

Full Length Research Paper

Glycated haemoglobin, lipids and drug adherence in Type 2 diabetes mellitus: experience in high income group

¹Ebesunun MO and ²Adedipe O

¹Chemical Pathology and Immunology, Obafemi Awolowo College of Health Science, Olabisi Onabanjo University Sagamu, Nigeria.

²Chemical Pathology and Immunology, University College Hospital Ibadan, Nigeria

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Adherence to drug regimen in diabetes mellitus has been observed to have contributed significantly to poor management in many populations. This study was designed to assess the relationship of HbA_{1c} to Morisky score in type II diabetes in high income group. Sixty subjects consisting of 30 type 2 diabetes mellitus patients. age range (38-60 years) and 30 age and sex matched non -diabetes controls (40-59 years) were selected for this study. Anthropometric and biochemical parameters were determined using standard procedures. Results showed significant increases in plasma glucose and glycated haemoglobin (HbA_{1c} %) ($p < 0.001$), triglyceride ($p < 0.01$) and decrease in plasma high density lipoprotein cholesterol ($p < 0.05$) in type 2 diabetic patients when compared with the corresponding control. Morisky score was significantly correlated with fasting plasma glucose ($r = 0.633$ $p < 0.05$) and HbA_{1c} % ($r = 0.549$, $p < 0.05$). An association between FPG and HbA_{1c}% and medication adherence rate of 66.7% was obtained for type II DM. Adherence to medication regimens showed a correlation with glycemic control ($p < 0.05$). Self-reported Morisky medication adherence score could be used to predict the degree of haemoglobin glycation (HbA_{1c} %) and therefore the risk of developing diabetic complications.

Keywords: Diabetes, drug adherence, HbA_{1c}, fasting plasma glucose, lipids.

INTRODUCTION

Diabetes mellitus (DM), a metabolic syndrome characterized by disturbance of carbohydrate, fat and protein metabolism results from defects in insulin secretion and or insulin action or both (World Health Organization (2006)). It is known to be one of the commonest causes of death in the developed world (Sacks (2001)). Obesity is commonly associated with type 2 diabetes and this has been shown to cause or aggravate insulin resistance. Several studies have demonstrated that chronic diabetes complications are the results of poor glycemic control. Central to good glycemic control is strict adherence to antidiabetic treatment. The treatment of DM is centered on reduction and avoidance

of obesity, adequate physical activity, modification of dietary habits, and use of oral antihyperglycemic agents and administration of insulin in some cases (World Health Organization (2004); Nyenwe et al (2003)).

Study has shown that the level of glycated hemoglobins in the blood is directly related to the average blood glucose levels over the life span of the hemoglobin in the circulation (Cramer (2004)). Available report has shown that Nigeria presents with the largest number of diabetes mellitus in Africa (Sacks (2001)). Report also indicates that the prevalence of type 2 diabetes in Nigeria is about 4-5% (Schteingart (1997)).

There is paucity of information on medication adherence rate in type 2 diabetes mellitus in high income group. This study was designed to assess the relationship of HbA_{1c} to Morisky score level in high income diabetes mellitus patients.

*Corresponding Author's Email: onoebe@yahoo.com

MATERIALS AND METHODS

Thirty high income group workers (24 males and 6 females) with mean age of 48 ± 6.3 years of a multinational oil company who were diagnosed as type 2 DM and taking at least one oral antihyperglycemic agent with or without insulin were selected for this study. These were classified into high income group using the WHO classification method (Robertson et al (2003)). The diagnosis of type 2 DM was assessed by the attending consultant Physician using clinical history and fasting plasma glucose (FPG) ≥ 7.0 mmol/L (≥ 126 mg/dl) and casual plasma glucose (random plasma glucose) of ≥ 11.0 mmol/L (≥ 200 mg/dl) or the 2-hour plasma glucose of > 11.0 mmol/L after a 75g oral glucose load. Thirty apparently healthy, free living volunteers matched for age and socioeconomic class were included as controls. A structured standard questionnaire to include the Morisky survey, a 4-item questionnaire that predicts patient medication-taking behavior, was administered to each patient. The relationship of HbA_{1c} to Morisky score was evaluated to other variables related to patient demographics. Inclusion criteria are; type 2 diabetes employee of an oil company, use of at least an oral anti hyperglycemic agent with or without insulin supplement.

Patients with liver diseases, renal disease, taking oral contraceptive, pregnant women and individuals on lipid lowering drug /diet were excluded from the study.

Anthropometric measurement

The weight and height were measured using standard digital weighing scale (Seca GMBH co. Germany) with a meter rule for height measurement. The Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (World Bank Data and statistics on economic class (2006)).

Blood collection and Analysis

Overnight fasting (10-14hours) blood samples were collected from each subject into fluoride oxalate and EDTA bottles. The plasma was separated from the cells and stored at -70°C until analyzed for HbA_{1c} using COBAS INTEGRA[®] 400 system. Total Hb and HbA_{1c} concentrations were estimated after haemolysis of the anticoagulated whole blood sample. Total haemoglobin was measured colourimetrically while HbA_{1c} was determined immunoturbidimetrically. The ratio of both concentrations yields the final percent HbA_{1c} (HbA_{1c} %) (Zander et al (1984); Goldstein et al (2004)).

Total cholesterol was determined using COBAS INTEGRA[®] 400 system based on enzymatic colorimetric method (CHOD/PAP) (Allain et al (1974)). HDL-cholesterol was determined using COBAS INTEGRA[®] 400 system based on direct homogeneous enzymatic colorimetric assay (Sugiuchi et al (1995)) and triglycerides determination using the COBAS INTEGRA[®] 400 system was based on enzymatic colorimetric method with glycerol phosphate oxidase (GPO) and 4-aminophenazone (PAP (Fossati and Prencipi (1982); McGowan et al (1983)). The low density lipoprotein cholesterol was calculated using Friedwald formula (Friedwald et al (1972)). $\text{LDLC} = \text{TC} - (\text{HDLc} + \text{TG}/5)$. The plasma glucose was immediately analyzed using glucose oxidase method (Neely (1972)).

Accuracy and precision of biochemical tests were monitored by including commercial quality control samples within each batch of test assay.

STATISTICS

All results were subjected to statistical analysis using the SPSS software for windows version 14. The student t test was used to compare the difference between two means. Pearson correlation coefficient was used to assess association between physical and

biochemical parameters. Differences were regarded as significant at $p < 0.05$ at 95% confidence.

RESULTS

Figure 1 shows the scatter plot of the correlation between the respective HbA_{1c}% and the corresponding FPG in all the diabetes mellitus patients. The two parameters were significantly correlated.

Figure 2 shows the scatter plot of the correlation between the respective HbA_{1c}% and the corresponding self-reported Morisky medication adherence score in the Type 2 diabetes mellitus patients. The two parameters were significantly correlated.

Figure 3 shows mean self-reported medication adherence scores and their corresponding mean HbA_{1c}% and FPG (mmol/L). The least adherent group (score 3) showed the poorest glycemic control (highest HbA_{1c}% and FPG) and the most adherent group (score 0) showed the best glycemic control (least HbA_{1c}% and FPG).

Table 1 shows mean \pm SD of all parameters in diabetes mellitus and control subjects. There were significant increases in plasma TG ($p < 0.01$) and fasting plasma glucose ($p < 0.001$) compared with the corresponding control values. While the plasma HDLC ($p < 0.05$) and HbA_{1c} (%) ($p < 0.001$) were significantly decreased when compared with the corresponding controls values. No significant changes were obtained in the other parameters.

Table 2 shows Pearson's correlation coefficient (r) of all parameters in type 2 diabetes mellitus group. Fasting plasma glucose showed a significant correlation with the Morisky medication adherence score ($r = 0.633$, $p < 0.05$) and HbA_{1c}% ($r = 0.770$, $p < 0.05$) respectively. There was a positive significant correlation between Morisky medication adherence score and HbA_{1c}% ($r = 0.549$, $p < 0.05$). A strong significant positive correlation was also obtained between TC and LDLc ($r = 0.938$, $p < 0.05$). No significant correlations were obtained in the other parameters.

DISCUSSION

The subjects studied were high income group type 2 diabetes matched with controls for age and income. The results of the study showed markedly elevated plasma glucose and HbA_{1c}% in the diabetes mellitus compared with the control value. When WHO criterion for glycemic controls of FPG (5-7.2mmol/L, HbA_{1c} % < 5-7%) (American Diabetes Association (1998)) was applied, most of the patients demonstrated poor glycemic control. However, 16.7% (5 patients) HbA_{1c}% had less than 7% (within WHO reference value). This finding is at variance with an earlier study that showed that 36% type 2 diabetes had HbA_{1c}% less than 7% (Adebisi et al.,

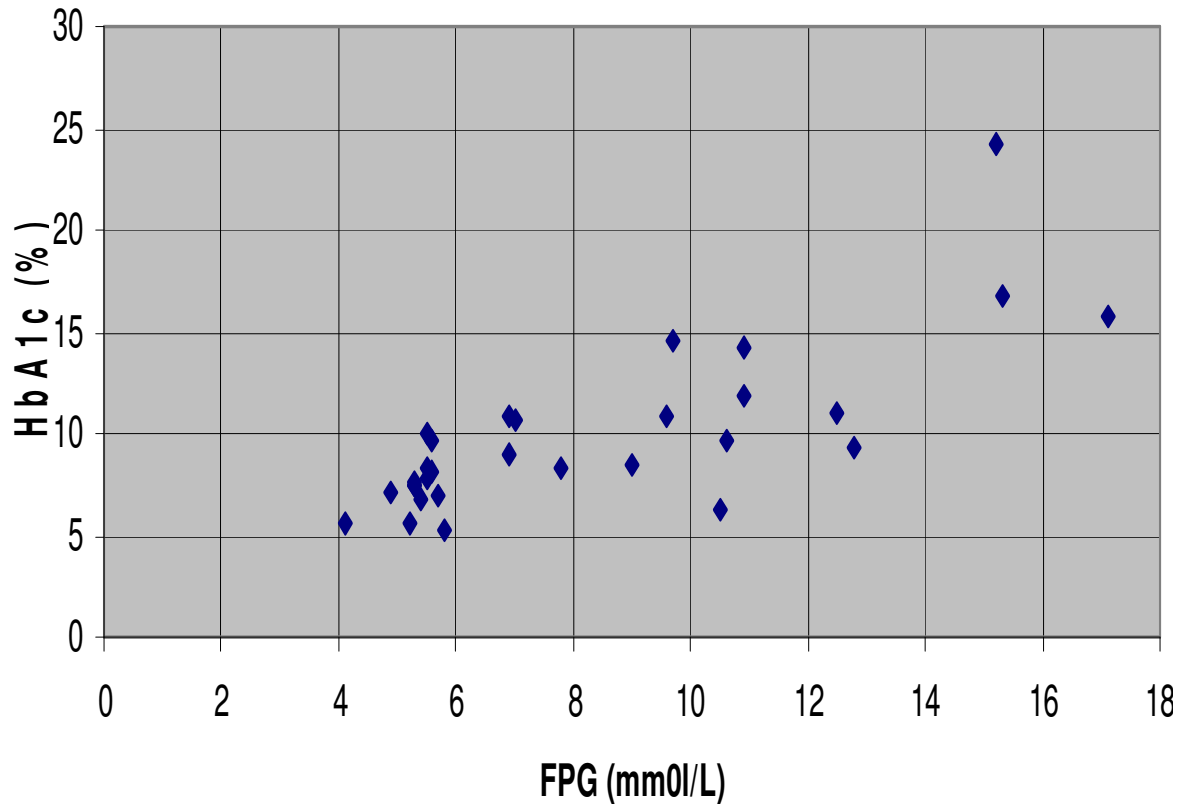


Figure 1. Relationship between Glycosylated Haemoglobin (HbA1c) and FPG Among the 30 Type 2 Diabetes Mellitu Study Group

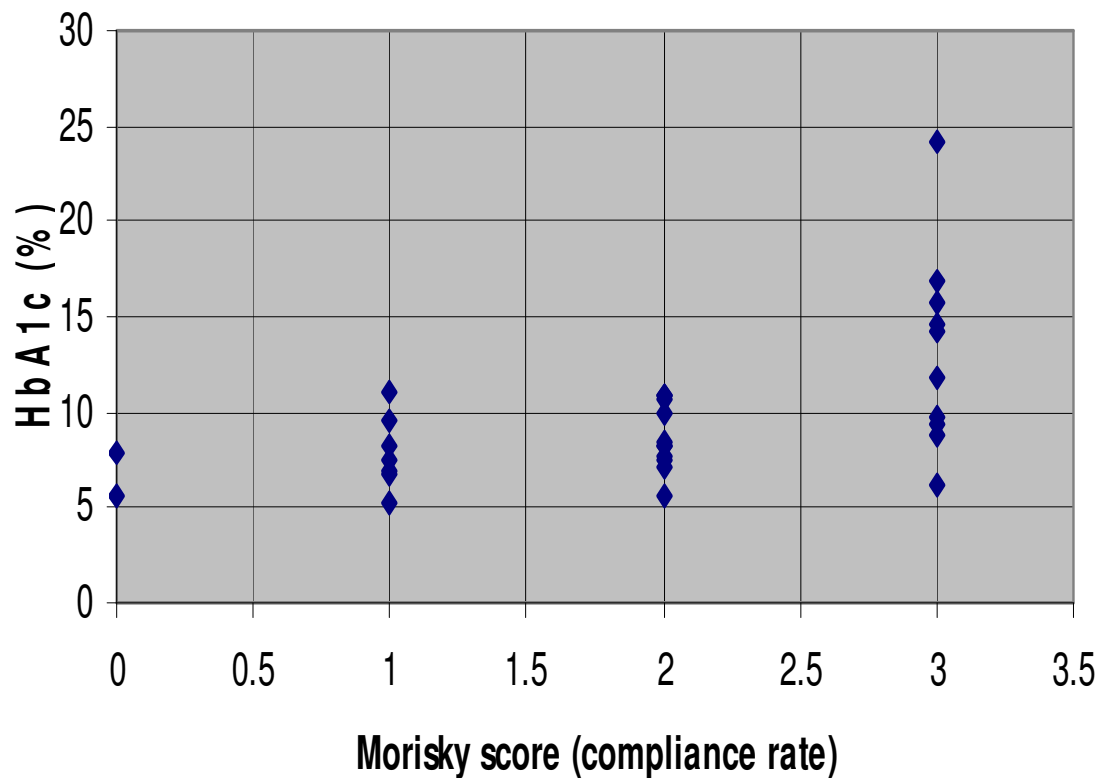


Figure 2. Glycemic index (HbA1c) vs Morisky score

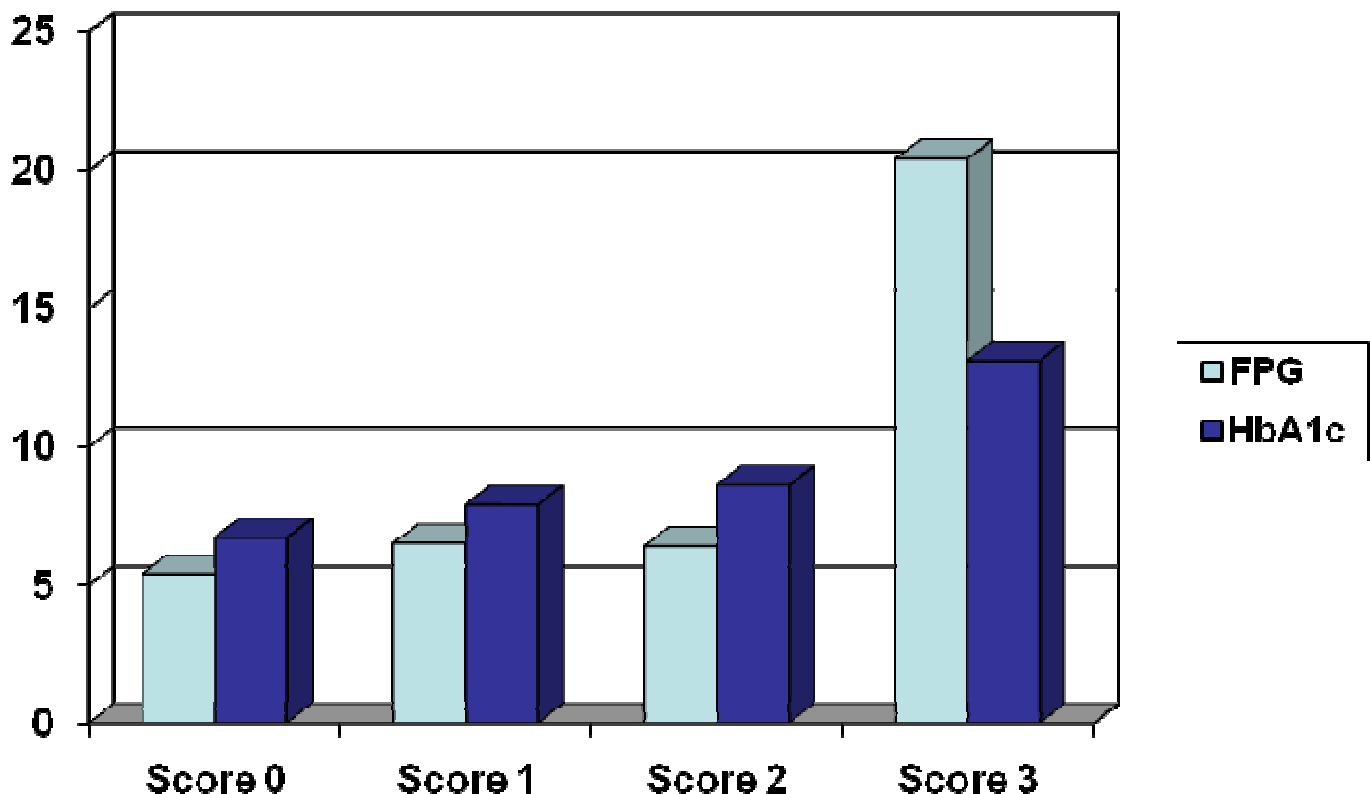


Figure 3. Pictogram showing means self-reported medication adherence scores and their corresponding mean HbA1c% and FPG (mmol/L).

(2003).

The results also indicated that the patients had some degree of dyslipidaemia with the mean plasma triglyceride significantly elevated and the HDLC statistically reduced. Mobilizations of free fatty acid from the liver can lead to increase synthesis of plasma TG and this could be a contributing factor to pancreatic lipotoxicity, which could lead to β - cell failure and invariably leads to poor glycemic control. On the other hand elevated plasma TG may in part may be as a result of poor glycemic control in our patients. Although the BMI (obese) of our patients was high using WHO classification, this was however not significant because the control subjects who were also high income group had BMI in the overweight range. However, studies have linked increased body weight and BMI to insulin resistance (Kasuga (2006)). The higher the body weight the more the risk of poor glycemic control.

The age, disease duration and BMI were not correlation with glycated haemoglobin, suggesting that the degree of HbA1c glycation does not depend on disease duration, age or BMI.

The medication adherence rate of the patients was 66.7% from self reported Morisky medication adherence scores. This is slightly higher than the reported

adherence rate of 50% in type 2 diabetes mellitus in previous studies (Littenberg (2006); Wens et al (2005); Schectman (2002)) and lower than 79.7% (using prescription –refill data) reported. However, the diabetic groups with good adherence (scores 1 and 2) showed significantly lower FPG and HbA1c (%) than the poorly adherent group (score 3) in which a better glycemic control has been obtained with good adherence. The mean adherence score of 2 (good adherence) observed in this group did not indicate good glycemic control, suggesting a probable treatment failure. Another possible explanation would be that the patients reported medication adherence score were likely inaccurate.

The correlation between HbA1c (%), and self-reported Morisky medication adherence score suggests that medication adherence score could be used to predict the degree of haemoglobin glycation (HbA1c %).

CONCLUSION

This study has demonstrated elevated plasma HbA1c (%), fasting plasma glucose triglyceride and reduced HDLC in high income diabetes mellitus patients with poor glycemic control. Self-reported Morisky medication

Table 1. Mean \pm sd of all parameters in diabetes mellitus and control subjects

Variables	Non-diabetic Control	Diabetes Mellitus t-value subjects		p-value
	N=30	N=30		
Age (yrs)	48.4 \pm 5.79	8.8 \pm 6.30	0.25	>0.05
BMI (kg/m ²)	28.8 \pm 2.75	30.2 \pm 3.68	1.67	>0.05
FPG (mmol/L)	4.8 + 0.51	8.2 + 3.57	5.16	<0.001
HbA1c (%)	6.4 + 0.87	9.8 + 4.0	4.55	<0.001
TC (mmol/L)	4.8 + 0.70	4.7 + 0.81	0.51	>0.05
TG (mmol/L)	0.9 + 0.29	1.3 + 0.69	2.92	<0.01
HDLC (mmol/L)	1.4 + 0.46	1.2 + 0.28	2.03	<0.05
LDLC (mmol/L)	3.2 + 0.73	3.2 + 0.78	0.00	>0.05

FPG = Fasting Plasma Glucose

HbA1c = Glycosylated Haemoglobin

n = no of subjects

X \pm SD = Mean \pm standard deviation

P = level of statistical significance

TC = Total Cholesterol

TG = Triglycerides

HDLC = High Density Lipoprotein Cholesterol

LDLC = Low Density Lipoprotein Cholesterol

Table 2. Pearson correlation of all parameters

Variables	BMI	FPG	HbA1c	TC	TG	HDLC	LDLC	Morisky Score
BMI								
FPG								0.633**
HbA1c		0.770**						0.549**
TC							0.938**	
TG								
HDLC								
LDLC								
Morisky Score			0.549**					

** = Significant at the 0.05 level

BMI = Body Mass Index

FPG = Fasting Plasma Glucose

HbA1c = Glycosylated Haemoglobin

TC = Total Cholesterol

TG = Triglycerides

HDLC = High Density Lipoprotein Cholesterol

LDLC = Low Density Lipoprotein Cholesterol

adherence score could be used to predict the degree of haemoglobin glycation (HbA1c %) and thus suggesting that the degree of haemoglobin glycation (HbA1c %) can be used to predict the FPG level in the study group. The Morisky score may be an efficient tool for identifying patients with poor medication-taking behaviour

Duality

This study did not receive any financial support from any

organization nor institution. It was a part of research for a higher degree in Chemical Pathology. There are no conflicts of interest among the authors.

Contributors

MOE was involved in the conception, design, interpretation and drafting of the manuscript.

AO was involved in the conception, collection of data and analysis of result as well as drafting.

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