AssessmentofBiomarkersof GlycationinTypeI,TypeIIand Gestational Diabetes Mellitus

ABSTRACT

Diabetes Mellitus, a leading global health challenge, necessitates reliable diagnostic and management biomarkers. This study assessed the efficacy of glycation markers in monitoring glycemic status across Type I, Type II, and gestational diabetes in Port Harcourt, Nigeria. A cross-sectionalanalysis of120participants (40 per diabetes type) evaluatedfastingbloodglucose(FBG), glycated hemoglobin (HbA1c), glycated albumin (GA), fructosamine (FA), and 1,5-anhydroglucitol (1,5-AG),alongwithantioxidantmarkers(glutathioneandalpha-tocopherol).Findingsindicatedthat HbA1c remains the most reliable indicator of glycemic status, with a strong correlation to FBG (r^2 = 0.99).GAandFAdemonstratedutilityasshort-termmarkersbutwerelessrobustthanHbA1c.

Notably, FBG and 1,5-AG showed inverse correlations, suggesting their potential for assessing short-term glycemic fluctuations. Insulin levels were the only statistically significant differential marker among diabetes types. These results support incorporating multiple biomarkers into diagnostic frameworks, particularly where HbA1c reliability may be limited (e.g., anemia or renal dysfunction).

Keywords:Diabetesindicators;glycationmarkers;HbA1c;fastingbloodglucose.

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by impaired glucose metabolism and elevated blood glucose levels. The condition can result from various etiological factors, including reduced insulin secretion, insulin resistance, and excessive glucose production. Diabetes is a multifactorial disease, withcausesrangingfromautoimmuneresponses andgeneticpredispositionstoenvironmentaland lifestyle factors such as diet, obesity, physical inactivity, smoking, and alcohol consumption. Additional contributing factors include vascular diseases, infections, and complications such as diabetic ketoacidosis, stroke, kidney disease,and nerve damage [1]. Although uncontrollable risk factors such as genetics and age cannot be changed, individuals can lower their risk by making healthier lifestyle choices, including a balanceddietandregularphysicalactivity [1].

Diabetes presents in various forms, classified according to its underlying pathogenic mechanisms. Type 1 diabetes mellitus (T1DM), typically diagnosed in children and young adults, results from autoimmune destruction of pancreaticbetacells,leadingtoinsulindeficiency [1].

Insulin therapy is crucial for managing T1DM, which often presents suddenly with severe symptoms, such as ketosis. In contrast, Type 2 diabetes mellitus (T2DM), typically developing in adulthood, is characterized by insulin resistance and reduced insulin secretion, with factors like obesity, aging, and lifestyle choices often contributing to its progression [2]. Type 3 diabetes,alsoreferredtoasgestationaldiabetes, occursduringpregnancyandisassociatedwitha higher risk of developing Type 2 diabetes later in life [3]. Diabetes can lead to serious health complications, such as cardiovascular disease, kidney damage, and vision impairment.

Diabetes is diagnosed and monitored using variousglycemicbiomarkers,withglycated hemoglobin (HbA1c) traditionally serving as the gold standard. However, alternative biomarkers such as fructosamine, glycated albumin (GA), and1,5-anhydroglucitolhavegained attentionfor their potential to provide more timely and accurate insights into glycemic control, particularly in situations where HbA1c may be unreliable [4]. These markers are especially valuable in cases of anemia, renal dysfunction,or gestational diabetes, where HbA1c may not accurately capture short-term fluctuations in blood glucose levels.

The increasing global prevalence of diabetes is concerning. According to the International DiabetesFederation(IDF), more than 537million adults worldwide are living with diabetes, a number expected to rise to 643 million by 2030 and 783 million by 2045. In Sub-Saharan Africa, Nigeria has the highest number of diabetes cases, with an estimated 11.2 million affected adults [5-7]. This underscores the urgent needfor improved diagnostic tools and management strategies to tackle the expanding diabetes epidemic, especially in resource-limited regions.

The incidence of diabetes mellitus is increasing, and late-stage presentations with poor prognosis are common. In Nigeria, despite the establishment of diagnostic centers, many patients continue to present with advanced symptoms, such as excessive hunger, fatigue, blurred vision, and slow-healing wounds, often resulting from uncontrolled blood sugar levels. This highlights the need for enhanced diagnostic techniques and regular monitoring to prevent complications and improve patient outcomes. This study aims to investigate more effective methods for diagnosing and monitoring diabetes mellitus in patients at the University of Port Harcourt Teaching Hospital in Rivers State, Nigeria.

Given the rising prevalence and poor prognosis ofdiabetes-relatedcomplications,thisstudyaims to identify improved diagnostic and monitoring strategies for diabetes mellitus in Nigeria. The findingsmaycontributetothedevelopmentof

more reliable biomarkers for early detection and better management, ultimately enhancing treatment outcomes and reducing complications. Thisresearchwillbenefitresearchers,healthcare providers, and educators, and serve as a valuable reference for future studies on diabetes management in the region. Additionally, it will address theneed for more comprehensive policy development and programs to combat diabetesin Nigeria and Sub-Saharan Africa as a whole[8].

This study primarily aims to evaluate glycation biomarkers in Type I, Type II, and Gestational Diabetes Mellitus, with the goal of identifying the most reliable marker for diagnosing, monitoring, and managing the disease. It seeks to examine the relationship between various glycation markers and blood glucose levels, determining which marker provides the most accurate index for diabetes diagnosis and monitoring. Additionally, the study will assess whether long-term glycation markers, such as HbA1c, offer more precise insights compared to short-term markers like fructosamine and glycated albumin in the diagnosis and management of Diabetes Mellitus. To achieve this, the study will analyze several biomarkers, including insulin, fasting blood glucose, albumin, total protein, glycated hemoglobin (HbA1c), fructosamine, glycated albumin, 1,5-anhydroglucitol, alpha-tocopherol (Vitamin E), and glutathione, evaluating their effectiveness in diagnosing, monitoring, and treating diabetes mellitus.

.

2. MATERIALSANDMETHODS

This study was conducted in Port Harcourt, specifically within the Obio-Akpor Local GovernmentArea[9].andinvolved120 subjects diagnosed with Type I, Type II, andTypeIIIdiabeteswhowereattending healthcare facilities in the region. The Type I groupconsistedof40participants,the TypeIIgroupalsoincluded40participants, andtheTypeIIIgroupcomprised40 participants.

The inclusion criteria for the study required that participants be registered with the hospital, diagnosed with diabetes, attending a diabetes clinicfortreatment,andagedbetween 18 and 60 years. Conversely, the exclusion criteriaincludedsuspecteddiabetespatients who were not registered with the healthcare facility, as well as unconfirmed diabetes patients.

Subjectswhomettheseeligibility criteria and provided written consent were recruitedforthestudy.Asimple randomization technique was used to select participants. Each subject drew a number from a container, which contained the numbers "0" and "1." Those who picked "1" were included in the study,whilethosewhopicked"0"wereexcluded.

For sample collection, 5 ml of blood was drawn from each participant. After withdrawing the needle from the vein, the puncture site was pressed with dry cotton wool to stop any bleeding. Of the collected blood, 3 ml was transferred into a heparin bottle for the preparation and analysis of various biomarkers, excluding glycated hemoglobin. The remaining 2 ml was placed into an EDTA tube for glycated hemoglobin determination. Blood samples collected in heparin bottles were processed by centrifugingat4000rpmfor5minutes.After spinning, the plasma was separatedfrom thebloodcellsandstoredat-20°Cuntil analysis.

The biomarkers analyzed in the study included insulin, fructosamine (FA), 1.5 anhydroglucitol (1,5AG),andglycatedalbumin(GA),whichwere measured using the ELISA technique. Fasting blood glucose (FBG) was measured using the glucose oxidase method, albumin was analyzed using the bromocresol green(BCG) method, and total protein (TP) was assessed using the biuret method. Glycated hemoglobin (HbA1c) was measured using the i-Croma sandwich immunoassay, while alpha-tocopherol (VitaminE) and glutathione (GSH) were measured using the colorimetric method.

For statistical analysis, a one-way ANOVA was performed to determine if there were significant differences in the biomarker concentrations acrossthethreediabetesgroups(TypeI,TypeII, and Gestational). Additionally, Pearson's correlation analysisandregressionwereusedtoexplorethe relationships between the biomarkers and to assesscause-and-effectpatterns.Thestatisticalsignificancelevelwassetatp
< 0.05.

3. RESULTSANDDISCUSSION

Table 1 shows the demographic parameters of diabetic subjects in their various groups. The mean±SD age of Type 1 diabetic subjects was 20±7years, the mean±SD age of Type 2 diabetic subjects was 42±10years and the mean±SD age of Type 3 was 33±8years.

Table1.DemographicParameters

	Type1subjects	Type2subjects	Gestational
Age(yrs)	20±7	42±10	33±8
Males	22	21	0
Females	18	19	40

Table2.ComparingGlycationBiomarkersinType1,Type2andGestationalDiabetesGroups

	Type1	Type2	Gestational	F-value	P-value	Remark
FBG	5.9±4.9	7.2±4.8	8.2±5.5	2.14	0.12	NS
INS	21.5±1.1	75.9±16.5	144.5±20.8	16.1	<0.05	SS
ALB	3.5±0.5	3.4±0.6	3.3±0.7	1.92	0.15	NS
TP	5.9±1.2	5.9±1.2	5.6±1.3	0.91	0.41	NS
FA	236.8±5.4	234.1±4.7	247.5±5.3	1.86	0.16	NS
GA	15.7±4.2	14.8±3.7	14.1±5.4	1.27	0.29	NS
A1C	6.05±4.5	7.2±4.9	8.6±6.0	2.35	0.10	NS
1,5AG	16.0±7.5	16.1±10.9	14.7±7.8	0.31	0.74	NS
GSH	4.9±0.5	4.2±0.4	5.3±0.5	1.22	0.29	NS
Toco	16.0±0.9	15.4±0.9	17.0±1.1	1.46	0.24	NS

Key:Diabetessubjects;TypeI:N=40;Type2:N=40;Gestational:N=40

Table3.ComparingtherelationshipbetweenFBGandFAinType1,Type2andGestational Diabetes Group

	Type1		Type2		*Gestational*	
	FBG	**FA**	**FBG**	**FA**	**FBG**	**FA**
Mean±SD	5.9±0.8	236.8±5.5	7.2±0.8	234.1±4.8	8.2±0.9	247.5±5.3
r^2	0.54		0.52		0.45	
F-value	15.68		13.87		9.54	
P-value	<0.05		<0.05		<0.05	
Remark	SS		SS		SS	

Keys:TypeI:N=40;TypeII:N=40;Gestational:N=40; FBG=Fastingbloodglucose;FA= Fructosamine

Table4.ComparingtherelationshipbetweenFBGandGAinType1,Type2andGestational Diabetes Group

	Type1		Type2		Gestational	
	FBG	**GA**	**FBG**	**GA**	**FBG**	**GA**
Mean±SD	5.9±0.8	15.7±5.4	7.2±0.8	14.8±5.5	8.2±0.9	14.8±5.4
r^2	0.64		0.61		0.59	
F-value	25.96		22.96		20.20	
P-value	<0.05		<0.05		<0.05	
Remark	SS		SS		SS	

Keys:TypeI:N=40;TypeII:N=40;Gestational:N=40;FBG=Fastingbloodglucose;GA=Glycated Albumin

Table5.ComparingtherelationshipbetweenFBGandA1cinType1,Type2andGestational Diabetes Group

	Type1		Type2		Gestational	
	FBG	**A1c**	**FBG**	**A1c**	**FBG**	**A1c**
Mean±SD	5.9±0.8	6.05±4.5	7.2±0.8	7.2±4.9	8.2±0.9	8.6±6.0
r^2	0.56		0.99		0.99	
F-value	17.50		2572.09		1139.45	
P-value	<0.05		<0.05		<0.05	
Remark	SS		SS		SS	

Keys:TypeI:N=40;TypeII:N=40;Gestational:N=40;FBG=Fastingbloodglucose;A1c=Glycated haemoglobin

Table6.ComparingtherelationshipbetweenFBGandGlutathioneinType1, Type2andGestational Diabetes Group

	Type1		Type2		Type3	
	FBG	**GSH**	**FBG**	**GSH**	**FBG**	**GSH**
Mean±SD	5.9±0.8	4.9±0.5	7.2±0.8	4.2±0.4	8.2±0.9	5.3±0.5
r^2	-0.68		-0.76		0.39	
F-value	11.0		9.2		2.5	
P-value	<0.05		<0.05		>0.05	
Remark	SS		SS		NS	

Keys:TypeI:N=40;TypeII:N=40;TypeIII:N=40;FBG=FastingBloodGlucose;GSH= Glutathione

Table7.ComparingtherelationshipbetweenFBGandTocophenolinType1,Type2and Gestational Diabetes Group

	Type1		Type2		Type3	
	FBG	**Toco**	**FBG**	**Toco**	**FBG**	**Toco**
Mean±SD	**5.9±0.8**	**16.0±0.9**	**7.2±0.8**	**15.4±0.9**	**8.2±0.9**	**17.0±1.1**
^{2}	-0.32		-0.38		0.35	
F-value	6.2		8.4		9.5	
P-value	<0.05		<0.05		<0.05	
Remark	SS		SS		SS	

Keys:TypeI:N=40;TypeII:N=40;TypeIII:N=40;FBG=FastingBloodGlucose;TOC=Tocophenol

Out of a total of 120 subjects recruited for the study, 43 were males and 77 were females. The Type 1 group comprised 22 males and 18 females, giving a total of 40 participants that made up the group. Type 2 group comprised 21 males and 19 females, giving a total of 40 participants that made up the group. Type 3 group comprised only females which were 40 participants. The values for other analytes, including Fasting Blood Glucose, Insulin, Albumin, Total Protein, Fructosamine, Glycated Albumin, Glycated Hemoglobin, 1,5-Anhydroglucitol, Glutathione, and Alpha-Tocopherol, are presented in Table 2.

The result presented in Table 2 shows that the mean level of fasting glucose was statistically insignificant in all groups of the diabetic populationstudied.Thisimpliesthatfastingblood glucose does not serve as a differential diagnostic marker for diabetes because it does not discriminate or differentiate among type 1, type 2 and gestational diabetes. This finding was consistent with other parameters evaluated inthis study except for insulin. Therefore, insulin canserveasadifferential markerforthetypes of DM

4. DISCUSSION

Diabetes is a group of disease that is characterizedwithtoomuch glucosein theblood and the laboratory diagnosis for diabetesrequires the determination of routine investigations such as fasting blood glucose, random blood glucose, postprandial glucose estimation, oral glucose tolerance, urinalysis and glycatedhaemoglobin.Insulinmeasurementmay be required to determine the type of diabetes asit is often deficient in type 1 diabetes, hence the name Insulin Dependent Diabetes. Glycated haemoglobin is the commonly used glycation marker to measure how the body managed glucose for a period of 3months based on that erythrocytes have a life span of 3months and glucose generally binds with proteins in the body in a term referred to as glycation; when the concentration of glucose is high in the blood it leads to corresponding increase in protein glycation. Generally, glycated haemoglobin has been the glycation marker of choice but thisstudy seeks to identify other glycation markers like fructosamine and glycated albumin to determine their suitability in diabetes diagnosis relative to glycated haemoglobin and their relationship with blood glucose level.

The demographic parameters, samples were collected from carefully selected group of 120 patients with type I, II and III diabetes mellitus, the subjects were 43 male and 77 female within different ages, blood samples were carefully collected from 40 patients with type I diabetes mellituswithintheageof20±7,40sampleswere

also collected from patients with type II diabetes mellitus within the age of 42±10 and another 40 samples were carefully collected from pregnant women within the age of 33±8 years of age to test for type III diabetes mellitus.

The result presented in Table 2 shows that the mean level of fasting glucose was statistically insignificant in all groups of the diabetic populationstudied.Thisimpliesthatfastingblood glucose does not serve as a differential diagnostic marker for diabetes because it does not discriminate or differentiate among type 1, type 2 and gestational diabetes. This finding was consistent with other parameters evaluated inthisstudy exceptforinsulin.Reportshaveshown that diabetes is classified based on insulin activity; Insulin-dependent diabetes and Non-insulin dependent diabetes. This classification is based on insulin dependency which implies that insulinwasthedifferentiatingmarkerbetweenthoset ypesofdiabetes;therefore,there shouldbeasignificantdifferencein insulin level among the groups. The findings on insulin were consistent with current knowledge because insulin showed significant difference in mean level among the groups studied. Comparing the three groups, insulin had the lowest level in type 1 diabetes than in other groups.

Certain other non-glycemic markers like protein and albumin showed no significant difference in theirmeanlevelsamongthegroups.Thisimplies that the various types of diabetes does notimpact of the distribution on concentration of protein in the blood.The same finding was consistent with albumin. Albumin level had not any significant difference among the three types of diabetes. On a differential basis, glutathione levels were consistent in three diabetic groups, meaning that there was no significant difference in the mean levels among the groups. This finding was also consistent with tocophenol. There was no significant difference among the mean levels of tocophenol in the three diabetic groups studied.

For a glycation marker to be considered more effective, it should be associated with blood glucose levels. Therefore, Table 3 presents the correlation and regression analysis between fasting blood glucose (FBG) levels and fructosamine (FA). The results show a moderate positive correlation in Type I and Type II diabetes, while a weak positive correlation was observed in Type III diabetes.

According to a study by [10] The findings of this study revealed a significant association between Fasting Blood Glucose (FBG) and fructosamine, with notable correlations observed between serum fructosamine levels FBG and other lipid profilesinastudy[11].Bloodglucoselevelshave been previously reported. While both fructosamineandHbA1careliableindicatorsof glycemic control, fructosamine is considered the better predictor of blood glucose levels [11]. In a study of 25 patients with Type I, II, and III diabetes, serum fructosamine was found to be a better indicator of average blood glucose concentrations over the previous 3-6 weeks, while HbA1c was more useful for reflecting glucose levels over the past 8-10 weeks [12].The effectiveness of Fasting Blood Glucose (FBG) for the routine detection of Type I, II, and gestational diabetes has been documented [12] Diabetes can be diagnosed using plasma glucose criteria, such as the fasting plasma glucose (FPG) value, the2-hour plasmaglucose (2-h PG) value during a 75-g oral glucose tolerance test (OGTT), or A1C criteria. Several other studies haveindicated that FBG alone is not an efficient or reliable screening method for types I, II, and III [13]. Likewise, relying solely on fructosamine for screening types I, II, and III may not be justified. In this study, the serum fructosamine assay showed a 3.125% false positive rate and a 9.375% false negative rate when compared to FBG values for assessing hyperglycemia. Astudy suggests that while fructosamine (FA) can be a useful indicator of glycemic control, it has several limitations in conditions associated with altered protein levels. This case highlights the unreliabilityofFAasamarkerofglycemiccontrol in patients with nephrotic syndrome, regardlessoftheir serum albumin or total protein levels [14]. A study that was conducted in the Southeast Asian population shows that Fructosamineshows a consistent correlation with HbA1c for monitoring glycaemic control [15]. Therefore, the combined assessment of fructosamine and FBG offers a more reliable approach for identifying type III compared to measuring either parameter alone. As fructosamine reflects the average glucose levels over the past 2-3 weeks, it is not influenced by food intake on the day of testing. Furthermore, no significant difference was observed between the measured serum fructosaminelevels [16].Therefore,fructosamine can be measured at any time of the day, and the same blood sample can be used to analyze both FBGandfructosamine.Asaresult,pairedvalues of FBG and fructosamine could be employed for diagnosingtypeIII,potentiallyeliminatingthe

need for unnecessary OGTT in many cases, as previously suggested [17].

The results, as shown in Table 4, present a correlation and regression analysis between glucose levels and GA (FBG and GA). The analysisindicatesapositiveassociationbetween theseparameters inType I, TypeII, andgestational.
Astudyontherelationshipbetweenfastingblood glucose and glycemic indices found that GA levels correlate more strongly with plasma glucose levels and the glucose fluctuation index than HbA1c or 1,5-AG, particularly in individuals with poor glucose control [18]. In this study, the relationship between FBG and GA was more positive compared to FA, with correlation coefficients of 0.64, 0.61, and 0.59 for Type I, Type II, and Type III, respectively. Albumin,being the most abundant serum protein, is likely the primary glycated component in fructosamine. As such, any changes in albumin levels affect both GA and FA. There are varying reports onthe suitability of glycated albumin (GA) or fructosamine (FA) as independent indicators for the assessment and management of diabetes. The present review highlights that, in certain clinical conditions, GA offers significant advantages for monitoring glycemic status compared to other currently availablebiomarkers. However, in pathological conditions characterized by altered albumin metabolism (such as nephrotic syndrome and hyperthyroidism, where albumin metabolism is increased), the value of GA may underestimate actual glycemic levels. Specifically, in patients with kidney disease, GA is considered reliable if the albumin concentration in the urine does not exceed 3.5 g/24 h. Additionally, chronic inflammation, as seen in smokers, patients with non-alcoholic liver disease, hypertriglyceridemia, and hyperuricemia,canalsoinfluence GA levels. Conversely, in conditions where albumin metabolism is reduced (such as cirrhosis and hypothyroidism), GA levels may be higher than the actual mean glycemia, thus limiting its use in glycemic monitoring due to the reducedsynthesis of albumin. Notably, in patients with cirrhosis,theGA/HbA1cratiocorrelateswithliver function, offering an indirect assessment of liver health.WhileliteraturesupportstheuseofGAas a reliable biomarker for glycemic status, consensus on the appropriate decisionthresholdsfordifferentclinicalconditionsre mains lacking.

The results shown in Table 5 present a correlationandregressionanalysisbetween glucose levels and HbA1c (FBG and HbA1c). A strongpositiveassociationwasobservedinType I, Type II, and Type III. According to a study the association between HbA1c and FBS was relatively strong, especially in individuals with diabetes [19] In another study, fasting blood glucose (FBG) shows a positive correlation with HbA1c in non-diabetic patients, while itnegatively correlates with random blood sugar due to LDL levels. In diabetic patients, however, FBG remains highly correlated with HbA1c [19]. Currently, HbA1c is widely accepted as the preferred indicator for assessing glycemiccontrol, rather than glycated albumin (GA) or fructosamine (FA). This is largely due to the extensive body of research supporting HbA1c, which has demonstrated greater stability and standardization for clinical use. In contrast, FA and GA are more commonly utilizedin veterinary medicine than in human clinical practice.

This study considered both short-term and long-term glycation markers. Theoretically, short-term markers (FA and GA) are expected to show a stronger association with FBG than long-term markers (A1c), but the opposite was observed. A1c exhibited a more positive correlation with FBGacrossalltypesofdiabetes,exceptinType 1. This finding suggests that A1c is the preferred glycation marker in this study, relative to theother markers.In Type 1, the correlationstrength was seen as follows: GA>A1c>FA. In Type II, the correlation strength was seen as follows: A1c>GA>FA while in Type III, A1c>GA>FA. A 2015 study evaluated blood glucose, A1c, and FA in both fasting conditions and 2 hours postprandial (PP) after a standard meal. The results showed a stronger correlation between 2-hour PP glucose levels and A1c compared to FA. [20-22] This finding isconsistent with the results of this study, suggesting that the glycation process may vary acrossdifferentproteins. Someproteinsglycated more rapidly and respond to changes in blood glucose levels faster than others. Therefore, attention should be directed more toward the glycation process itself rather than the half-life of the protein. Based on this, A1c remains a relatively reliable marker for the diagnosis and management of diabetes.

Due to the competitive inhibition of 1,5-AG reabsorption in the kidney tubule by glucose, blood 1,5-AG levels may respond with high sensitivity within 24 hours [23], indicating even transient elevations in glucose levels over the courseofafewdays[24],Byimplication,an

increase in glucose levels should result in a decrease in blood 1,5-AG levels. This observation aligns with the findings of this study. In all the groups studied there were negative relationships between FBG and 1, 5-AG so that increase in one leads to the decrease of theother and vice versa. This pattern, if well understood, can be used as complementary marker for glycemic monitoring.

This study also evaluated some antioxidantssuchasglutathioneandtocophenolwith theview of determining the level of relationship they have with fasting blood glucose. Table 6 revealed a significantnegativecorrelationbetweenFBGand glutathione as seen in Type I and Type II diabetesbutaweakpositivecorrelationinType III. According to a study when the correlation between glutathion levels and fasting blood glucose, HbA1c, fructosamine, urea, uric acid, creatinine, was analyzed using Pearson's correlation test. A strong negative correlationwas found with fasting blood glucose. Additionally,moderatenegativecorrelationswere observed between GSH levels, HbA1c, fructosamine and urea, [25]. A recent study in 2024 demonstrated a negative correlation between serum alpha-tocopherol (Vitamin E) levels and several other indicators. The results revealed that Vitamin E was negativelycorrelated with direct bilirubin, fasting blood glucose,fastinginsulin,andfastingC-peptide(r =−0.246,−0.282,−0.504,−0.513;P-values= 0.008, 0.002, <0.001, <0.001, respectively). In contrast, Vitamin Ewas positively correlated with total cholesterol, triglycerides, and low-density lipoprotein(r=0.452,0.333,0.368,respectively; P-values=<0.001,<0.001,<0.001).No significant correlation was found with other indicators [26]. This means that an increase in bloodsugar will leadto a decrease in glutathione and vice versa. Table 7 revealed a significant negative correlation between FBG and tocophenol in Type I and Type II diabetes but a weak positive correation in Type III. This means that an increase in blood sugar will lead to a decrease in tocophenol and vice versa. This findingisintunewithcurrentknowledgebecause diabetes is believed to increase oxidative stress which in turn deplicts antioxidant levels.

5. CONCLUSION

The growing interest in nontraditional glycemic biomarkers stems from the limitations of the HbA1c assay. It is crucial to recognize the conditionsunderwhichHbA1clevelsmaybe difficult to interpret. The use of alternative markers can be valuable in diabetes management as complementary tools alongside standard measures. There is generally a strong correlation between HbA1c and serum fructosamine as well as glycated albumin. While fructosamine and glycated albumin have been proposed as useful tools for monitoring glycemic control, they should not be considered independent markers for diabetes management but rather as additional assessment tools. Currently, there are no definitive guidelines for incorporating alternative biomarkers as adjuncts to standard glycemic markers, such as HbA1c and fasting blood glucose. Therefore, including serum 1,5-anhydroglucitol may be useful for assessing day-to-day glycemic excursions. In conclusion, GA, FA, and 1,5-AG play asignificant clinical role in supporting the management of diabetes.

DISCLAIMER(ARTIFICIALINTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

As per international standards or university standards,Participants'writtenconsenthasbeen collected and preserved by the author(s).

COMPETINGINTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. AmericanDiabetesAssociation.Standards of medical care in diabetes. DiabetesCare. 2007;(Suppl 1):S4–S41. DOI:10.2337/dc07-S004.PMID17192377
2. Yau M, Sperling MA. Treatment ofdiabetes mellitus in children and adolescents.UpToDate;2021,June28. Available:https://www.uptodate.com/
3. Kandimalla R, Thirumala V, Reddy PH. Is Alzheimer's disease a Type 3 diabetes? A criticalappraisal. Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease. 2017;1863(5):1078-1089. Available:https://doi.org/10.1016/j.bbadis.2016.08.018

4. ParrinelloCM,SelvinE.BeyondHbA1c andglucose:Theroleofnontraditional glycemicmarkersindiabetesdiagnosis, prognosis, and management. Current Diabetes Reports. 2014;14(11):548. Available:https://doi.org/10.1007/s11892-014-0548-3
5. International Diabetes Federation. Diabetes around the world in 2021; 2021. Available:https://diabetesatlas.org/https://idf.org/our-network/regions-and-
6. International Diabetes Federation. Diabetes in Nigeria members/africa/members/nigeria/;2021.
7. Gezawa ID, Puepet FH, Mubi BM, Uloko AE, HaliruI.Prevalenceof overweight and obesity in Maiduguri, North-Eastern Nigeria. Nigerian Journal of Medicine. 2013;22(3):171–174. Available:https://pubmed.ncbi.nlm.nih.gov
8. DahiruT, Aliyu AA, Shehu AU. Areview of population-based studies on diabetes mellitus in Nigeria. Sub-Saharan Afr JMed. 2016;3:59-64.
9. Census; 2006. Available:https://propertypro.ng/guide/axes/obio-akpor-rivers/
10. HanHA,SobkiSH,AlhomidaAS,Khan SA.Pairedvaluesofserumfructosamine andbloodglucoseforthescreeningof gestational diabetes mellitus: A retrospective study of 165 Saudi pregnant women. Indian Journal of Clinical Biochemistry. 2007;22(1):65-70. Available:https://doi.org/10.1007/BF02912884
11. Peng Y-F, Wei Y-S. The relationships between serum fructosamine concentrations and lipid profiles in community-dwelling adults. Plos One. 2017;12(7):e0181099. Available:https://doi.org/10.1371/journal.pone.0181099PMCID: PMC5537271
12. Chen H-S, Chen R-L, Chang Z-Y, Li H-D. A comparison of fructosamine and HbA1c for home self-monitoring blood glucose levelsintype2diabetes.ZhonghuaYiXue Za Zhi (Taipei). 2002;65(4):151-155.PMID: 12135193
13. American Diabetes Association Professional Practice Committee. Classificationanddiagnosisofdiabetes: Standards of medical care in diabetes—2022.DiabetesCare.2022;45 (Supplement_1):S17–S38. Available:https://doi.org/10.2337/dc22-S002PubMed ID: 34964875
14. Mula-Abed WS, Al-Naemi AH. Performance indicators and validity of serum fructosamine assay as a diagnostic test in a screening program for diabetes mellitus. Saudi Medical Journal. 2003;24 (5):477-484. Available:https://pubmed.ncbi.nlm.nih.gov/12847621
15. Chandran K, Lee SM, Shen L, Tng EL. Fructosamine and HbA1c: A Correlational Study in a Southeast Asian Population. J ASEAN Fed Endocr Soc. 2024;39(1):26-30. Available:https://doi.org/10.15605/jafes.039.01.14
16. SenapathiSHV,BhavsarR,KaurR,Kim P, Sachmechi I. A case report of fructosamine'sunreliabilityasaglycemic control assessment tool in nephrotic syndrome. Cureus. 2017;9(9):e1694. Available:https://doi.org/10.7759/cureus.1694
17. Agarwal MM, Punnose J. Screening for gestational diabetes in high-risk populations: the United Arab Emirates experience.AnnSaudiMed.2001;21(1-2): 117-9. DOI: 10.5144/0256-4947.2001.117. PMID: 17264610
18. Suwa T, Ohta A, Matsui T, Koganei R, Kato H, Kawata T, Sada Y, Ishii S, Kondo A, Murakami K, Katabami T, Tanaka Y. Relationship between clinical markers of glycemia and glucose excursion evaluated by continuous glucose monitoring (CGM). Endocrine Journal. 2010;57(2):135–140.
19. KhanHA,SobkiSH,KhanSA.Association betweenglycaemiccontrolandserumlipid profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. Clin Exp Med. 2007;7(1):24-9. DOI: 10.1007/s10238-007-0121-3. PMID: 17380302
20. KetemaEB,KibretKT.Correlationof fastingandpostprandialplasmaglucose with HbA1c in assessing glycemic control: Systematic review and meta-analysis. Archives of Public Health. 2015;73:43. Available:https://doi.org/10.1186/s13690-015-0088-6 PMCID: PMC4582842, PMID:
21. American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: Standards of Care in Diabetes—2022. Diabetes Care 2021;45(Suppl1):S17–S38.
22. GhazanfariZ,HaghdoostAA, MohammadAlizadehS,AtapourJ,

Zolala F. A comparison of HbA1c and fasting blood sugar tests in the general population. International Journal of PreventiveMedicine.2010;1(3):187–194.
Available:https://doi.org/10.4103/2008-7802.65767 PMCID: PMC3075530, PMID: 21566790

23. DunganKM,BuseJB,LargayJ,KellyMM, Button EA, Kato S, Wittlin S. 1,5-Anhydroglucitol and postprandial hyperglycemiaasmeasuredbycontinuous glucose monitoring system in moderately controlledpatientswithdiabetes.ClinCare Educ Nutr; 2006.
24. Stettler C, Stahl M, Allemann S, Diem P, Schmidlin K, Zwahlen M, Riesen W, Keller U, Christ E. Association of 1,5-Anhydroglucitol and 2-h postprandialbloodglucoseintype2diabetic patients.DiabetesCare.2008;31(8):1534–1535.
Available:https://doi.org/10.2337/dc08-0385
25. Kalkan IH, Suher M. The relationship between the level of glutathione, impairment of glucose metabolism, and complications of diabetes mellitus. Pakistan Journal of Medical Sciences. 2013;29(4):938–942.
Available:https://doi.org/10.12669/pjms.294.2859 PMCID: PMC3817774
26. Zhang J, Hou Y, Zhang Z, Shi Y, Wang Z, Song G. Correlation between serum vitamin E and HOMA-IR in patients with T2DM.Diabetes,MetabolicSyndromeand Obesity: Targets and Therapy. 2024;17: 1833–1843.
Available:https://doi.org/10.2147/DMSO.S50738