at 15minutes at 3000 revolution per minute. Harvested serum was kept frozen at -20^{0}C until analysis.

Anthropometric Variables

Anthropometric variables were measured according to standard procedures. Blood pressure was according to Onwubere and Kadiri (2005), weight and height and body mass index was measured according to World Health Organization (2005).

Biochemical analysis

Trinder (1969) glucose oxidase method was used to estimate glucose, HbA1c by immunoturbidometric method (Hamwi *et al*., 1995). The enzymatic CHOD-PAP method was used for total cholesterol and triglycerides while HDL-Cholesterol was evaluated by Burstein *et al*., (1970) method. LDL-Cholesterol and VLDL-Cholesterol were determined by Friedewald (1972) equation. Quality assurance was maintained by the use of standards and quality control materials which were treated as test samples. During analysis, manufacturer's instructions were followed to ensure accuracy and precision.

Statistical Analysis

Data were analyzed to obtain mean± standard deviations which were compared using statistical package for social sciences (SPSS) IBM Chicago version 23 with ≤ 0.05 considered significant while Pearson correlation was at ≤0.001

RESULTS

Tables and figures were used in presentation of the study results. Distribution of respondents with diabetes mellitus subjects accounting for eighty percent (80%) and apparently healthy subjects, twenty percent (20%) as shown in figure 1.

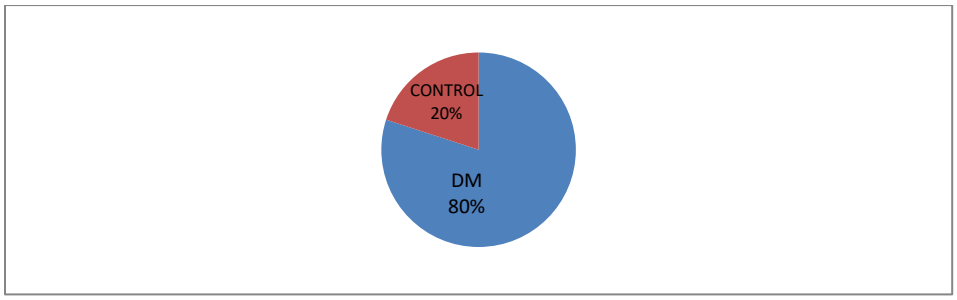

Figure I: Percentage of study respondents

There was no significant difference observed with age of both participants and control subjects. However, systolic blood pressure, diastolic blood pressure, weight and body mass index were significantly higher in diabetics than in control subjects as shown in the table below.

Table 1: Anthropometric variables of diabetes mellitus and non-diabetic subjects

PARAMETERS	NIDDM (n=320)	Control (n=80)	t - values	P values
Age (Years)	54.74±9.63	52.45±7.30	0.991	0.324ŧ
SBP (mmHg)	127.37±10.89	119.30±8.56	3.080	0.003*
DBP (mmHg)	80.40±12.00	61.70±5.00	6.798	0.000*
Wt (Kg)	72.25±6.21	58.20±3.67	9.673	0.000*
Ht (m^2)	1.69±0.13	1.77±0.08	-2.654	0.009*
BMI	42.78±4.20	32.76±1.70	10.417	0.000*

*Significant, ŧ Not Significant

Fasting blood glucose and glycosylated haemoglobin were significantly ($p<0.05$) higher in Diabetics mellitus than non-diabetic individuals.

Table 2: Glycemic indices of diabetes mellitus and non-diabetic individuals

PARAMETERS	NIDDM (n=320)	Control (n=80)	t - values	P values
FBG (mg/dl)	221.53±15.92	91.90±16.83	32.189	0.000*
HbA1c (%)	10.89±10.90	5.78±1.30	2.085	0.040*

***Significant**

Table 3: Lipid profile variables of diabetes mellitus and non-diabetic individuals

PARAMETERS	NIDDM (n=320)	Control (n=80)	t - values	P values
TC (mg/dl)	225.93±20.73	184.10±15.57	8.435	0.000*
TG (mg/dl)	186.68±27.48	125.35±19.38	9.395	0.000*
VLDL (mg/dl)	37.34±5.50	25.07±3.88	9.395	0.000*
LDL (mg/dl)	143.92±22.05	99.18±12.86	8.691	0.000*
HDL(mg/dl)	44.68±6.68	59.85±3.57	-9.789	0.009*

*Significant

In the same manner, Diabetic had a significantly higher cholesterol (TC), triglycerides (TG), very low density lipoprotein (VLDL) and low density lipoprotein (LDL) than non-diabetic individuals. However, there was significantly lower high density lipoprotein (HDL-C) in diabetes mellitus than non-diabetic individuals.

There was a positive correlation of glycosylated haemoglobin with total cholesterol, triglycerides and low density lipoprotein but negative correlation with high density lipoprotein as shown in figure II- V below.

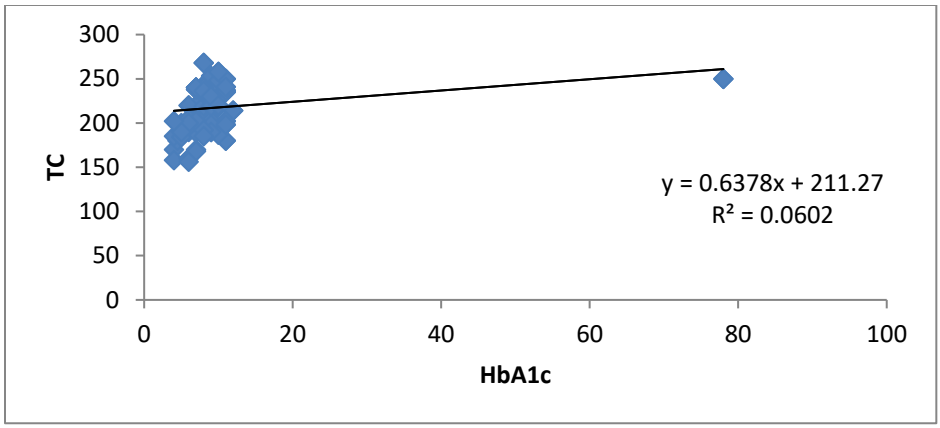

Figure 2: Positive correlation of total cholesterol and glycosylated haemoglobin

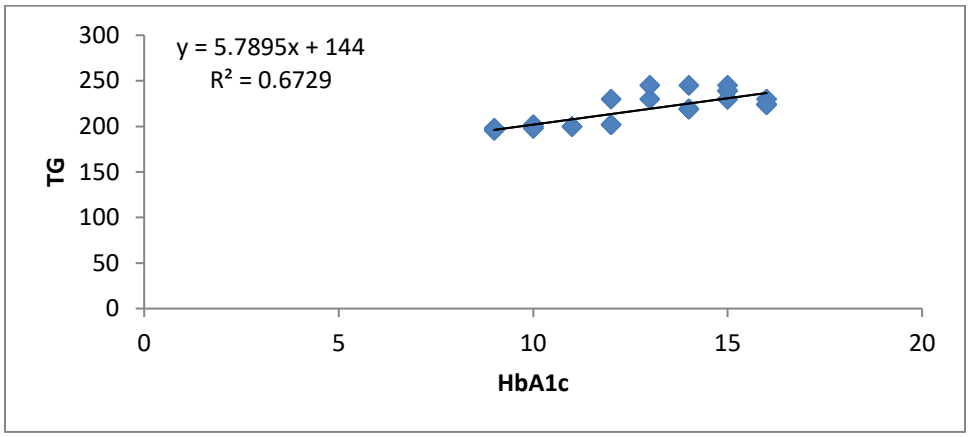

Figure 3: Positive correlation of triglycerides and glycosylated haemoglobin

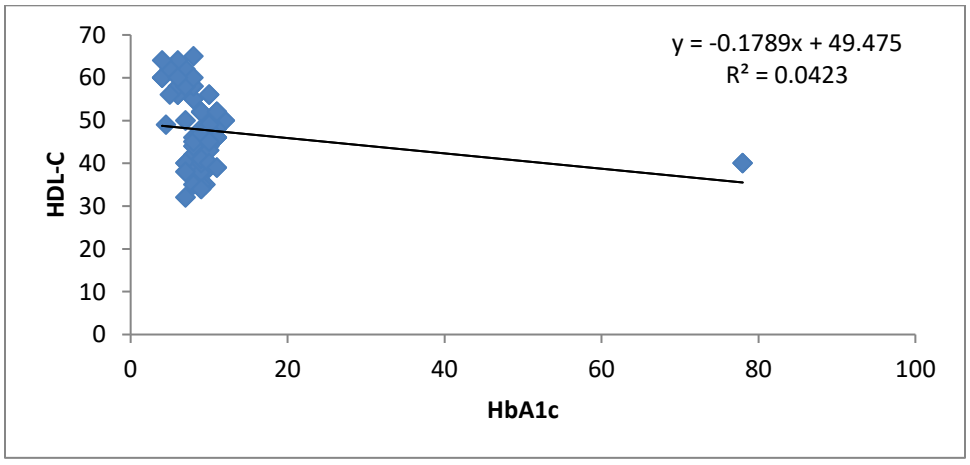

Figure 4: Negative association of HDL-C andHbA1c

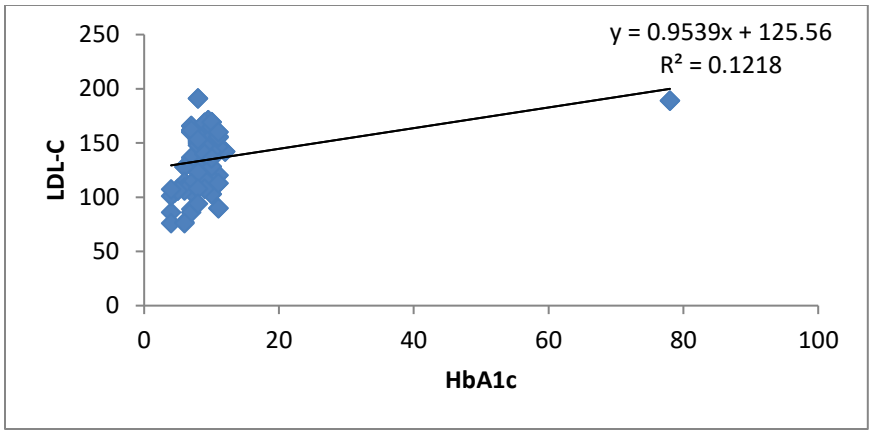

Figure 5: Positive correlation of low density lipoprotein - cholesterol and glycosylated haemoglobin

DISCUSSION

Diabetes mellitus, a multifactorial and a public health disease worldwide because of the complications and disability associated with it has gained so much attention. Adu *et al*. (2015) observed that diabetes mellitus have altered lipid profile and high propensity to cardiovascular complications. Glycosylated haemolobin (HbA1C) is known as a traditional glycemic index in the assessment of glycemic control in diabetes mellitus and since there is altered lipid pattern in diabetes mellitus, this study examines the association of glycemic indices with atherogenic dyslipidemia in diabetic individuals. There was a significantly higher blood pressure (systolic and diastolic) among diabetic subjects than control subjects when compared. This is in line with earlier study by Adu (2022), who observed similar findings. Also, Adu and Akpojisheri (2021), in their study observed a prevalence of 46% hypertension among diabetes mellitus. This confirms the findings that diabetes mellitus had higher blood pressure than non-diabetic individuals. The increase has been identified as a risk factor in diabetes mellitus subjects and has been observed as a result of the effect of diabetes mellitus on the renin-angiotensin system (Towfighi, 2011).

There was a statistically significant higher body mass index (BMI) among Diabetic subjects than non-diabetics when compared. This is in line with earlier studies by Ogbera *et al*. (2009), Adu (2014). Adu (2022) observed that 40% of diabetic subjects are obese and 34% are overweight due to high body mass index. This higher BMI may be attributed to the improper metabolism of carbohydrates in diabetes mellitus leading to excess weight as earlier observed by Bai *et al*. (2022)

There was statistically significant higher blood glucose and glycosylated haemoglobin among diabetics than non-diabetics in this study. This is in tandem with earlier submission by Adu (2014; 2022). Blood glucose and glycosylated haemoglobin has been established as traditional biomarkers for diabetes mellitus. Fasting blood sugar has been observed to positively correlate with blood pressure and BMI. This shows that as blood glucose increases, blood pressure and body mass index tend to increase also. In a study by Bini *et al*. (2014), similar results were observed and this may be due to effect of diabetes mellitus exerted on the renin- angiotensin system (Towfighi, 2011).

There was statistically significant higher cholesterol, triglycerides, very low density lipoprotein and low density lipoprotein in diabetes mellitus than apparently healthy control individuals. This is in lie with earlier report by Adu (2014) in diabetes mellitus individuals. However, there was significantly lower high density lipoprotein

cholesterol in Diabetes than non-diabetic control individuals. This is in line with Adu (2014) that observed similar pattern of results in diabetic subjects. It was observed that, elevated low density lipoprotein is a risk factor for cardiovascular diseases, but Talayero and Sacks (2011) in their study observed that hypertriglyceride is a sole risk for cardiovascular diseases. Ogbera *et al*. (2009) observed that diabetes mellitus subjects exhibit lipid abnormalities which are termed atherogenic dyslipidemia due to the atherogenic effect they exhibit on the subject. Kuvin *et al*. (2002) opined that low high density lipoprotein cholesterol level correlated significantly with endothelial malfunction and weak vasodilation. Rasha (2008) in an earlier study observed that increased total cholesterol may be due to insufficient muscular exercise or blockage of cholesterol metabolism in the system. However, in another study, Choudhury *et al*. (2011) attributed high total cholesterol to increase very low density and low density lipoprotein that is found in the diabetes mellitus subjects but Adu (2013) observed that the hypercholesterolemia observed in diabetes mellitus is as a result of dysfunctional response of the enzymes in cholesterol synthesis (3- hydroxyl- 3- methylglutararyl- CoA reductase and hepatic cholesterol 7α- hydroxylase) leading to obstruction in the cholesterol pathway.

Glycosylated haemoglobin (HbA1c) is observed to be positively correlated with cholesterol, triglycerides and low density lipoprotein which implies that they are directly proportional to HbA1c. This show poor management of glucose level in the blood of the subject. Also, glycosylated haemoglobin is negatively correlated with high density lipoprotein, which therefore implies that as glycosylated haemoglobin is increasing, high density lipoprotein cholesterol is decreasing. This shows that HbA1c is indirectly proportional to high density lipoprotein but directly proportional to total cholesterol, triglycerides and low density lipoprotein.

CONCLUSION

It has been shown that glycosylated haemoglobin is positively associated with blood glucose as well as total cholesterol, triglycerides, low density lipoprotein but negatively associated with high density lipoprotein. It is therefore pertinent to note that, glycosylated haemoglobin can be used as a surrogate marker of dyslipidemia and dual biomarker for both glycemic control and diabetic atherogenic dyslipidemia.

CONFLICT OF INTEREST: There was no conflict of interest

FUNDING: None

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