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Research Article

Correlation of Estimated Average Glucose with Single Point Glucose Values in Patients Attending a Clinical Laboratory Facility in South-Western Nigeria: A retrospective Study

Olabisi T. Bamidele[1,2], Stanley I.R. Okoduwa[3], Olanrewaju E. Olasehinde[1], Ngozi E. Okonkwo[1], Frank C. Ibeaja[1], Ayomide Faleye[1], Olatunde A. Olayanju[1,*]

[1] *Department of Chemical Pathology, Babcock University Teaching Hospital, Ilishan-Remo, Nigeria*
[2] *Department of Chemical Pathology, School of Basic Clinical Sciences, Babcock University, Ilishan-Remo, Nigeria*
[3] *Department of Biochemistry, School of Basic Medical Sciences, Babcock University, Ilishan-Remo, Nigeria*

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***CORRESPONDENCE**
olayanjuo@babcock.edu.ng
+2347032055262

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ABSTRACT

Regular monitoring of glycaemic levels in patients with diabetes mellitus forms a major fulcrum for ensuring a desirable treatment outcome and a good quality of life in affected individuals. Glycated haemoglobin (HbA1c) measurement is a common and dependable option for determining long-term glycaemic control. Unfortunately, it is relatively expensive and not readily available in most low-income settings. Measuring fasting plasma glucose (FPG) is the cheaper alternative if it correlates with HbA1c. A retrospective study into clinical records to identify all patients who had HbA1c and FPG was conducted on the same day between January 2021 and July 2022. Estimated average glucose was calculated from the HbA1c and the values were correlated with the FPG. Factors predicting values for HbA1c were also determined. The results obtained showed that a total of 315 patients had clinical records required for the study, 147(46.7%) males and 168 (53.3%) females. They were grouped into diabetic (n=111, with median FPG of 155 mg/dL), impaired fasting glucose (n=67, with median FPG of 108 mg/dL) and non-diabetic (n=137, with median FPG of 92 mg/dL) participants. The estimated average glucose for the three groups was 160 mg/dL, 117 mg/dL and 112 mg/dL, respectively. The FPG of the diabetic group showed a moderate correlation with the estimated average glucose (0.630 and a p-value < 0.001), and factors which predicted a high HbA1c were increasing age, FPG and the presence of diabetes mellitus. This data further encourages the continued use of FPG in monitoring glycaemic control in diabetic patients, especially in resource-poor locations where HbA1c is either too expensive or unavailable.

Keywords: *Fasting Plasma Glucose, HbA1c, Estimated Average Glucose, Diabetes, Impaired Fasting Glucose, Glycaemic*

INTRODUCTION

Current methods for monitoring blood glucose regulation after initiating treatment and lifestyle changes in the management of diabetes and prediabetes rely on single-time-point measurements of plasma glucose, and average measures of overall glycaemia using glycated haemoglobin or continuous glucose monitors (Chehregosha *et al*., 2019; Nolen, 2019). Single-time-point measurements of glucose in the form of self-monitoring blood glucose (SMBG) or laboratory-based plasma glucose measurements such as fasting plasma glucose (FPG), random plasma glucose (RPG), and two-hour post-prandial (2HPP) glucose checks

are very common in the developing countries although globally the use of continuous glucose monitors is being advocated (Nolen, 2019; Siddiqui *et. al*, 2020, Adams *et al*., 2021).

The use of SMBG aims at collecting multiple blood glucose checks at many time points using portable glucometers (Wang *et al*., 2019; Aliyu *et al*., 2019; Olamoyegun *et al*., 2021; Tran *et al*., 2023). HbA1c measurements give an average estimate of glucose over 10-12 weeks, it is used in the monitoring of long-term glycaemic control in a person with diabetes. Levels <7% in persons with diabetes have been shown to delay the development of microvascular complications. There is a perceived preference for the use of FPG to HbA1c and/or SMBG in assessing long-term glycaemic control in Nigeria and other developing countries, this may be due to the higher cost of tests and the unavailability of testing methods in some areas of the country (Balogun *et al*., 2020, Tandon *et al*., 2021; Adams *et al*., 2021). While HbA1c is given in percentage (%), FPG is expressed in mg/dL or mmol/L. The American Diabetes Association and the American Association of Clinical Chemists have advocated the estimation of average glucose from HbA1c with the use of Nathan's equation to give glucose values in mg/dL. This unit is relatable to the patients (Kariyawasan *et al.*, 2021, Sriwimol *et al.*, 2022). In a resource-poor setting like Nigeria, with a growing burden of diabetes and insufficient coverage of health insurance scheme, patients are scheduled to do a pre-appointment one-time FPG to assess the adequacy of glycaemic control to aid the continued use or titration of hypoglycaemic agents (Balogun *et al*., 2020). This method of glucose monitoring has a major shortcoming in assessing glycaemic control in the short term and may not be truly reflective of glycaemic control since the prior clinic visit (Okpara *et al.*, 2023). Due to the patient's lack of funds, inaccessibility to standard laboratories and/or illiteracy, the clinician is left to manage patients with diabetes who are unable to provide the best indicators of long-term glycaemic control such as results of self-monitoring blood and/or HbA1c, with single point FPG and two-hours postprandial glucose (Balogun *et al*., 2020).

This study aimed to evaluate the popular practice in most hospital settings in Nigeria for the monitoring of glycaemic control in persons with diabetes. The essence is to find possible correlations between the HbA1c-derived estimated average glucose values and FPG of patients. The findings of this study are expected to provide vital information on the usefulness of glycated haemoglobin and FPG, tests routinely used for monitoring glycaemic control in persons with diabetes.

MATERIALS AND METHODS

Study Design and Setting

The research was a retrospective study using data obtained from the laboratory records of the Chemical Pathology Laboratory at the Babcock University Teaching Hospital, Ilishan-Remo, Nigeria. This semi-automated laboratory provides services to its patients, neighbouring government, and private healthcare facilities within Ogun and Lagos States, Nigeria. Ethics approval was obtained from the Babcock University Health Research and Ethics Committee to use secondary data from the Chemical Pathology laboratory test record. The data was anonymised to ensure confidentiality by de-identifying the data. An ethical clearance number (BUHREC No 809/23) was also obtained.

Data sources: Secondary data obtained from the laboratory record book were used in the study. All patients sent for FPG and HbA1c on the same day between January 2021 and July 2022 were included in this study. Records without major identifiers including age, gender and/or clinical diagnosis were excluded from the study.

Variables: The patient's record was divided into three groups based on their clinical diagnosis and laboratory results. The diabetic, impaired fasting glucose and non-diabetic (normal) groups were identified and formed the basis for analysis.

Biochemical Classifications

The Diabetic group was defined biochemically as those whose FPG exceeded 126 mg/dL on two separate occasions or HbA1c values greater than or equal to 6.5% on two separate occasions. The impaired FPG had FPG between 100-125 mg/dL, and the non-diabetic or normal population had FPG less than 100 mg/dL (ElSayed *et al*., 2022).

Laboratory Analysis

The analysis of HbA1c on whole blood samples was done using the fluorescence immune-chromatographic method on an SD Biosensor (Republic of South Korea) while plasma glucose estimation was done using the glucose oxidase method on an automated chemistry analyser (TC matrix 4AS auto-analyzer). Quality control for glucose estimation was within specified limits of 2 standard deviations.

Statistical Analysis

Data was subjected to a normality test and reported according to distribution pattern. Categorical variables were reported as number and frequency while continuous variables were reported as median and interquartile range. Estimated average glucose (eAG) values were calculated from patients' HbA1c results using Nathan's regression equation: (eAG =28.7 x HbA1c –46.7). The relationship

between eAG and FPG was determined using Spearman's correlation analysis, and regression analysis was done to determine the relationship between a selected variable and the HbA1c. A *p*-value less than 5% was considered significant.

RESULTS

The total number of patients whose clinical records passed the selection criteria was 315, and the majority of them were non-diabetic adults with a median FPG of 91.8 (86.4-95.4) mg/dl. The other patients were either known diabetic patients or patients with impaired fasting glucose. The number of patients in these two groups and their FPG levels are reported in Table 1. There was a total of 147 (46.7%) males in the study, and the gender distribution in each of the

The median eAG for the total participants was 116.9 (108.3-142.7) mg/dL, comparable to that of the patients in the impaired group. The median eAG for the diabetic group was higher at 159.9 (136.9-211.6) mg/dL. Other details regarding the glycaemic studies of the participants including HbA1c and FPG are reported in Table 1.

Table 1. Basic Demographic and Glycaemic status of all Participants, Patients with Diabetes Mellitus, Patients with Impaired Fasting Glucose, and Non-diabetic Participants.

	All participants (N=315)	Diabetic (n=111;35.2%)	Impaired (n=67;21.3%)	Normal (n=137;43.5%)
Sex (M)	147 (46.7)	54 (48.6)	28 (41.8)	65 (47.4)
(F)	168 (53.3)	57 (41.4)	39 (48.2)	72 (42.6)
Age (years)	53 (45-62)	57 (50-65)	53 (44-61)	49.0 (40.5-60.0)
eAG (mg/dL)	116.9 (108.3-142.7)	159.9 (136.9-211.6)	116.9(108.3-125.5)	111.2 (102.5-116.9)
FPG (mg/dl)	106.6 (91.8-133.2)	154.8 (129.6-214.2)	108 (102.6-113.4)	91.8 (86.4-95.4)

M = male, F= female, eAG: Estimated average glucose, FPG: Fasting plasma glucose

In the three groups investigated in this study, the median eAG was consistently greater than the median FPG; 159.9 (136.9-211.6) mg/dl vs 106.6 (91.8-133.2) mg/dl in the diabetic group, 116.9(108.3-125.5) mg/dl vs 108 (102.6-113.4) mg/dl in the impaired group, and 111.2 (102.5-116.9) mg/dl vs 91.8 (86.4-95.4) mg/dl in the non-diabetic group, although there was a downward trend in each of the two parameters across the three groups. The same trend was observed in the values of the HbA1c across the three groups (Figure 1). The HbA1c values were not significantly different between males and females in the total participants with 7.1 % vs. 7.3%; p=0.173, and this trend was also seen in the three groups (Table 2). Participants who were 50 years and above had a significantly higher HbA1c than the younger participants with 5.9% vs. 5.5%; p=0.025 generally, but when the same analysis was done across the three groups, this effect was not seen (Table 2).

Table 2. Comparing HbA1c Values Across Gender and Age Groups, in the Three Categories of Participants

	All participants		Diabetic		Impaired		Normal	
	HbA1c	p-value	HbA1c	p-value	HbA1c	p-value	HbA1c	p-value
Male	5.7	0.384	7.1	0.173	5.8	0.580	5.4	0.859
Female	5.7		7.3		5.6		5.5	
Age <50 (n=118)	5.5	0.025	7.2	0.175	5.6	0.580	5.4	0.863
Age ≥50 (197)	5.9		7.3		5.8		5.6	

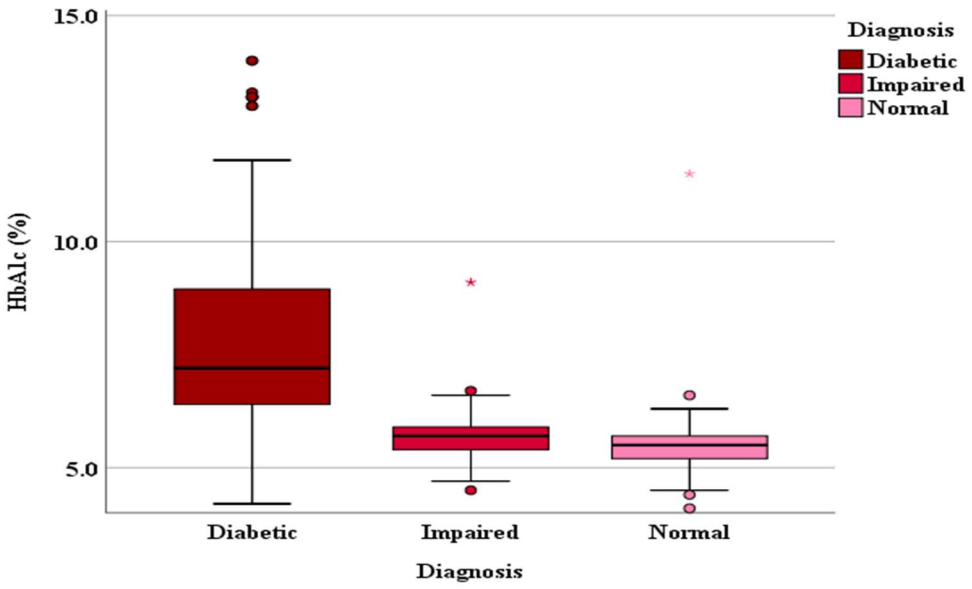

Figure 1. Graphical Presentation of the HbA1c for the Participants with Diabetes, Impaired Fasting Glucose and Non-diabetic Participants

The correlation analysis for the total participants showed that the fasting plasma glucose was positively correlated with the eAG having a correlation coefficient of 0.671 and a p-value < 0.001. When the correlation analysis was stratified across the 3 different groups, the diabetic group showed the strongest correlation between fasting plasma glucose and the eAG having a correlation coefficient of 0.630 and a *p*-value < 0.001. The impaired group and the non-diabetic group also showed a positive correlation between the fasting plasma glucose and the eAG, but the relationship was less compared to the diabetic group, even though both were also statistically significant (Figures 2-5).

Regression analysis showed that age (p=0.014), fasting plasma glucose (<0.01) and the diagnosis category (p=0.01) were independent predictors of HbA1c, while the sex was not (Table 3).

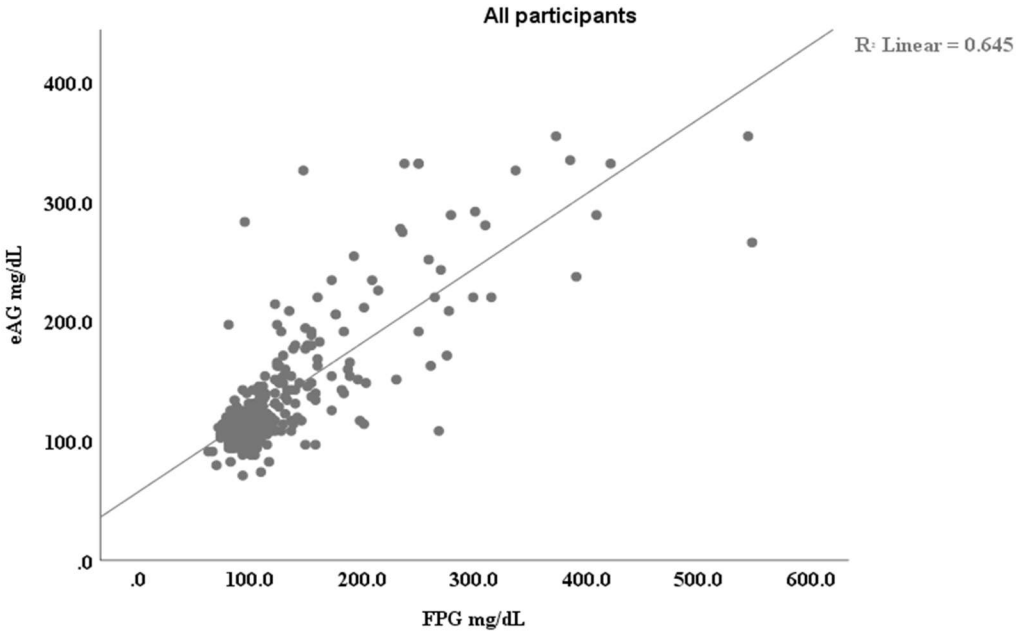

Figure 2. Scatter Plot Showing the Correlation between Estimated Average Glucose and the Fasting Plasma Glucose for all the Participants.

NB: Coefficient of correlation = 0.671, p-value <0.001, eAG: Estimated average glucose

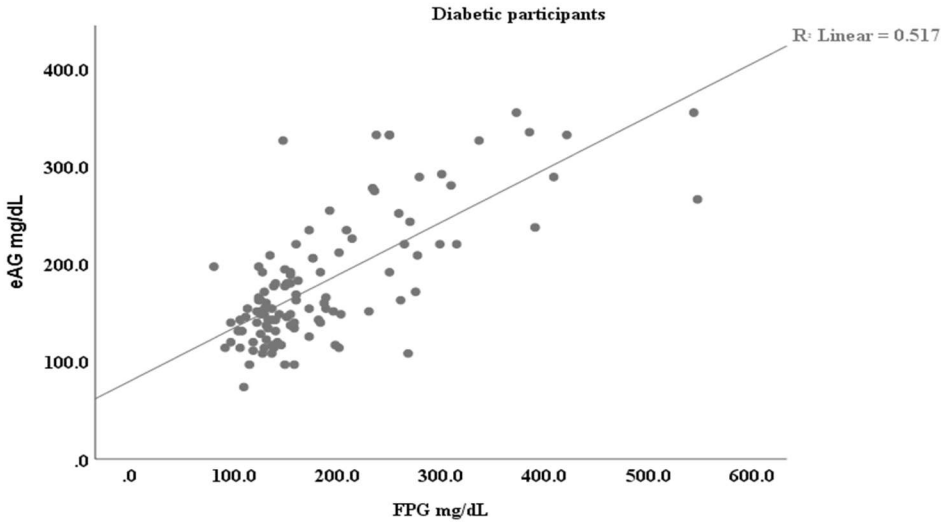

Figure 3. Scatter plot showing the correlation between estimated average glucose and the FPG for diabetic participants.

NB: Coefficient of correlation = 0.630, p-value < 0.001, eAG: Estimated average glucose .

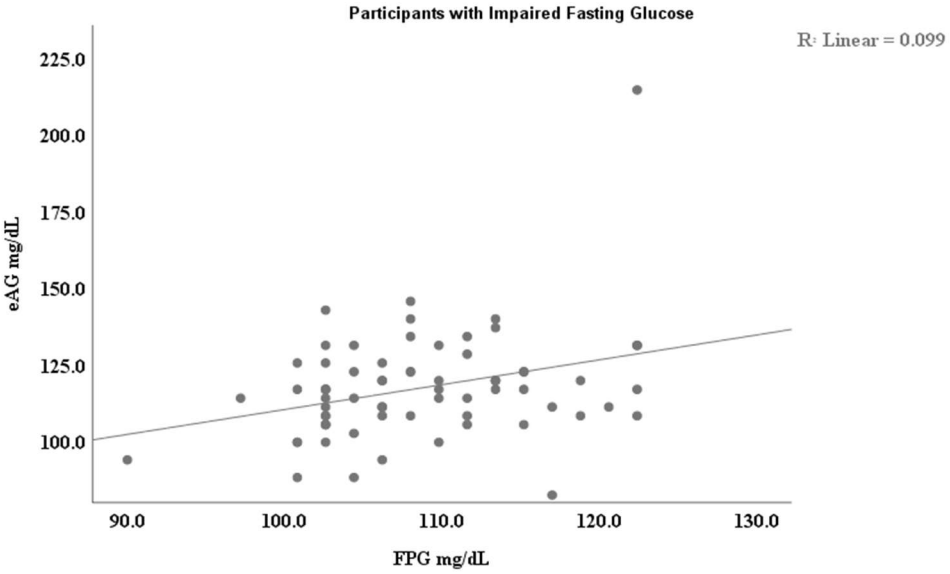

Figure 4. Scatter Plot Showing the Correlation Between Estimated Average Glucose and the HbA1c for Participants with Impaired Fasting Glucose.

NB: Coefficient of correlation = 0.273 p-value =0.023, eAG: Estimated average glucose

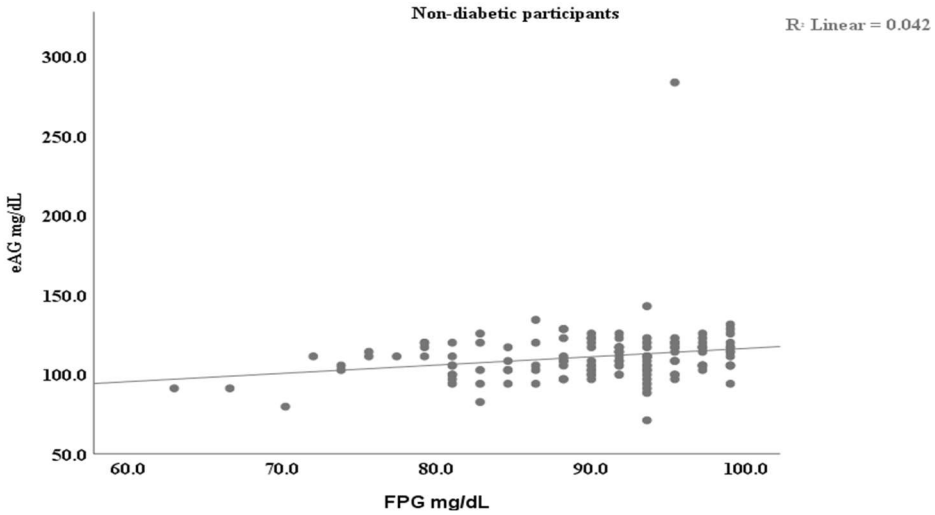

Figure 5. Scatter Plot showing the Correlation Between Estimated Average Glucose and the Fasting Plasma Glucose for the Non-Diabetic Participants.

NB: Coefficient of correlation = 0.218, p-value=0.011, eAG: Estimated average glucose

Table 3. Regression analysis Showing the Relationship between Selected Variables and the Value of HbA1c.

Variables	C.I (95%)	*p*-value
Age	5.463 (4.690-6.236)	0.014
Sex	6.785 (6.123-7.448)	0.234
FPG	3.610 (3.350-3.871)	<0.001
Diagnosis	8.898 (8.467-9.329)	<0.001

FPG: Fasting plasma glucose, C.I:

DISCUSSION

The management of diabetes mellitus is lifelong and a crucial part of the exercise that determines the treatment outcome and the quality of life of affected patients is the depth of monitoring the patient receives. In this study, the correlation of fasting plasma glucose, a cheaper and more readily available test, with the HbA1c, the test that evaluates the quality of long-term glycaemic control, was explored. It was shown that the fasting plasma glucose of the patients in the diabetic group had a strong positive correlation with their HbA1c. It also showed that patients in the non-diabetic group and those in the impaired fasting plasma glucose group also had a positive correlation, but the association was weak. Furthermore, increasing age, fasting plasma glucose level and the presence of diabetes mellitus were independent predictors of high HbA1c values, while there was no difference in the HbA1c levels across the genders.

Similar to a study by Karnchanasorn *et al.,* (2016), our current study demonstrated a positive correlation between HbA1c and FPG amongst diabetics, although the study was done in the diagnosis of diabetes as against monitoring of glucose control in our study (Karnchanasorn *et al*., 2016). The advantage of HbA1c remains its ability to monitor long-term glycaemic control however it is expensive and not readily available in most developing countries (Balogun *et al*., 2020). The use of SMBG amongst type 2 diabetics remains a challenge in developing countries and studies done in some parts of Nigeria left the use of SMBG between 20- 40%, higher use was seen amongst those with tertiary education (Iwuala *et al*., 2015 Nkpozi *et al*., 2019).

We demonstrated that HbA1c values increase with age, a similar finding with other studies (Masuch *et al*., 2019; Jang *et al*., 2019; Ibeh *et al*., 2021; Kone *et al*., 2023) while some studies also associated elevations in HbA1c with gender and race (Miller *et al*., 2020; Williams *et al*., 2020; Mustafa *et al*., 2023), there was no significant association of HbA1c with gender in our study population. Higher HbA1c in the diabetics in this study suggests the long-term duration of hyperglycaemia which is a basis of the disease diagnosis as seen in other studies, or this may support the findings of higher HbA1c in persons of African descent (Khosla *et al*.,

2021; ElSayed *et al*. 2022), a high fasting plasma glucose was also associated with high HbA1c values as seen in some studies (Hodel *et al*., 2020).

Fasting plasma glucose may be the first index of good glycaemic control following the initiation of glucose-lowering therapy (Adeniyi *et al*., 2013). Most studies in Nigeria use RPG and FPG and very few use HbA1c in the diagnosis and monitoring of DM because as against the latter, the former tests are relatively cheaper and more available (Uloko *et al*., 2018). The findings of this study show that a single fasting plasma glucose test result has a positive correlation with eAG and can be useful in monitoring glycaemic control in a resource-poor environment with limited availability of equipment for HbA1c. This is especially useful in the diabetic population where it is essential to know the adequacy of glycaemic control in other to adjust or continue treatment with the glucose-lowering regimen.

CONCLUSION

The increased prevalence of diabetes in resource-poor settings calls for an environment-driven management alternative. While continued research is essential to generate further evidence, there is a positive correlation between FPG with HbA1c among individuals with diabetes and this may be used as an alternative to predict long-term glycaemic control when HBA1c is not available. There is a critical need for the government, policy makers, and other stakeholders to design and implement context and content-specific, culturally acceptable options for testing for glycaemic control in individuals with diabetes mellitus.

AUTHORS' CONTRIBUTIONS

Author OTB, SIRO, OEO, NEO, FCI, AF, OAO conceptualize the research. OTB, NEO, FCI participated in data acquisition. Data analysis was done by OTB, OAO. Article writing was done by OTB, OAO, SIRO. Manuscript review was done by OTB, SIRO, OEO, NEO, FCI, AF, OAO. The manuscript was finally approved by OTB, SIRO, OEO, NEO, FCI, AF, OAO

INSTITUTIONAL REVIEW BOARD

The researchers obtained ethics approval from the Babcock University Health Research and Ethics Committee to use secondary data from the Chemical Pathology laboratory test record with an ethical clearance number (BUHREC No 809/23). The data was anonymised to ensure confidentiality by de-identifying the data.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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