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A comparative analysis of HbA1c, glycated albumin, and fasting plasma glucose for glycemic assessment in people living with HIV

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ABSTRACT

Background: People living with HIV (PLWH) are at increased risk for metabolic disorders, including diabetes and prediabetes. While hemoglobin A1c (HbA1c) is widely used for glycemic assessment, its reliability in PLWH is questioned due to altered red blood cell turnover. Glycated albumin (GA) has been proposed as an alternative, but its diagnostic utility remains unclear in PLWH. This study aims to compare the correlations of HbA1c and GA with fasting plasma glucose (FPG), evaluate their diagnostic performance, and identify factors influencing discrepancies between them in PLWH.

Methods: This retrospective cross-sectional study included 236 PLWH with documented FPG, HbA1c, and GA levels. Correlations between glycemic markers were assessed using Pearson's correlation coefficients. Diagnostic performance for prediabetes and diabetes was evaluated using receiver operating characteristic (ROC) curves, and a GA cut-off was determined using the Youden index. Multivariable logistic regression was performed to identify predictors of HbA1c-GA mismatch.

Results: HbA1c showed a moderate correlation with FPG ($r = 0.33$, p value < 0.001), while GA had a weaker correlation ($r = 0.18$, p value $= 0.005$). The area under the ROC curve (AUC) for detecting glycemic abnormalities was 0.66 for HbA1c and 0.57 for GA. The optimal GA cut-off for prediabetes derived from ROC analysis was 12.42 %, improving sensitivity but reducing specificity. Multivariable analysis identified low mean corpuscular volume (MCV <80 fL) as an independent predictor of HbA1c-GA mismatch (odds ratio = 4.94, 95 % confidence interval: 1.95–12.50, $p$value < 0.001).

Conclusion: HbA1c or GA alone do not reliably capture glycemic abnormalities in PLWH. A lower GA cut-off (12.42 %) for prediabetes improves sensitivity but remains suboptimal. A combined approach incorporating FPG is recommended to enhance prediabetes and diabetes screening accuracy in this population.

1. Introduction

Fasting plasma glucose (FPG), a primary screening method recommended by the World Health Organization (WHO) for type 2 diabetes and prediabetes. At a cutoff of ≥126 mg/dL, FPG demonstrates a sensitivity of approximately 56 % and a specificity of 98 % versus the 2-h oral glucose tolerance test (OGTT) for diabetes.[1] A meta-analysis found FPG highly specific for identifying prediabetes (94 percent) but less sensitive because older studies used an FPG cutoff of 110–125 mg/dL instead of the American Diabetes Association (ADA)'s updated threshold (100–125 mg/dL).[2] Hemoglobin A1c (HbA1c) is another widely used marker, which reflects the average blood glucose levels over two to three months. Using HbA1c ≥ 6.5 % yields 68 % sensitivity and 96 % specificity for diabetes, whereas for prediabetes, the sensitivity is about 49 %

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and specificity 79 %.[2] Its accuracy can be affected when red blood cell (RBC) turnover is abnormal, such as anemia, hemoglobinopathies, or chronic kidney disease.[3] On the other hand, glycated albumin (GA) has gained attention as an alternative marker for glycemic monitoring, reflecting average glucose levels over two to four weeks. It remains unaffected by RBC turnover, though its accuracy can be influenced by conditions causing hypoalbuminemia, such as cirrhosis or nephrotic syndrome.[4] Although data on the sensitivity and specificity of GA for diagnosing diabetes mellitus are relatively limited, a Taiwanese study suggests that a GA level of 16.5 % correlates with HbA1c cutoff of 6.5 %, while 14.5 % aligns with the prediabetes (HbA1c cutoff of 5.7 %).[5] In addition, some researchers propose a conversion formula for GA and HbA1c: GA = (HbA1c − 2.015) × 4.[6]

People living with HIV (PLWH) face a disproportionately higher risk of developing prediabetes and diabetes mellitus compared with the general population.[7] Although the advent of antiretroviral therapy (ART) has substantially improved survival rates among PLWH, it has also introduced new challenges, especially regarding metabolic complications such as dyslipidemia and diabetes mellitus, which can increase cardiovascular risk. One study found DM prevalence among PLWH was 10.3 %. DM prevalence was 3.8 % higher in HIV-infected adults compared with general population, which was potentially caused by chronic immune activation, ART-induced toxicities, and extended life expectancy.[8] Consequently, metabolic disorders now pose an important public health concern in PLWH, underscoring the need for early detection of diabetes for them.

Current guidelines for HIV care generally recommend screening for diabetes in a manner similar to the general population—namely, by routinely measuring FPG and, when borderline values (100–125 mg/dL) are detected, proceeding with confirmatory testing such as HbA1c or an OGTT.[9] However, growing evidence suggests that HbA1c may underestimate true glycemia in PLWH.[10] In one study, PLWH had glucose levels approximately 29 mg/dL higher than expected for their measured HbA1c.[11] Proposed mechanisms include shortened RBC lifespan, medication effects (particularly nucleoside reverse transcriptase inhibitors), and persistent inflammation.[12] Because of these potential inaccuracies, some experts recommend relying more on FPG rather than HbA1c for both diagnosing diabetes and monitoring glycemic trends in PLWH.[13] The 2025 ADA guidelines still caution against using HbA1c as a diagnostic test in PLWH. Instead, the ADA recommends screening for diabetes and prediabetes with FPG before initiating or switching ART, and again 3–6 months after any regimen change. If initial results are normal, annual FPG monitoring is advised to detect emerging metabolic complications.[14]

Despite the frequent use of HbA1c for glycemic assessment in PLWH, its correlation with FPG in this population remains uncertain. GA, which reflects shorter-term glycemia and is less influenced by RBC lifespan, could serve as an alternative marker. However, evidence on GA's correlation with FPG and its diagnostic performance for prediabetes and diabetes in PLWH is limited. Moreover, it is unclear whether certain clinical or laboratory factors might affect the accuracy of GA or HbA1c, leading to a "mismatch" in which one measure is disproportionately higher or lower than the other under similar conditions. Therefore, this study aims to (1) compare the correlation of HbA1c and GA with FPG, (2) evaluate their diagnostic performance in detecting glycemic abnormalities in PLWH, and (3) identify factors that contribute to discrepancies between GA and HbA1c.

2. Method

This retrospective cross-sectional study was carried out at a regional hospital in southern Taiwan between January 2019 and December 2020. Our study included adult PLWH (aged 18 years or older) who attended regular outpatient follow-ups during this period. Only patients with documented measurements for HbA1c, GA, and FPG were included, and we collected additional clinical and laboratory data from electronic medical records. Patients were excluded if they had missing glycemic data or were on medications known to affect glucose metabolism (such as corticosteroids or anti-diabetic drugs). We also screened for conditions known to distort HbA1c or GA (cirrhosis, hemoglobinopathies, nephrotic syndrome, overt thyroid disease, marked anemia [Hb < 10 g/dL], and severe obesity [mean body mass index (BMI) ≥35 kg/m^2]). Only one patient had marked anemia and two had severe obesity; no other such conditions were identified, so no additional exclusions were applied.

Demographic data, including age and sex, were extracted from the hospital's electronic database. In addition, we collected clinical information and laboratory parameters relevant to both metabolic and HIV-specific assessments. Metabolic parameters included FPG, HbA1c, GA, lipid profiles, and homeostatic model assessment of insulin resistance (HOMA-IR). HIV-related parameters included CD4 count and HIV RNA viral load. Additional laboratory markers, such as hemoglobin concentration, mean corpuscular volume (MCV), renal function (estimated glomerular filtration rate [eGFR], calculated using the Modification of Diet in Renal Disease [MDRD] formula), and serum albumin levels, were also recorded.

FPG was measured after an overnight fast (≥8 h) using a standardized enzymatic method on the UniCel® DxC 800 Synchron Clinical System with GLUCm reagent (Beckman Coulter, USA). HbA1c was determined by ion-exchange HPLC on the VARIANT™ II TURBO system with the VARIANT II TURBO HbA1c Kit-2.0 (Bio-Rad Laboratories, USA), and GA was quantified using the Lucica® Glycated Albumin-L enzymatic assay (Asahi Kasei Pharma Corporation, Japan). HOMA-IR was calculated from fasting insulin and glucose levels using the following formula: HOMA-IR = (FPG [mg/dL] × fasting insulin [μIU/mL])/405. To reduce daily fluctuations and obtain a more stable measure of glycemic status, each participant's fasting plasma glucose (FPG) was calculated as the mean of all available FPG readings from the three months prior to the HbA1c and GA blood draw.

For diagnostic performance analysis, glycemic abnormalities were defined using FPG measurements based on ADA criteria. An FPG of 100–125 mg/dL was considered indicative of prediabetes, while values of ≥126 mg/dL defined diabetes mellitus. We then evaluated the diagnostic performance of HbA1c and GA using these FPG thresholds as the reference standard. For prespecified biomarker thresholds, HbA1c followed ADA criteria (prediabetes 5.7–6.4 %; diabetes ≥6.5 %). For GA, we used population-based receiver operating characteristic (ROC) cutoffs from a Taiwanese cohort (14.5 % for prediabetes; 16.5 % for diabetes), reflecting the best available local evidence.[5] Diagnostic performance against FPG ≥100 mg/dL was therefore computed at HbA1c ≥ 5.7 % and GA ≥14.5 %; as a sensitivity analysis. A mismatch between HbA1c and GA was defined as an absolute difference greater than 0.5 % between the measured GA and GA estimated from measured HbA1c using the formula GA = (HbA1c – 2.015) × 4, as described in previous studies. Based on this criterion, participants were subsequently categorized into mismatch and non-mismatch groups.

Statistical analyses were conducted using SPSS version 22.0. We first summarized all demographic, clinical, and laboratory variables using descriptive statistics. Continuous data are reported either as mean ± standard deviation (SD) or as median with interquartile range (IQR), depending on their distribution, while categorical data are presented as frequencies and percentages.

Pearson's correlation analysis was used to evaluate the relationships between HbA1c, GA, and FPG. To assess the diagnostic performance of HbA1c and GA in detecting prediabetes and diabetes when these conditions are considered together, we calculated sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. Additionally, ROC curve analyses were performed to determine the area under the curve (AUC) for both markers. Specifically, we used ROC analysis to evaluate GA's diagnostic performance in PLWH and applied the Youden index to identify a proposed optimal GA cut-off that maximizes the sum of sensitivity and specificity.

Mismatch between HbA1c and GA was defined as an absolute difference of |GA – estimated HbA1c| greater than 0.5, with estimated HbA1c calculated using the conversion formula GA = (HbA1c – 2.015) × 4. Comparative analyses between the mismatch and non-mismatch groups were initially performed using univariate methods, with t-tests applied for continuous variables and chi-square tests for categorical variables. Multivariable logistic regression model was constructed by including both variables with significant univariate associations and clinically relevant factors (e.g., HIV RNA, serum albumin) to identify independent predictors of HbA1c-GA mismatch. The results from the logistic regression were expressed as odds ratios (OR) with corresponding 95 % confidence intervals (CI), and a p value <0.05 was considered statistically significant.

The study protocol was reviewed and approved by the Institutional Review Board of Kaohsiung Medical University Hospital (approval number KMUHIRB - SV(I)20210055). Informed consent was obtained from all subjects involved in the study.

3. Result

From January 2019 to December 2020, a total of 318 PLWH attending outpatient follow-up at the regional hospital were screened for inclusion. After applying our exclusion criteria, 74 patients were removed due to missing measurements for GA, FPG, or HbA1c, 2 were excluded because of missing body weight data, and an additional 6 patients were excluded for receiving active diabetes treatment. Consequently, 236 participants met the inclusion criteria and were included in the final analysis.

Baseline characteristics of the 236 participants are detailed in Tables 1 and 2. In brief, the cohort had a median age of 36 years (IQR: 31–42) and was predominantly male (98.7 %). Renal function was preserved (mean eGFR 97.70 ± 23.81 mL/min/1.73 m^2, with 58.5 % ≥ 90 mL/min/1.73 m^2), and serum albumin was within normal limits (mean 3.94 ± 0.59 g/dL, 96.2 % ≥ 3.5 g/dL). Hematologic evaluation showed that 9.3 % of participants had an MCV <80 fL. HIV-related parameters revealed a mean CD4 count of 637.6 ± 326.3 cells/μL (92.4 % ≥ 200 cells/μL) and that 89.4 % had HIV RNA levels <200 copies/mL.

Table 1
Baseline demographic and clinical characteristics.

Characteristics	Overall (n = 236)
Age (yr) — Median (IQR)	36 (31–42)
Distribution — no. (%)	
15–29 yr	45 (19.1 %)
30–44 yr	145 (61.4 %)
45–59 yr	41 (17.4 %)
≥60 yr	5 (2.1 %)
Sex — no. (%)	
Male	233 (98.7 %)
Female	3 (1.3 %)
eGFR (mL/min/1.73m^2) — Mean ± SD	97.70 ± 23.81
Distribution — no. (%)	
≥90	138 (58.5 %)
60–89	93 (39.4 %)
30–59	5 (2.1 %)
Albumin (g/dL) — Mean ± SD	3.94 ± 0.59
Distribution — no. (%)	
≥3.5 g/dL	227 (96.2 %)
<3.5 g/dL	9 (3.8 %)
MCV (fl) — Mean ± SD	93.36 ± 58.17
Distribution — no. (%)	
80-100 fL	214 (90.7 %)
<80 fL	22 (9.3 %)
CD4 (cells/μL) — Mean ± SD	637.6 ± 326.3
Distribution — no. (%)	
≥200 cells/μL	218 (92.4 %)
<200 cells/μL	18 (7.6 %)
HIV RNA (copies/mL)	
Distribution — no. (%)	
<200 copies/mL	211 (89.4 %)
≥200 copies/mL	25 (10.6 %)

Abbreviations: eGFR, estimated glomerular filtration rate; MCV, mean corpuscular volume.

Table 2
Baseline metabolic characteristics.

Characteristics	Overall (n = 236)
BMI(kg/m^2) — Mean ± SD	23.67 ± 3.40
Distribution — no. (%)	
<18.5 kg/m^2	9 (3.8 %)
18.5–23.9 kg/m^2	128 (54.2 %)
24.0–26.9 kg/m^2	65 (27.5 %)
≥27.0 kg/m^2	34 (14.4 %)
FPG (mg/dL) — Mean ± SD	102.0 ± 9.6
Distribution — no. (%)	
<100 mg/dL	102 (43.2 %)
100–125 mg/dL	128 (54.2 %)
≥126 mg/dL	6 (2.5 %)
HbA1c (%) — Mean ± SD	5.28 ± 0.39
Distribution — no. (%)	
<5.7 %	187 (79.2 %)
5.7–6.4 %	48 (20.3 %)
≥6.5 %	1 (0.4 %)
GA (%) — Mean ± SD	12.36 ± 1.28
Distribution — no. (%)	
<14.5 %	224 (94.9 %)
14.5–16.4 %	11 (4.7 %)
≥16.5 %	1 (0.4 %)
HOMA-IR — Mean ± SD	2.65 ± 4.41
Distribution — no. (%)	
<2.5	179 (75.8 %)
≥2.5	57 (24.2 %)
Total cholesterol (mg/dL) — Mean ± SD	174.06 ± 34.21
LDL (mg/dL)— Mean ± SD	106.86 ± 28.36
Triglycerides (mg/dL)— Mean ± SD	137.77 ± 98.24

Abbreviations: BMI, body mass index; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; GA, glycated albumin; HOMA-IR, homeostatic model assessment of insulin resistance; LDL, low-density lipoprotein.

Table 2 presents the metabolic profiles of the cohort. The mean body BMI was 23.67 ± 3.40 kg/m^2. Based on the Taiwan adult BMI classification,[15] 3.8 % had BMI <18.5 kg/m^2, 54.2 % were 18.5–23.9 kg/m^2, 27.5 % were 24.0–26.9 kg/m^2, and 14.4 % were ≥27.0 kg/m^2. The mean FPG was 102.0 ± 9.6 mg/dL; 43.2 % of subjects had FPG <100 mg/dL, 54.2 % were in the 100–125 mg/dL range, and 2.5 % had FPG ≥126 mg/dL. Glycemic control markers showed a mean HbA1c of 5.28 ± 0.39 %, with 79.2 % of participants having HbA1c values < 5.7 %, 20.3 % between 5.7 % and 6.4 %, and 0.4 % ≥ 6.5 %. The mean GA was 12.36 ± 1.28 %, with 94.9 % of patients having GA <14.5 %, 4.7 % between 14.5 % and 16.4 %, and 0.4 % ≥ 16.5 %. The mean HOMA-IR was 2.65 ± 4.41; 24.2 % had HOMA-IR ≥2.5.

The correlation between HbA1c and FPG was assessed using Pearson's correlation coefficient. A positive correlation was observed (r = 0.33, $p < 0.001$). The correlation between GA and FPG was also evaluated, showing a weaker positive correlation (r = 0.18, $p = 0.005$). Scatter plots of HbA1c vs. FPG (Fig. 1) and GA vs. FPG (Fig. 2) illustrate these relationships.

Using FPG ≥100 mg/dL as the reference standard, the diagnostic performance of HbA1c and GA for detecting prediabetes and diabetes is summarized in Table 3 and depicted in Fig. 3. At a cut-off of HbA1c ≥ 5.7 %, sensitivity was 28.0 %, specificity was 87.4 %, and the overall accuracy reached 69.49 %. In contrast, using GA threshold of ≥14.5 % yielded a sensitivity of 6.4 % and specificity of 96.4 %, with an accuracy of 54.24 %. ROC analysis (see Fig. 3) revealed an AUC of 0.66 for HbA1c and 0.57 for GA. Applying the Youden index to optimize GA's performance resulted in a revised GA cut-off of ≥12.42 %. This adjusted threshold increased sensitivity to 51.2 % but reduced specificity to 64.86 %, yielding an overall accuracy of 57.63 %.

A mismatch between HbA1c and GA was defined as an absolute difference of |GA – estimated HbA1c| greater than 0.5, with the

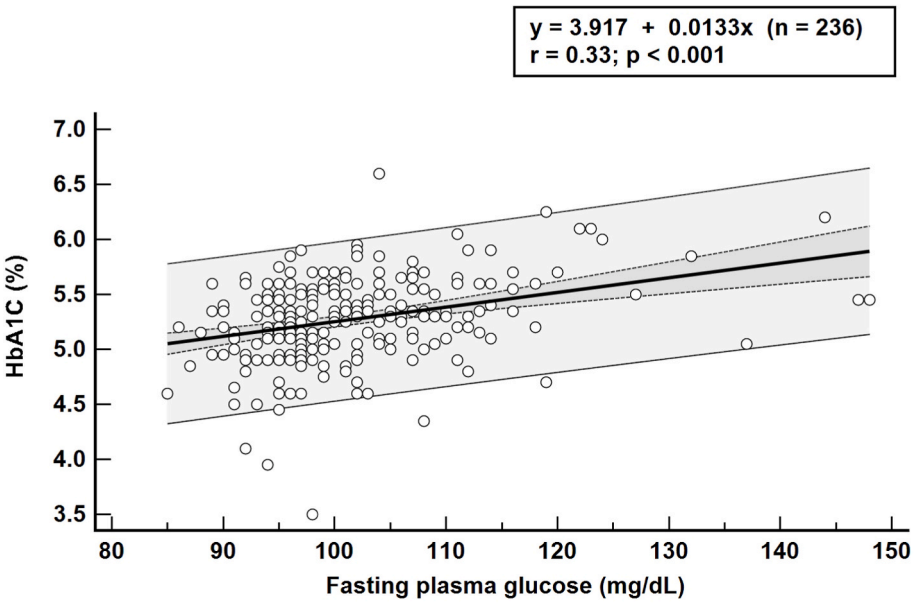

Fig. 1. Correlation between HbA1c and fasting plasma glucose (FPG). A scatter plot illustrating the correlation between HbA1c (%) and fasting plasma glucose (mg/dL). The solid line represents the linear regression model ($y = 3.917 + 0.0133x$), and the shaded area represents the 95 % confidence interval. The Pearson correlation coefficient was $r = 0.33$, $p < 0.001$.

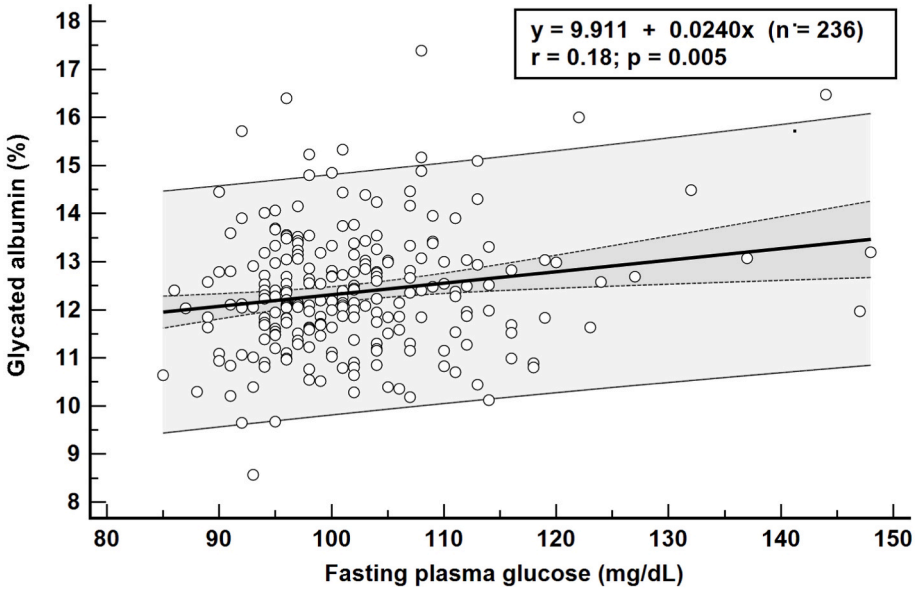

Fig. 2. Correlation between glycated albumin and fasting plasma glucose. A scatter plot illustrating the correlation between glycated albumin (%) and fasting plasma glucose (mg/dL). The solid line represents the linear regression model ($y = 9.911 + 0.0240x$), and the shaded area represents the 95 % confidence interval. The Pearson correlation coefficient was $r = 0.18$, $p = 0.005$.

Table 3
Diagnostic performance of HbA1c and GA with different cut-off values compared to FPG in detecting prediabetes and diabetes.

Marker	Cut-off Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
HbA1c	≥5.7 %	28.0	87.4	71.4	51.9	69.49
Glycated albumin	≥14.5 %[a]	6.4	96.4	66.7	47.8	54.24
	≥12.42 %	51.2	64.86	62.14	54.14	57.63

[a] The GA cut-off of ≥14.5 % was based on previous study,[5] while the GA cut-off of ≥12.42 % was derived from ROC curve analysis in this study as the proposed GA threshold to optimize sensitivity and specificity. Abbreviations: GA, glycated albumin; HbA1c, hemoglobin A1c; FPG, fasting plasma glucose; PPV, positive predictive value; NPV, negative predictive value.

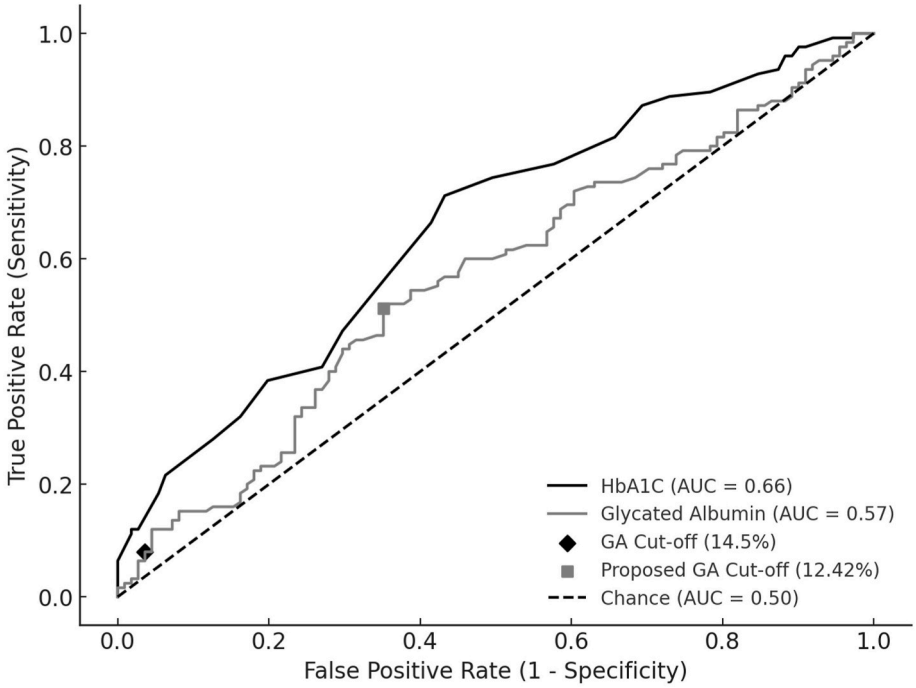

Fig. 3. Receiver operating characteristic curves of HbA1c and GA for detecting prediabetes and diabetes. ROC curves comparing the diagnostic performance of HbA1c (black solid line) and GA (gray solid line) for detecting glycemic abnormalities. The area under the curve (AUC) was 0.66 for HbA1c and 0.57 for GA. The diamond symbol represents the GA cut-off of 14.5 % derived from Hsu et al.,[5] while the square symbol represents the optimized GA cut-off (12.42 %) derived from this study. The dashed line represents the chance level (AUC = 0.50).

Table 4
Univariate analysis of factors associated with HbA1c and glycated albumin mismatch in PLWH.

Variables	Non-mismatch (n = 174)	Mismatch (n = 62)	*p* value
Categorical variables	n (%)		
BMI (kg/m^2)			0.457
<18.5	8 (4.6 %)	1 (1.6 %)	
18.5–23.9	96 (55.2 %)	32 (51.6 %)	
24.0–26.9	48 (27.6 %)	17 (27.4 %)	
≥27.0	22 (12.6 %)	12 (19.4 %)	
HOMA-IR			0.598
<2.5	134 (77.0 %)	45 (72.6 %)	
≥2.5	40 (23.0 %)	17 (27.4 %)	
eGFR (mL/min/ 1.73m^2)			0.268
<60	5 (2.9 %)	0 (0.0 %)	
60–89	71 (40.8 %)	22 (35.5 %)	
≥90	98 (56.3 %)	40 (64.5 %)	
Albumin (g/dL)			0.056
<3.5	4 (2.3 %)	5 (8.1 %)	
≥3.5	170 (97.7 %)	57 (91.9 %)	
CD4 (cells/μL)			0.880
≥200	161 (92.5 %)	57 (91.9 %)	
<200	13 (7.5 %)	5 (8.1 %)	
HIV RNA (copies/mL)			0.353
<200	158 (90.8 %)	53 (85.5 %)	
≥200	16 (9.2 %)	9 (14.5 %)	
MCV (fl)			<0.001*
≥80	165 (94.8 %)[77.1 %]	49 (79.0 %)[22.9 %]	
<80	9 (5.2 %)[77.1 %]	13 (21.0 %)[59.1 %]	

Data are presented as n (column %) except for MCV, for which [row %] is additionally shown in brackets. For MCV, row percentages indicate the proportion of mismatch within each MCV subgroup. *indicates $p < 0.05$.

estimated HbA1c calculated using the formula GA = (HbA1c – 2.015) × 4. Using this criterion, 62 of the 236 participants (26.3 %) were classified as having a mismatch, while 174 participants (73.7 %) showed concordant results (Table 4). Univariate analysis (Table 4) demonstrated that a significantly higher proportion of individuals in the mismatch group had an MCV <80 fL compared to those with concordant results (21.0 % vs. 5.2 %; $p < 0.001$). Other variables, including BMI, HOMA-IR, eGFR, serum albumin, CD4 count, and HIV RNA levels, did not differ significantly between the groups. Subsequently, multivariable logistic regression analysis (Table 5 and Fig. 4) was performed to identify independent predictors of the HbA1c-GA mismatch. In this analysis, an MCV <80 fL emerged as a significant predictor, with an OR of 4.94 (95 % CI: 1.95–12.50; $p < 0.001$). Additionally, serum albumin <3.5 g/dL showed a trend toward significance (OR 3.86, 95 % CI: 0.92–16.12; $p = 0.064$). No significant associations were observed for BMI≥27 kg/m^2, CD4 count <200 cells/μL, or HIV RNA levels ≥200 copies/mL. These findings indicate that a lower MCV is independently associated with discrepancies between HbA1c and GA in this cohort of PLWH.

4. Discussion

Our cohort consisted of 236 PLWH who were screened to ensure complete data on glycemic markers and clinical variables. The median

Table 5
Multivariable logistic regression analysis of factors associated with HbA1c and Glycated Albumin mismatch in PLWH.

Variable	β coefficient	Odds Ratio (OR)	95 % CI	*p* value
BMI ≥27.0 kg/m^2	0.481	1.62	0.71–3.66	0.248
Albumin <3.5 g/dL	1.350	3.86	0.92–16.12	0.064
CD4 < 200 cells/μL	−0.186	0.83	0.23–2.96	0.774
HIV RNA ≥200 copies/mL	0.584	1.79	0.65–4.95	0.260
MCV <80 fL	1.598	4.94	1.95–12.50	<0.001*

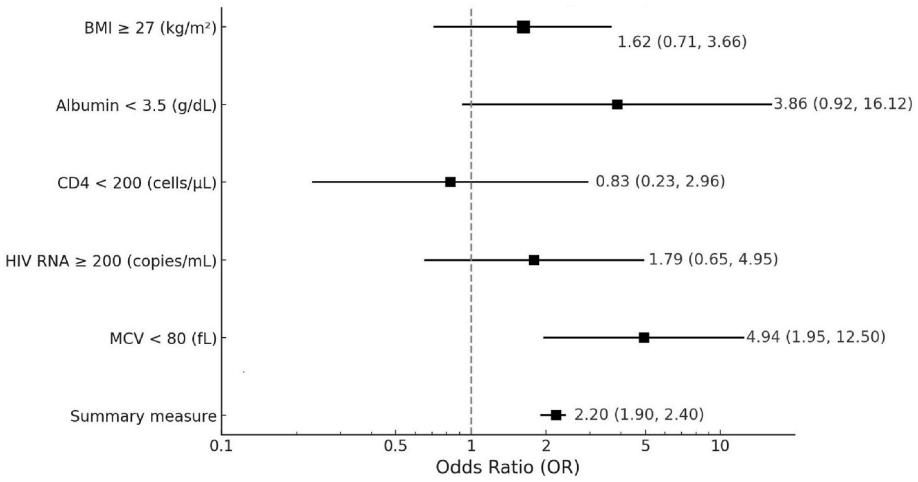

Fig. 4. Forest plot of multivariable logistic regression analysis for factors associated with HbA1c and glycated albumin mismatch. Odds ratios (OR) with 95 % confidence intervals for clinical and metabolic factors associated with HbA1c-GA mismatch. MCV <80 fL (OR = 4.94, 95 % CI: 1.95–12.50) and albumin <3.5 g/dL (OR = 3.86, 95 % CI: 0.92–16.12) showed higher odds of mismatch, while CD4 < 200 cells/μL was not significantly associated (OR = 0.83, 95 % CI: 0.23–2.96). The diamond represents the summary measure.

age was 36 years, and the group was predominantly male, with well-preserved renal function and largely normal albumin levels. Our study demonstrated that HbA1c correlated modestly with FPG (r = 0.33, $p <$ 0.001) in PLWH, while GA showed a weaker positive correlation (r = 0.18, p = 0.005). These results indicate that, despite concerns about potential underestimation of glycemia in PLWH, HbA1c remains a viable marker for reflecting long-term glycemic status. Our findings of a modest correlation between HbA1c and FPG in PLWH align with recent evidence from Daultrey et al.,[16] who demonstrated a strong association between HbA1c and continuous glucose monitoring (CGM) mean sensor glucose (r = 0.78) in a smaller cohort. While our correlation (r = 0.33) appears lower, differences in study design and measurement methods may account for this discrepancy. Notably, Daultrey et al. suggest that HbA1c remains a viable screening tool in PLWH despite concerns about its accuracy from previous literature; however, their study was limited by a small sample size and a relatively short CGM monitoring period of 10 days. These limitations raise questions about the generalizability of their conclusions. The 2025 ADA guidelines still caution against using HbA1c as a diagnostic test in individuals with HIV and advocates using FPG to detect prediabetes and diabetes for PLWH.[14]

While GA was significantly correlated with FPG (r = 0.18, p = 0.005), this association was surprisingly weaker than that observed for HbA1c. Despite that GA reflects glycemic status over a shorter term and is not influenced by RBC turnover, one might expect it to correlate more strongly with FPG. A possible explanation is that factors unique to PLWH—such as chronic inflammation or alterations in albumin metabolism—may interfere with GA levels, thereby reducing its correlation with FPG. However, current literature has not yet clearly delineated the underlying mechanisms for this observation.

Our study demonstrated that both HbA1c and GA exhibit suboptimal performance in detecting glucose abnormalities (prediabetes and diabetes) in PLWH. Coelho et al. demonstrated that HbA1c exhibits markedly lower sensitivity for diagnosing diabetes in PLWH compared to FPG and OGTT.[17] Although research on GA is limited in this population, current literature suggests that its primary role is in the monitoring of glycemic control post-treatment in diabetic patients, due to its ability to reflect short-term glycemic fluctuations.[18] Nevertheless, several studies have reported that GA's sensitivity for diagnosing diabetes is lower than desired, and its performance in identifying prediabetes is similarly inadequate.[19,20] Based on our ROC analysis using the Youden index, our proposed GA cutoff is 12.42 %. This threshold is lower than the 14.5 % reported by Hsu et al. (which corresponds to an HbA1c of 5.7 % for prediabetes in the general population),[5] and it increases sensitivity from 6.4 % to 51.2 % at the expense of a decrease in specificity, which drops from 96.4 % to 64.86 %. This finding aligns with a Korean study, which reported notably lower optimal GA cutoffs of 14.3 % for diabetes and 12.5 % for prediabetes.[19] However, even after we lower the GA threshold, the diagnostic performance remains suboptimal. These results underscore the notion that, in PLWH, GA alone is insufficient to accurately identify glucose abnormalities. Consequently, a multimodal approach that incorporates FPG alongside GA may be necessary to enhance diagnostic accuracy in this population.

Mismatch was defined as an absolute difference greater than 0.5 between measured GA and estimated HbA1c (using GA = (HbA1c – 2.015) × 4). This phenomenon was observed in 26.3 % of our cohort. Notably, patients with a mismatch had a significantly higher prevalence of MCV <80 fL (21.0 % vs. 5.2 %, $p <$ 0.001). Previous studies have reported that both low and high MCV, such as microcytosis due to iron deficiency anemia (IDA) or hemolysis, may influence HbA1c measurements.[12,21] In our cohort, no patients had MCV >100 fL. Although serum albumin levels are known to influence GA measurements,[18] our analysis did not reach statistical significance regarding hypoalbuminemia (albumin <3.5 g/dL), likely due to the low number of affected patients. In both univariate and multivariable analyses, HIV-related factors such as HIV RNA and CD4 count were not associated with mismatch. Thus, in PLWH, lower MCV appears to contribute to discrepancies between GA and HbA1c measurements, while HIV viral load and immune status do not seem to affect this discordance.

Our study has several limitations. It is a retrospective cross-sectional study. FPG was calculated as the mean of readings over the three months prior to HbA1c and GA measurements, potentially yielding lower correlations than CGM. Although FPG was averaged over the prior three months, the retrospective windows of HbA1c and GA are not fully aligned; nevertheless, patient-level FPG variability was low, supporting the comparability of these measures. Additionally, we used FPG as the reference standard to assess diagnostic performance of GA and HbA1c, although OGTT is considered a superior gold standard for diagnosing prediabetes and diabetes. This choice may miss dysglycemia with normal fasting glucose and underestimate abnormal glycemia. Furthermore, the absence of a matched HIV-negative control group precluded direct comparison of absolute GA and HbA1c values, limiting our ability to assess biomarker distortion attributable to HIV-related hematologic alterations. Our relatively small, single-center sample and unmeasured confounders, such as variations in ART regimens and nutritional status, may further limit the generalizability of our findings.

Our study provides insights that both HbA1c and GA have limitations

in detecting prediabetes and diabetes in PLWH, with GA demonstrating a weaker correlation with FPG and suboptimal diagnostic performance. While a lower GA threshold for prediabetes (12.42 %) improves sensitivity, its accuracy remains insufficient. A combined approach with FPG for better identification of glycemic abnormalities in this population is warranted. Future research should focus on validating and refining GA thresholds specific to PLWH and using CGM to verify the performance of HbA1c and GA in larger cohorts.

In conclusion, HbA1c or GA alone do not reliably capture glycemic abnormalities in PLWH. A lower GA cut-off (12.42 %) for prediabetes improves sensitivity but remains suboptimal. A combined approach incorporating FPG is recommended to enhance prediabetes and diabetes screening accuracy in this population.

CRediT authorship contribution statement

Chih-Wei Liang: Writing – original draft, Formal analysis, Data curation. **Shin-Huei Kuo:** Investigation, Data curation. **Chun-Yuan Lee:** Methodology, Formal analysis. **Shang-Yi Lin:** Validation, Formal analysis. **Ya-Ting Chang:** Validation, Formal analysis. **Chung-Hao Huang:** Validation, Formal analysis. **Tun-Chieh Chen:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chun-Yu Lin:** Validation, Supervision. **Jih-Jin Tsai:** Validation, Supervision. **Yen-Hsu Chen:** Validation, Supervision. **Po-Liang Lu:** Validation, Supervision.

Declaration of competing interest

The authors declared no conflicts of interest in the article.

Data availability

All data generated or analyzed during this study are included in this published article.

References

1. Hoyer A, Rathmann W, Kuss O. Utility of HbA(1c) and fasting plasma glucose for screening of type 2 diabetes: a meta-analysis of full ROC curves. *Diabet Med*. 2018;35(3):317–322.
2. Barry E, Roberts S, Oke J, Vijayaraghavan S, Normansell R, Greenhalgh T. Efficacy and effectiveness of screen and treat policies in prevention of type 2 diabetes: systematic review and meta-analysis of screening tests and interventions. *Br Med J*. 2017;356, i6538.
3. Little RR, Roberts WL. A review of variant hemoglobins interfering with hemoglobin A1c measurement. *J Diabetes Sci Technol*. 2009;3(3):446–451.
4. Wu WC, Ma WY, Wei JN, et al. Serum glycated albumin to guide the diagnosis of diabetes mellitus. *PLoS One*. 2016;11(1), e0146780.
5. Hsu P, Ai M, Kanda E, et al. A comparison of glycated albumin and glycosylated hemoglobin for the screening of diabetes mellitus in Taiwan. *Atherosclerosis*. 2015;242(1):327–333.
6. Tahara Y. Analysis of the method for conversion between levels of HbA1c and glycated albumin by linear regression analysis using a measurement error model. *Diabetes Res Clin Pract*. 2009;84(3):224–229.
7. Nansseu JR, Bigna JJ, Kaze AD, Noubiap JJ. Incidence and risk factors for prediabetes and diabetes mellitus among HIV-infected adults on antiretroviral therapy: a systematic review and meta-analysis. *Epidemiology*. 2018;29(3):431–441.
8. Hernandez-Romieu AC, Garg S, Rosenberg ES, Thompson-Paul AM, Skarbinski J. Is diabetes prevalence higher among HIV-infected individuals compared with the general population? Evidence from MMP and NHANES 2009-2010. *BMJ Open Diabetes Res Care*. 2017;5(1), e000304.
9. Ambrosioni J, Levi L, Alagaratnam J, et al. Major revision version 12.0 of the European AIDS Clinical Society guidelines 2023. *HIV Med*. 2023;24(11):1126–1136.
10. Eckhardt BJ, Holzman RS, Kwan CK, Baghdadi J, Aberg JA. Glycated Hemoglobin A (1c) as screening for diabetes mellitus in HIV-infected individuals. *AIDS Patient Care STDS*. 2012;26(4):197–201.
11. Kim PS, Woods C, Georgoff P, et al. A1C underestimates glycemia in HIV infection. *Diabetes Care*. 2009;32(9):1591–1593.
12. Diop ME, Bastard JP, Meunier N, et al. Inappropriately low glycated hemoglobin values and hemolysis in HIV-infected patients. *AIDS Res Hum Retrovir*. 2006;22(12):1242–1247.
13. Monroe AK, Glesby MJ, Brown TT. Diagnosing and managing diabetes in HIV-infected patients: current concepts. *Clin Infect Dis*. 2015;60(3):453–462.
14. Diagnosis and classification of diabetes: standards of care in Diabetes-2025. *Diabetes Care*. 2025;48(Supplement_1):S27–s49.
15. Statistics of Health Promotion 2022. *Health Promotion Administration*. Ministry of Health and Welfare; 2024. R.O.C (TAIWAN).
16. Daultrey H, Oliver NS, Wright J, Levett TJ, Chakera AJ. What is the influence of HIV serostatus on HbA1c? A prospective analysis using continuous glucose monitoring. *Diabetes Care*. 2024;47(8):1379–1385.
17. Coelho AR, Moreira FA, Santos AC, et al. Diabetes mellitus in HIV-infected patients: fasting glucose, A1c, or oral glucose tolerance test - which method to choose for the diagnosis? *BMC Infect Dis*. 2018;18(1):309.
18. Freitas PAC, Ehlert LR, Camargo JL. Glycated albumin: a potential biomarker in diabetes. *Arch Endocrinol Metab*. 2017;61(3):296–304.
19. Hwang YC, Jung CH, Ahn HY, et al. Optimal glycated albumin cutoff value to diagnose diabetes in Korean adults: a retrospective study based on the oral glucose tolerance test. *Clin Chim Acta*. 2014;437:1–5.
20. Ikezaki H, Furusyo N, Ihara T, et al. Glycated albumin as a diagnostic tool for diabetes in a general Japanese population. *Metabolism*. 2015;64(6):698–705.
21. Radin MS. Pitfalls in hemoglobin A1c measurement: when results may be misleading. *J Gen Intern Med*. 2014;29(2):388–394.