ORIGINAL ARTICLE

Relationships between hemoglobin A_{1c} and spot glucose measurements in Nigerians with type 2 diabetes mellitus

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Abstract

Background: Glycosylated hemoglobin, HbA_{1c} is the most acceptable measure of chronic glycemia. It is not widely available and/or affordable in Nigeria. The mean of the monthly fasting plasma glucose (MFPG) of the preceding 3 months is often used as surrogate for assessing chronic glycemia.

Objective: To determine the relationships among fasting plasma glucose (FPG), 2-hour post-prandial glucose (2-hPG), HbA1c, and MFPG.

Materials and Methods: Hospital records were used to derive the MFPGs of diabetic subjects from the mean of their monthly FPGs of the preceding three months. Other data extracted included the patient's age, sex, body mass index (BMI), waist circumference (WC), and duration of diabetes mellitus (DMDU). FPG, 2- hPG and HbA_{1c} were determined during this index consultation.

Results: Ninety five persons (65 males, 30 females) with type 2 were included in the study. Their mean age and DMDU were 54.7 ± 8.9 years and 8.1 ± 6.1 years, respectively. Their mean WC, BMI, FPG, 2-hPG, HbA1c, and MFPG were 100.2 ± 11.0 cm, 24.2 ± 4.3 kgm/2, 7.5 ± 2.4 mmol/l, 10.4 ± 4.1 mmol/l, 8.2 ± 2.2%, and 5.9 ± 2.2 mmol/l, respectively. The males were significantly older (57.5 ± 8.4 vs 49.3 ± 7.6, $P<0.001$) while the females had higher waist circumference and BMI than their male counterparts: 104.8 ± 11.6 cm vs 92.8 ± 10.1 cm, $P<0.004$; and 25.8 ± 4.9 kg/m^2 vs 23.3 ± 3.7 kg/m^2, $P<0.005$, respectively. There were no significant differences in FPG, 2-hPG, MFPG and HbA1c levels between male and female subjects. There were significant positive correlations between FPG and HbA1c ($r=0.45$, $P=0.05$) and between 2-hPG and HbA1c ($r=0.52$, $P=0.01$), but there was no positive correlation between MFPG and HbA1c ($r=-0.20$, $P=0.18$).

Conclusion: There is no positive correlation between MFPG and HbA_{1c} and thus MFPG may not be a good surrogate for HbA1c in assessment of chronic glycemia in our patients.

Key words: Diabetes mellitus, fasting plasma glucose, glycosylated hemoglobin (HbA1c), 2-h post-prandial glucose

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Introduction

Hemoglobin A_{1c} is formed from irreversible glycosylation of erythrocyte hemoglobin in proportion to circulating plasma levels of glucose.[1,2] HbA_{1c} level provides an index of the average blood glucose concentration over the previous 2-3 months.[3-5] Presently, HbA_{1c} is the most acceptable and widely used measure of chronic glycemia.[2] Elevated HbA_{1c} levels have been associated with long-term complications of diabetes mellitus.[6,7] Its level is therefore used to determine whether treatment is adequate. Many Nigerians with diabetes mellitus do not achieve good long term glycemic control when HbA_{1c} is used as an index of chronic glycemia.

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Idogun and Olumese[8] reported that only 53% of 64 type 2 diabetic patients seen in a tertiary medical centre in Benin City had good glycemic control. Adebisi *et al.*,[9] found only 36% of diabetic patients had $HbA_{1c} \leq 7.2\%$ in Ilorin.

Unfortunately HbA_{1c} is not widely available and/or affordable in most hospitals in Africa,[10] Nigeria inclusive. In Nigeria, the mean of the three most recent fasting plasma glucose (MFPG) results documented in the patient's last three hospital consultations is often calculated and used as surrogate for long term glycemia in place of HbA_{1c}. However, it is not known with certainty if there is a strong correlation between the calculated mean fasting plasma glucose (MFPG) and HbA_{1c} in Nigerians with type 2 diabetes mellitus. This study is to determine the relationship among HbA_{1c}, fasting plasma glucose, 2-h post-prandial plasma glucose and the mean of the last three FPG levels of Nigerians with type 2 diabetes mellitus with a view to determining the suitability or otherwise of using MFPG as a surrogate for HbA_{1c}.

Materials and Methods

Hospital records of all patients with type 2 DM seen at the diabetes clinic over a 3-month period were retrieved for the study. Data documented included the patient's age, sex, body mass index (BMI), waist circumference (WC), and duration of diabetes mellitus. All consenting patients with type 2 diabetes mellitus were educated about the aim of the study and were instructed to come to the Diabetes Clinic fasting on test days.

On arrival at the Diabetes Clinic in the morning, blood samples were drawn for determination of FPG (after 8-10 hour overnight fast) and HbA_{1c}. After which subjects drank within 5 minutes a glucose solution prepared by dissolving 75 g anhydrous glucose in 250 ml of water. Two hours later, blood samples were drawn to determine the 2-h postprandial plasma glucose (2-hPG). The mean fasting plasma glucose (MFPG) values was derived from the mean of the monthly FPG of the preceding three months documented in the patient's hospital record.

Plasma glucose was determined by the glucose oxidase method of Trinder.[11] HbA_{1c} level was determined with an automated HbA_{1c} point-of-care-testing analyser, the Bio-Rad in2it (Bio-Rad Laboratories Deeside, CH5 2NU, UK) using a drop of blood obtained by finger prick.

All the study subjects voluntarily gave informed consent. The Hospital Ethics and Research Committee approved the study.

Exclusion criteria

All pregnant subjects with type 2 diabetes mellitus, all type 1 DM patients, all type 2 DM subjects who were unwilling to give consent for the study, those who were ill, and any subject who could not complete every aspect of the study were excluded.

Definition of terms

Good long term glycaemic control was defined according to the American Diabetes Association criteria[12] as a $HbA_{1c} < 7\%$.

Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 16. Data are expressed as mean±SD. Significance of difference in mean values was determined using a two-tailed unpaired *t*-test. Correlations among FPG, 2-hPG, MFPG, and HbA_{1c} were estimated using Pearson or Spearman correlation coefficients as appropriate. Level of statistical significance was set at $P<0.05$.

Results

Ninety five persons (65 males, 30 females) with type 2 were included in the study. Their mean age was 54.7 ± 8.9 years. The mean duration of diabetes mellitus was 8.1 ± 6.1 years. The mean of their waist circumstance, BMI, FPG, 2-hPG, HbA_{1c}, and MFPG were 100.2 ± 11.0 cm, 24.2 ± 4.3 kgm^{-2}, 7.45 ± 2.4 mmol/l, 10.4 ± 4.1 mmol/L, 8.2 ± 2.2%, and 5.9 ± 2.2 mmol/l. The characteristics of the study subjects by gender are summarized in [Table 1]. The males were significantly older (57.5 ± 8.4 vs 49.3 ± 7.6, $P<0.001$) while the females had higher waist circumference and BMI than their male counterparts: 104.8 ± 11.6 cm vs 92.8 ± 10.1 cm, $P<0.004$; and 25.8 ± 4.9 kg/m^2 vs 23.3 ± 3.7 kg/m^2, $P<0.005$, respectively. There were no significant differences in FPG, 2-hPG, MFPG, and HbA_{1c} levels between male and female subjects. Thirty-five (37%) of them had good long-term glycaemic control of the diabetes mellitus (HbA1c<7%)

There were significant positive correlations between FPG and HbA_{1c} ($r=0.45$, $P=0.05$) and between 2hPG and HbA_{1c} ($r=0.52$, $P=0.01$). There was no positive correlation observed between MFPG and HbA_{1c}; $r=-0.20$, $P=0.18$ [Table 2].

Table 1: Characteristics of the study subjects mean±SD

Parameter	Male	Females	*P* value
Age (years)	57.5 ± 8.4	49.3 ± 7.6	<0.001
BMI (kgm/2)	23.3 ± 3.7	25.8 ± 4.9	0.005
WC (cm)	92.8 ± 10.1	104.8 ± 11.6	0.004
DMDU (years)	8.0 ± 6.0	8.2 ± 6.2	0.892
FPG (mmol/l)	7.3 ± 2.4	7.7 ± 2.6	0.462
2hPG (mmol/l)	10.59 ± 4.2	9.93 ± 4.0	0.487
MFPG (mmol/l)	5.8 ± 2.3	6.3 ± 1.6	0.359
HbA_{1c} (%)	8.2 ± 2.3	8.2 ± 2.0	0.994

BMI = Body mass index, WC = Waist circumference, DMDU = Duration of diabetes, FPG = Fasting plasma glucose, 2hPG = Two hour postprandial plasma glucose, MFPG = Mean fasting plasma glucose, HbA_{1c} = Glycosylated haemoglobin A_{1c}

Table 2: Correlation coefficient (*r*) between plasma glucose values and glycosylated haemoglobin (HbA_{1c})

	FPG	2hPG	MFPG	HbA_{1c}
FPG	1	0.66**	−0.18	0.45*
2hPG	0.66**	1	−0.20	0.52**
MFPG	−0.18	−0.20	1	−0.20
HbA_{1c}	0.45*	0.52**	−0.20	1

*Correlation is significant at the 0.05 level (2- tailed); **Correlation is significant at the 0.01 level (2- tailed); FPG = Fasting plasma glucose; 2hPG = 2-h postprandial plasma glucose; MFPG = Most recent fasting plasma glucose ; HBA_{1c} = hemoglobinA_{1c}

Discussion

Our study showed that in Nigerians with type 2 diabetes mellitus, there was a significant positive correlation between fasting plasma glucose and HbA_{1c} and an even stronger correlation between 2-h post-prandial plasma glucose and HbA_{1c}. There was no positive correlation between the MFPG and HbA_{1c}. These findings have important implications for our diabetic patients. The fasting plasma glucose is commonly done few days before or on the day of outpatient consultations. There are no local studies to validate any relationship between FPG and HbA_{1c}. Otieno *et al.*,[13] reported that the morning random blood glucose (RBS) level had a linear relationship with glycated hemoglobin taken simultaneously when the RBS is less than 10 mmol/l. Gill *et al.*,[14] documented a positive correlation between RBS and HbA_{1c} (r=0.54). Further study is desirable to validate this in our locale.

The mean of the monthly fasting plasma glucose (MFPG) of the last three months was within acceptable target glycemic levels in our study. This gives a false sense of a good long-term glycemic control whereas the HbA_{1c} clearly showed that a majority (63%) of our patients had poor long term glycemic control as evidenced by values of HbA_{1c}>7.0%. Our patients are generally not adherent to diet and anti-diabetic drugs. They tend to maintain better glycemia immediately before and after the consultation. This is, however, not substained on a long-term basis.

The correlation between FPG and HbA_{1c} (r=0.45) and between 2-h postprandial glucose and HbA_{1c} (r=0.52) found in this study were smaller than those of r=0.71 and r=0.79 for FPG vs HbA_{1c} and 2hPG vs HbA_{1c}, respectively, documented by Van-'t Riet *et al.*,[15] in patients with diabetes mellitus in a Dutch population. Nathan *et al.*,[4] also reported that HbA_{1c} correlated closely with a complete measure of average glycemia over the preceding 8-12 weeks. Nathan and colleagues measured mean glucose levels by continuous glucose monitoring, which measured interstitial glucose levels every 5 min, for 12 weeks. A strong correlation between mean blood glucose and HbA_{1c} in type 2 diabetes mellitus was also documented by Makris *et al.*,[5] among Greek patients with type 2 diabetes (r=0.92). In the Greek study, mean blood glucose was calculated for each patient from self measurements of blood glucose using a portable glucometer, made six times a day (before eating and 2 h after a meal), three times a week for 1 month.

There was, however, no positive correlation between the MFPG and HbA_{1c} in our patients compared to those documented in Caucasians. In the Caucasian studies, mean blood glucose were determined by continuous blood glucose monitoring every 5 min, for 12 weeks by Nathan *et al.*,[4] six times a day, three times a week in the Makris *et al.*,[5] compared to the once-a-month FPG in our study. The mean of the glucose level from the continuous glucose monitoring is expectedly more likely to correlate with $HbA_{1c.}$ This is due to less day-to-day variability of fasting plasma glucose in diabetic patients when plasma fasting glucose is done on a daily basis[16] rather than it being done once a month.

In our study, 2hPG had a stronger correlation with HbA_{1c} than FPG as in previous studies.[17,18] In an analysis of glucose profiles and HbA_{1c} in the Diabetes Control and Complication Trial, Rohlfing *et al.*,[17] found that among individual time points, afternoon and evening plasma glucose (post lunch, pre-dinner, post-dinner, and bedtime) showed higher correlations with HbA_{1c} than the morning time points (pre-breakfast, post-breakfast, and pre-lunch). This finding is similar to that of Woerle *et al.*,[18] who noted that both FPG and 2-hPG levels increased as HbA_{1c} increased but that 2-hPG level increased at a rate 4 times greater than FPG and accounted for a greater proportion of HbA_{1c}.

Our patient characteristics such as age, gender and BMI were not associated with adequate glycaemic control. This observation was previously reported by Goudswaard *et al.*,[19] and was recently reaffirmed by Rätsep *et al.*[20]

In conclusion, MFPG derived from the mean of the monthly FPG done over the preceding 3 months in our patients with type 2 diabetes mellitus did not correlate positively with HbA_{1c} and thus may not be a good surrogate for HbA_{1c} as a measure of long-term glycemic control. FPG and 2-hPG both showed linear relationship with HbA_{1c}; however, a larger scale study is needed to determine their usefulness as possible predictors of long term glycemic control in resource-constraint environment. It is thus recommended that further studies involving patients who do their FPG weekly at least for 12 weeks should be done to assess if that will give a better correlation with HbA_{1c} as continuous glucose monitoring is not feasible in our environment.

Limitation of study

The sample size is rather small due to the high cost of HbA_{1c} and the difficulty in getting subjects with diabetes mellitus to participate in research in our practice locale.

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