Asian Journal of Research in Biochemistry

Volume 14, Issue 6, Page 124-130, 2024; Article no.AJRB.127523
ISSN: 2582-0516

Comparative Evaluation of Glycemic and Glycation Markers in Type I, Type II, and Gestational Diabetes Mellitus in Choba, Rivers State

Chinwebudu Miller Melford [a*], George G. Simeon [a], Martin Mie-Ebi Wankasi [a], Merlyn Baraclan [b] and Marguerite Alofa P. O'Brien-Melford [b]

[a] Department of Chemical Pathology, Faculty of Medical Laboratory Science, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria.
[b] Department of Medical Technology, College of Allied Medical Sciences, Cebu Doctors' University, Mandaue City, Cebu, Philippines.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/ajrb/2024/v14i6334

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/127523

Original Research Article

Received: 25/09/2024
Accepted: 27/11/2024
Published: 03/12/2024

ABSTRACT

Diabetes Mellitus is a leading global cause of death, highlighting the need for accurate diagnostic and management markers. This study aimed to assess various diabetes indicators and glycation markers related to glycemic status. Conducted in Rivers State (Choba), the study included 90

**Corresponding author: E-mail: melfordcmiller@gmail.com;*

Cite as: *Melford, Chinwebudu Miller, George G. Simeon, Martin Mie-Ebi Wankasi, Merlyn Baraclan, and Marguerite Alofa P. O'Brien-Melford. 2024. "Comparative Evaluation of Glycemic and Glycation Markers in Type I, Type II, and Gestational Diabetes Mellitus in Choba, Rivers State". Asian Journal of Research in Biochemistry 14 (6):124-30. https://doi.org/10.9734/ajrb/2024/v14i6334.*

participants diagnosed with Gestational, Type I, and Type II diabetes, with 30 individuals in each group. Blood samples were collected after fasting to measure Insulin (INS), Fasting Blood Glucose (FBG), Glycated Hemoglobin (A1c), Glycated Albumin (GA), Fructosamine (FA), and 1,5-anhydroglucitol (1,5-AG). Results showed no significant differences in FBG levels across the groups (F-value = 2.14, P = 0.12). However, INS levels were significantly higher in all groups (F-value = 16.1, P < 0.05). Other markers, including FA, GA, A1c, and 1,5-AG, did not differ significantly between the groups. Correlation analysis revealed significant relationships between A1c, GA, and FA with FBG. Notably, the correlation between FBG and A1c was strongest in Type II ($r^2 = 0.99$) and Gestational diabetes ($r^2 = 0.99$), while it was weaker in Type I ($r^2 = 0.56$). Overall, A1c emerged as the most reliable marker of glycemic status, providing valuable insights for the diagnosis and management of diabetes. HbA1c remains the gold standard for long-term glycemic control, alternative biomarkers such as fructosamine, GA, and 1,5-AG are gaining recognition for their clinical utility in managing diabetes.

Keywords: Diabetes mellitus; glycated hemoglobin; glycemic status.

1. INTRODUCTION

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves. The most common is type 2 diabetes, usually in adults, which occurs when the body becomes resistant to insulin or doesn't make enough insulin. In the past 3 decades the prevalence of type 2 diabetes has risen dramatically in countries of all income levels. Type 1 diabetes, once known as juvenile diabetes or insulin-dependent diabetes, is a chronic condition in which the pancreas produces little or no insulin by itself [1]. Gestational Diabetes Mellitus (GDM) is a condition in which women without history of diabetes experience hyperglycemia during pregnancy, especially at the second and third trimesters. In women who have had GDM, an elevated body mass index (BMI) may have a substantial impact for persistent hyperglycemia in their lives after gestation [2]. Accurate diagnostic markers are critical for timely diagnosis and effective management, which can prevent or mitigate these complications.

In clinical practice, several biomarkers are used to assess glycemic control and the risk of diabetes-related complications. Fasting Blood Glucose (FBS) is the standard measure for acute glycemic status, while Glycated Hemoglobin (HbA1c) is widely recognized as a long-term marker of glycemic control [3]. Additionally, other markers such as Insulin (INS), Glycated Albumin (GA), and 1,5-Anhydroglucitol (1,5-AG) are increasingly being evaluated for their potential to offer insights into insulin resistance, glycemic variability, and the effectiveness of diabetes management [4] While these biomarkers have been studied extensively in Type I and Type II diabetes, there is limited data on their comparative levels in Gestational Diabetes, especially in specific regions such as Rivers State, Nigeria. This study aims to compare the levels of FBS, Insulin, HbA1c, Glycated Albumin, and 1,5-AG across patients diagnosed with Gestational Diabetes, Type I, and Type II diabetes in a hospital in Choba, Rivers State. The results may provide valuable insights into their role as diagnostic and management markers for these conditions.

2. MATERIALS AND METHODS

This study was conducted in Rivers State specifically within the Choba region of Rivers State, Nigeria. A total of 90 participants were recruited, comprising individuals diagnosed with Type 1 Diabetes Mellitus (T1DM), Type 2 Diabetes Mellitus (T2DM), and Gestational Diabetes Mellitus (GDM), with 30 participants in each group. The T1DM group consisted of insulin-dependent individuals, the T2DM group included those primarily exhibiting insulin resistance, and the GDM group consisted of pregnant women diagnosed with diabetes during pregnancy.

Participants were selected based on the following inclusion criteria: they were registered patients at local healthcare facilities, diagnosed with any type of diabetes (T1DM, T2DM, or GDM), attending a diabetes clinic for treatment, and aged between 18 and 60 years. Exclusion criteria included individuals who were not officially registered with the healthcare facility or had unconfirmed diabetes diagnoses.

A simple randomization method was used to select participants who met the eligibility criteria and provided written informed consent. Participants drew a number from a container containing “A” and “B”. Those who picked “A” were included in the study, while those who picked “B” were excluded.

Blood samples (7 mL) were collected from each participant via venipuncture. After the needle was removed, pressure was applied to the puncture site to prevent bleeding. The collected blood was processed as follows: 5 mL was placed in a heparinized tube for analysis of various biomarkers (except glycated hemoglobin), and 2 mL was transferred into an EDTA tube for the determination of glycated hemoglobin (HbA1c). The heparinized samples were centrifuged at 5000 rpm for 5 minutes to separate plasma from blood cells, and the plasma was then stored in labeled bijou bottles at -20°C until analysis.

Biomarkers were assessed using the following methods: Fasting Blood Glucose (FBG) was determined using the glucose oxidase method; Glycated Hemoglobin (HbA1c) was measured using the i-Croma sandwich immunoassay; and Insulin, Fructosamine (FA), 1,5-Anhydroglucitol (1,5-AG), and Glycated Albumin (GA) were quantified by Enzyme-Linked Immunosorbent Assay (ELISA).

Data analysis was performed using One-Way Analysis of Variance (ANOVA) to assess differences in biomarker levels among the three groups (T1DM, T2DM, and GDM). Pearson’s correlation and regression analysis were used to explore relationships between biomarkers and to examine potential cause-and-effect associations. A p-value of < 0.05 was considered statistically significant for all analyses.

3. RESULTS AND DISCUSSION

Table 1 summarizes the demographic characteristics of the diabetic participants. The mean age of Type 1 diabetics was 20 ± 7 years, Type 2 diabetics 42 ± 10 years, and Gestational Diabetes participants 33 ± 8 years. Of the 90 participants, 33 were male and 57 were female. The Type 1 group included 17 males and 13 females, the Type 2 group consisted of 16 males and 14 females, and the Gestational Diabetes group had 30 females.

The results in Table 2 indicate that the mean fasting glucose levels were statistically similar across all diabetic groups. This suggests that fasting blood glucose is not a reliable marker for differentiating between Gestational Diabetes, Type I and Type II. This finding aligns with the results of other biomarkers measured in the study, with the exception of insulin. Therefore, insulin levels could be a more reliable marker for differentiating between the various types of diabetes.

Table 1. Demographic Parameters

	Type 1 subjects	Type 2 subjects	Gestational
Age (yrs)	20±7	42±10	33±8
Males	17	16	0
Females	13	14	30

Table 2. Comparing Glycation Biomarkers in Type 1, Type 2 and Gestational Diabetes Groups

	Type 1	Type 2	Gestational	F-value	P-value	Remark
FBG	5.9±4.8	7.2±4.7	8.2±5.6	2.14	0.12	NS
A1C	6.05±4.5	7.2±4.9	8.6±6.0	2.35	0.11	NS
FA	235.8±5.4	234.1±4.7	247.5±5.3	1.86	0.16	NS
INS	21.5±1.1	75.9±16.5	144.5±20.8	16.1	<0.05	SS
GA	15.7±4.3	14.8±3.8	14.1±5.4	1.27	0.29	NS
1,5 AG	16.0±7.5	16.1±10.9	14.7±7.8	0.31	0.73	NS

Key:
Diabetes subjects:
Gestational: N = 30
Type I: N = 30
Type 2: N = 30

3.1 Discussion

Diabetes Mellitus encompasses a group of metabolic disorders characterized by chronic hyperglycemia due to either defects in insulin secretion or insulin resistance [5]. Effective management of diabetes relies heavily on diagnostic tools that assess glucose metabolism, with critical tests such as fasting blood glucose (FBG), random glucose, oral glucose tolerance tests (OGTT), and glycated hemoglobin (HbA1c) serving as foundational elements for diagnosis and monitoring [5,6]. These markers help identify individuals at risk for diabetes complications, such as cardiovascular disease, nephropathy, and retinopathy [7].

Insulin levels play a crucial role in diagnosing and classifying diabetes. Type 1 diabetes (T1D) is characterized by an absolute insulin deficiency due to autoimmune destruction of pancreatic beta cells, whereas Type 2 diabetes (T2D) is primarily associated with insulin resistance and gradual beta-cell dysfunction [8,9]. The present study found significantly lower insulin levels in T1D patients compared to T2D and Gestational Diabetes Mellitus (GDM), where insulin resistance predominates, supporting the established role of insulin in differentiating these conditions.

HbA1c remains the gold standard for evaluating long-term glycemic control, as it reflects average blood glucose over the past 2-3 months [10]. Elevated HbA1c levels are strongly associated with an increased risk of diabetes-related complications [11]. However, HbA1c has limitations, particularly in reflecting short-term glucose fluctuations and being influenced by factors such as anemia or hemoglobinopathies [12].

Fructosamine and glycated albumin (GA) are emerging markers for assessing short-term glycemic control. Fructosamine reflects average glucose over the past 2-3 weeks and is particularly useful when HbA1c is less reliable [13]. Our study found a positive correlation between fructosamine levels and FBG in T1D, T2D, and GDM patients, consistent with previous research indicating fructosamine's ability to detect rapid glucose changes [14]. Additionally, fructosamine has shown better sensitivity than HbA1c in assessing acute changes in glucose levels [15].

GA, another marker for short-term glycemic control, reflects glycation over the past 2-3 weeks [16]. In this study, GA showed a stronger correlation with FBG than fructosamine, particularly in T1D patients. This finding aligns with prior studies suggesting that GA is more sensitive to short-term glucose fluctuations than HbA1c or fructosamine [17]. This could make GA a valuable tool for monitoring glycemic status, especially in individuals with poor long-term glucose control.

While HbA1c remains indispensable for long-term glycemic monitoring, short-term markers like fructosamine and GA offer critical insights, particularly in cases of rapid glucose fluctuations. In T1D, GA showed a stronger correlation with FBG than HbA1c, indicating its potential to better reflect acute changes in blood glucose. Conversely, HbA1c demonstrated a stronger correlation with FBG in T2D and GDM, supporting its role in long-term monitoring [18].

Despite their utility, short-term markers like fructosamine and GA are not without limitations. Our study observed false positive (3.125%) and false negative (9.375%) rates for fructosamine, suggesting that it may not be a reliable standalone diagnostic tool for all types of diabetes [19]. Previous research also highlights error rates in fructosamine assays, underscoring the need for caution when using it for diabetes screening [20].

1,5-Anhydroglucitol (1,5-AG) is another promising biomarker, responsive to short-term glucose fluctuations. The negative correlation between 1,5-AG and FBG in this study supports its potential as a sensitive marker for transient hyperglycemia, as elevated glucose levels reduce 1,5-AG concentrations [21]. As a marker reflecting brief periods of elevated glucose, 1,5-AG may complement existing tools for glycemic monitoring, especially in individuals with fluctuating blood sugar levels.

This study highlights the effectiveness of various glycation markers in diagnosing and managing diabetes. While HbA1c remains the most reliable marker for long-term glycemic control, short-term markers such as fructosamine and GA offer valuable insights, especially in contexts where rapid glucose changes occur or HbA1c is unreliable. Additionally, 1,5-AG is a sensitive marker for detecting short-term glucose fluctuations. A combined approach incorporating both long-term and short-term markers is recommended to enhance diabetes diagnosis and management.

4. CONCLUSION

The growing emphasis on nontraditional glycemic biomarkers has emerged in response to the limitations of the HbA1c test, particularly in clinical scenarios where HbA1c may not accurately reflect overall glycemic control. Certain conditions, such as anemia, hemoglobinopathies, and pregnancy, can affect HbA1c levels, making interpretation challenging and potentially misleading. In such cases, relying solely on HbA1c may not provide a full understanding of a patient's glycemic status. Therefore, alternative biomarkers have gained attention for their ability to complement traditional methods, such as HbA1c and fasting blood glucose (FBG), in the management of diabetes.

Among these alternative markers, fructosamine and glycated albumin (GA) are increasingly recognized for their role in monitoring short-term glycemic control. Both biomarkers are formed when glucose binds to proteins in the bloodstream, with their levels reflecting average glucose concentrations over a shorter time frame—typically 2 to 3 weeks—compared to HbA1c. Fructosamine and GA correlate well with HbA1c and FBG, making them useful for assessing glycemic status in situations where HbA1c is unreliable. However, while these markers provide valuable insights, they should be considered supplementary tools rather than primary diagnostic methods for diabetes management. Their role should be to complement, not replace, standard glycemic measures.

At present, there are no universally accepted guidelines for integrating alternative biomarkers into routine clinical practice alongside traditional markers like HbA1c and FBG. The lack of standardized recommendations means their use in diabetes care remains in development. In addition to fructosamine and GA, 1,5-anhydroglucitol (1,5-AG) is an emerging biomarker that reflects rapid fluctuations in glucose levels, providing useful information about daily glycemic excursions. While 1,5-AG can be particularly beneficial for individuals who experience frequent blood sugar fluctuations, it should also be used in conjunction with other markers rather than as a stand-alone diagnostic tool.

In conclusion, although HbA1c remains the gold standard for long-term glycemic control, alternative biomarkers such as fructosamine, GA, and 1,5-AG are gaining recognition for their clinical utility in managing diabetes. These markers offer distinct advantages, particularly in assessing short-term glycemic control and capturing glucose fluctuations that may not be detected by HbA1c alone. As research into these biomarkers progresses, they may play an important role in developing a more comprehensive, multifaceted approach to diabetes monitoring and management.

CONSENT

A simple randomization method was used to select participants who met the eligibility criteria and provided written informed consent.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

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.

COMPETING INTERESTS

Authors have declared that no competing interests exist

REFERENCES

1. World Health Organization (WHO). Diabetes. World Health Organization; 2024.
   Available: https://www.who.int/diabetes
   Accessed: November 2024.
2. Sisay M, Edessa D, Ali T, Mekuria AN, Gebrie A. The relationship between advanced glycation end products and gestational diabetes: A systematic review and meta-analysis. PLoS One. 2020; 15(10):e0240382.
   DOI: 10.1371/journal.pone.0240382
3. Gillett MJ. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care. 2009;32:1327–34.
   DOI: 10.2337/dc09-9033. [DOI]
   [PMC free article] [PubMed] [Google Scholar]
4. Xu H, Chen R, Hou X, Li N, Han Y, Ji S. The clinical potential of 1,5-anhydroglucitol as a biomarker in diabetes mellitus. Frontiers in Endocrinology (Lausanne). 2024;15:1471577.
   Availavle:https://doi.org/10.3389/fendo.2024.1471577

5. American Diabetes Association. Standards of medical care in diabetes—2023. Diabetes Care. 2023;46(Supplement 1):S1-S2.
6. Agarwal MM, Punnose J. Screening for gestational diabetes in high-risk populations: the United Arab Emirates experience. Ann Saudi Med. 2001;21(1-2):117-9.
DOI: 10.5144/0256-4947.2001.117
PMID: 17264610.
7. Wu H, Norton V, Cui K, Zhu B, Bhattacharjee S, Lu YW, Wang B, Shan D, Wong S, Dong Y, Chan S-L, Cowan D, Xu J, Bielenberg DR, Zhou C, Chen H. Diabetes and its cardiovascular complications: Comprehensive network and systematic analyses. Frontiers in Cardiovascular Medicine. 2022;9:841928.
Available:https://doi.org/10.3389/fcvm.2022.841928
8. Roep BO, Thomaidou S, van Tienhoven R, Zaldumbide A. Type 1 diabetes mellitus as a disease of the β-cell (do not blame the immune system?). Nature Reviews Endocrinology. 2020;17(3):150–161.
Available:https://doi.org/10.1038/s41574-020-00443-4
9. Roep BO, Thomaidou S, van Tienhoven R, Zaldumbide A. Type 1 diabetes mellitus as a disease of the β-cell (do not blame the immune system?). Nature Reviews Endocrinology. 2021;17(3):150-161.
Available:https://doi.org/10.1038/s41574-020-00443-4
10. American Diabetes Association Professional Practice Committee. Glycemic goals and hypoglycemia: Standards of care in diabetes—2024. Diabetes Care. 2024;47(Supplement_1): S111–S125.
Available:https://doi.org/10.2337/dc24-S006
11. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Turner RC. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): Prospective observational study. BMJ. 2000;321(7258):405-412.
Available:https://doi.org/10.1136/bmj.321.7258.405
12. Makris K, Spanou L. Is there a relationship between mean blood glucose and glycated hemoglobin? J Diabetes Sci Technol. 2011;5(6):1572–1583.
DOI: 10.1177/193229681100500634
PMCID: PMC3262729,
PMID: 22226280
13. Parrinello CM, Selvin E. Beyond HbA1c and glucose: the role of nontraditional glycemic markers in diabetes diagnosis, prognosis, and management. Curr Diab Rep. 2014;14(11):548.
DOI: 10.1007/s11892-014-0548-3
PMCID: PMC4214073,
NIHMSID: NIHMS636924,
PMID: 25249070.
14. Moini J. Treatment of diabetes. In: Epidemiology of Diabetes; 2019.
Available:https://www.sciencedirect.com/topics/medicine-and-dentistry/fructosamine
15. Fructosamine. In: Medical Clinics of North America; 2013.
Available:https://www.sciencedirect.com/topics/medicine-and-dentistry/fructosamine
16. Kohzuma T, Tao X, Koga M. Glycated albumin as biomarker: Evidence and its outcomes. Journal of Diabetes and its Complications. 2021;35(11):108040.
Available:https://doi.org/10.1016/j.jdiacomp.2021.108040
17. Tarabichi S, Parvizi J. Preventing the impact of hyperglycemia and diabetes on patients undergoing total joint arthroplasty. The Journal of Arthroplasty. 2023;38(7):1303–1308.
Available:https://doi.org/10.1016/j.arth.2023.02.016
18. American Diabetes Association. Standards of medical care in diabetes—2023. Diabetes Care. 2023;46(Suppl. 1): S1-S2.
Available:https://doi.org/10.2337/dc23-S001
19. 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
20. Nansseu JRN, Fokom-Domgue J, Noubiap JJN, Balti EV, Sobngwi E, Kengne AP. Fructosamine measurement for diabetes mellitus diagnosis and monitoring: A systematic review and meta-analysis protocol. BMJ Open. 2015;5(5): e007689.
Available:https://doi.org/10.1136/bmjopen-2015-007689

21. Dungan, Kathleen M. "1,5-Anhydroglucitol (GlycoMark™) as a Marker of Short-Term Glycemic Control and Glycemic Excursions." Expert Review of Molecular Diagnostics. 2008;8(1): 9–19. Available:https://doi.org/10.1586/14737159.8.1.9

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/127523