

Original article

Diagnostic Accuracy and Cut-off Values of Atherogenic Lipid Indices for Identifying Elevated HbA1c in Adults

Siraj Hamad¹ , Ahmed Alsharksi² , Abdalla Ali³ ¹Higher Institute of Science and Technology, Department of Medical Laboratory, Misurata, Libya²Higher Institute of Science and Technology, Department of Nursing Technology, Tawergha, Libya³Department of Chemistry, Faculty of Education, Misurata University, LibyaEmail: ahmedlalsherkas87@gmail.com**Abstract**

Atherogenic dyslipidemia, characterized by elevated triglyceride (TG) levels and reduced high-density lipoprotein cholesterol (HDL-C), is closely associated with insulin resistance and an unfavorable cardiometabolic profile. The atherogenic index of plasma (AIP), calculated as the logarithm of the TG-to-HDL-C ratio, integrates these lipid parameters into a single indicator of atherogenic risk. This study aimed to evaluate the discriminatory performance of AIP and other lipid parameters in distinguishing individuals with HbA1c >6.5% from those with HbA1c ≤6.5%. The supplied study results included 200 adults divided into two equal groups according to HbA1c: 100 participants with HbA1c ≤6.5% and 100 with HbA1c >6.5%. Lipid measurements were obtained after a 12-hour fast. Receiver operating characteristic (ROC) analysis and the Youden index were used to assess discrimination and identify cut-off values. Mean age was 45.26 ± 10.71 years; 59% were female. AIP had the highest reported area under the ROC curve (AUC = 0.825, 95% CI: 0.765–0.883; p < 0.001). The reported optimal AIP cut-off was >0.145, with 78.0% sensitivity and 74.7% specificity. TG also showed good discrimination (AUC = 0.791, 95% CI: 0.728–0.854; p < 0.001), whereas total cholesterol (AUC = 0.682), LDL-C (AUC = 0.645), and HDL-C (AUC = 0.312) showed weaker or directionally inverse discrimination. Conclusion: This study highlights the potential value of AIP as an adjunctive marker for identifying an atherogenic lipid profile associated with elevated HbA1c. AIP should be interpreted as a complementary cardiometabolic indicator rather than a replacement for established glycemic assessment methods.

Keywords. Atherogenic Index of Plasma, HbA1c, Triglycerides, HDL Cholesterol, ROC Analysis.**Introduction**

Diabetes mellitus is a major metabolic disorder associated with substantial microvascular and macrovascular morbidity. Glycated hemoglobin (HbA1c) reflects average glycemia over approximately the preceding two to three months and is widely used for diabetes diagnosis and monitoring. An HbA1c value of 6.5% or higher may support the diagnosis of diabetes when measured using an appropriately standardized method; in the absence of unequivocal hyperglycemia, confirmatory testing is generally recommended. HbA1c classification therefore needs to be interpreted within accepted diagnostic criteria rather than as a stand-alone proxy for all aspects of metabolic health [1,2].

Insulin resistance and type 2 diabetes are frequently accompanied by a characteristic dyslipidemic pattern involving elevated triglyceride-rich lipoproteins, reduced HDL-C, and qualitative changes in low-density lipoprotein (LDL) particles. These abnormalities are metabolically interconnected and contribute to residual cardiovascular risk even when LDL-C is considered alongside other conventional risk factors [3,4]. Elevated TG and low HDL-C can reflect altered hepatic lipid handling, increased flux of triglyceride-rich lipoproteins, and changes in lipoprotein remodeling. The relationship is biologically plausible because insulin resistance can increase hepatic very-low-density lipoprotein production and impair the clearance of triglyceride-rich particles [3,4].

The atherogenic index of plasma (AIP) was proposed as the base-10 logarithm of the ratio of triglycerides to HDL-C, conventionally expressed using molar concentrations. AIP is associated with lipoprotein particle size and plasma atherogenicity and has been investigated as a readily calculated cardiometabolic marker [5]. Studies have reported associations between AIP and cardiovascular risk factors, while research in people with type 2 diabetes has also examined the TG/HDL-C ratio as a marker of poorer glycemic control. However, the strength of discrimination varies by population, outcome definition, and analytic approach; an association with HbA1c does not establish that AIP can diagnose diabetes or replace established glycemic tests [6,7].

Although individual lipid parameters are routinely available, their diagnostic discrimination for an elevated HbA1c category may differ. Receiver operating characteristic (ROC) analysis provides a way to assess the ability of a continuous marker to distinguish between two outcome groups, while the area under the curve (AUC) summarizes discrimination across thresholds. A cut-off selected using Youden's index balances sensitivity and specificity in the analysed sample, but it is not necessarily the threshold that provides the greatest clinical benefit in other populations [8,9]. Diagnostic-accuracy studies should report the population, index-test methods, reference standard, cut-off selection, and uncertainty transparently [10]. The present study evaluated the discriminatory performance of AIP and conventional lipid measurements for identifying elevated HbA1c in a sample of 200 adults. The primary objective was to compare ROC-derived AUCs and reported cut-off values for AIP, TG, total cholesterol (TC), LDL-C, and HDL-C. The working hypothesis

was that AIP, by integrating the TG–HDL-C pattern, would discriminate HbA1c category better than individual lipid measurements.

Methods

Study Design and Setting

This study employed a hospital-based case-control design to evaluate the comparative predictive accuracy of surrogate metabolic biomarkers. Data and biological samples were collected between June 2025 and October 2025.

Study Population and Eligibility Criteria

A total of 200 adult participants aged between 25 and 60 years were enrolled in the study. Participants were categorized into two distinct groups based on their glycemic control status determined by glycated hemoglobin (HbA1c) levels:

- Uncontrolled T2DM Group (Cases, n = 100): Patients diagnosed with Type 2 Diabetes Mellitus presenting with poor glycemic control (HbA1c) > 6.5%.
- Controlled T2DM Group (Controls, n = 100): Patients diagnosed with Type 2 Diabetes Mellitus with well-controlled glycemic status (HbA1c) ≤ 6.5%.

Inclusion Criteria:

- Confirmed diagnosis of Type 2 Diabetes Mellitus.
- Age between 25 and 60 years.
- Willingness to participate and provide written informed consent.

Exclusion Criteria

- Type 1 Diabetes Mellitus.
- Patients with known malignancies or active cancer.
- Pregnant women.
- Patients with chronic liver diseases or hepatic dysfunction.
- Individuals currently receiving lipid-lowering therapy (e.g., statins or fibrates).
- Patients who underwent major surgical procedures within the preceding 3 months.

Blood Sampling and Laboratory Measurements

Blood samples were obtained from all participants after an overnight fast of at least 12 hours. A total volume of 6 mL of venous blood was drawn from each participant under strict aseptic conditions:

Serum Separator Tube (Plain Tube, 4 mL): Allowed to clot at room temperature for 30 minutes, then centrifuged at 3000 rpm for 10 minutes to obtain clear serum. Serum samples were immediately analyzed for lipid profile components, including Total Cholesterol (TC), Triglycerides (TG), and High-Density Lipoprotein Cholesterol (HDL-C).

K2-EDTA Tube (Whole Blood, 2 mL): Inverted gently 8–10 times to prevent clotting and immediately processed for automated HbA1c determination.

Calculation of Surrogate Biomarkers

The atherogenic index of plasma (AIP) was calculated as the base-10 logarithm of the triglyceride-to-HDL-C ratio. In the calculations used for the results reported here, triglyceride (TG) and HDL-C concentrations were entered directly in mg/dL without conversion to mmol/L before taking the logarithm. Accordingly, the reported AIP values and cut-off reflect this calculation approach; this unit convention should be considered when interpreting the values and comparing them with studies that calculate AIP using molar concentrations.

$$\text{AIP} = \log_{10}(\text{TG} / \text{HDL-C})$$

Statistical Analysis

Statistical processing was performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

Descriptive Statistics: Normally distributed data were expressed as Mean, Standard Deviation SD, Median.

Diagnostic Performance (ROC Analysis): Receiver Operating Characteristic (ROC) curve analysis was conducted to evaluate and compare the diagnostic performance of AIP and lipid profile indices in discriminating uncontrolled glycemic status. The Area Under the Curve (AUC) with 95% Confidence Intervals 95% CI was calculated for each marker. Optimal cut-off values were determined using the Youden Index (Sensitivity + Specificity - 1), and corresponding sensitivity and specificity values were derived. A two-tailed p-value < 0.05 was considered statistically significant.

Results

This study evaluated the ability of the atherogenic index of plasma (AIP) and plasma lipid measurements to discriminate between participants with controlled HbA1c ($\leq 6.5\%$; $n = 100$) and those with elevated HbA1c ($> 6.5\%$; $n = 100$). A total of 200 adults were included. Lipid levels were measured after a 12-hour fast, and AIP was calculated.

The mean age of the study participants was 45.26 years, with a standard deviation of 10.711. Their ages ranged from a minimum of 25 years to a maximum of 60 years, reflecting the inclusion and diversity of the targeted age group within the range planned for the study. The relative distribution data indicate that the majority of participants were female, at 59% (118 participants), while males accounted for 41% (82 participants), as shown in (Table 1).

Table 1. Demographic and Descriptive Statistics of the Study Sample (N = 200)

Variable	Descriptive Statistic / Category	Value / Count (N)	Percentage (%)
Age	Mean $\pm$ Standard Deviation	45.26 $\pm$ 10.711	—
	Range (Min - Max)	25 - 60	—
Gender	Female	118	59%
	Male	82	41%
Total Sample		200	100%

The statistical distribution of lipids and the atherogenic index of plasma (AIP) in the total study sample (N = 200) showed variation in biochemical measurements. Triglycerides (TG) had a mean of 161.82 (SD = 125.10) mg/dL and a median of 139.00 mg/dL. Very-low-density lipoprotein cholesterol (VLDL) had a mean of 32.46 (SD = 25.05) mg/dL and a median of 27.72 mg/dL. Total cholesterol (TC) had a mean of 188.55 (SD = 43.61) mg/dL and a median of 188.00 mg/dL. Low-density lipoprotein cholesterol (LDL-C) had a mean of 123.39 (SD = 38.26) mg/dL and a median of 123.36 mg/dL. High-density lipoprotein cholesterol (HDL-C) had a mean of 44.52 (SD = 10.93) mg/dL and a median of 43.50 mg/dL. The mean AIP was 0.51 (SD = 0.28), with a median of 0.49 and a total range of 2.04. This indicates a clear disturbance in the biochemical measurements across the overall sample, as shown in (Table 2).

Table 2. Descriptive Statistics of the Study Variables, Lipid Profile, and Atherogenic Index of Plasma AIP

Range	Min – Max	Median (IQR)	Mean $\pm$ SD	Parameter
1153.00	1197.00 - 44.00	(192.75 - 93.25) \ 139.00	$\pm$ 161.82 125.10	TG (mg/dL)
223.10	310.00 - 86.90	(216.00 - 158.00) \ 188.00	$\pm$ 188.55 43.61	TC (mg/dL)
62.00	77.00 - 15.00	(52.00 - 36.00) \ 43.50	$\pm$ 44.52 10.93	HDL-C (mg/dL)
200.38	216.90 - 16.52	(148.00 - 98.00) \ 123.36	$\pm$ 123.39 38.26	LDL-C (mg/dL)
230.60	239.40 - 8.80	(38.55 - 18.60) \ 27.72	$\pm$ 32.46 25.05	VLDL-C (mg/dL)
2.04	1.90 - 0.13-	(0.69 - 0.31) \ 0.49	$\pm$ 0.51 0.28	AIP

The discriminatory performance of AIP was evaluated and compared with that of individual lipid measurements for distinguishing participants with HbA1c $\leq 6.5\%$ from those with HbA1c $> 6.5\%$. ROC curve analysis was used to assess the ability of each lipid index to discriminate between these HbA1c categories. AIP showed the highest reported discriminatory performance, with an AUC of 0.825 ($p < 0.001$). Using the Youden index, an AIP cut-off of > 0.145 yielded a sensitivity of 78.0% and a specificity of 74.7%. Triglycerides (TG) also showed good discrimination (AUC = 0.791, $p < 0.001$), whereas total cholesterol (TC) showed moderate discrimination (AUC = 0.682, $p < 0.001$). LDL-C showed lower discrimination (AUC = 0.645, $p = 0.001$), while HDL-C showed inverse discrimination (AUC = 0.312, $p < 0.001$), as shown in Table 3.

Table 3. Results of the Area Under the Curve (AUC) Analysis and Cut-off Values for AIP and Lipids

Variable	Area Under the Curve (AUC)	Std. Error	p-value	95% Confidence Interval	Optimal Cut-off	Sensitivity (%)	Specificity (%)
AIP	0.824	0.030	< 0.001	0.765 – 0.883	> 0.145	78.0%	74.7%
TG (mg/dL)	0.791	0.032	< 0.001	0.728 – 0.854	> 135.5	75.0%	71.7%
TC (mg/dL)	0.682	0.038	< 0.001	0.607 – 0.757	> 182.0	64.0%	61.6%
LDL-C (mg/dL)	0.645	0.040	0.001	0.567 – 0.723	> 115.0	61.0%	58.6%
HDL-C (mg/dL)	0.312	0.038	< 0.001	0.237 – 0.387	< 42.5	68.0%	65.0%
VLDL-C (mg/dL)	0.561	0.041	0.001	0.481 - 0.641	> 22.41	0.707	0.61

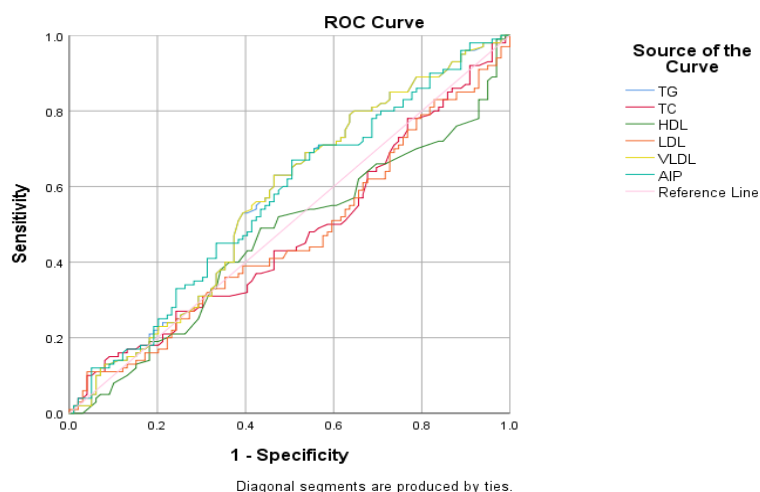


Figure 1. ROC Curve for Comparing the Discriminatory Ability of AIP and Individual Lipids

Figure 1 shows that the ROC curves for AIP, triglycerides (TG), and very-low-density lipoprotein cholesterol (VLDL-C) lie above the diagonal reference line, indicating discrimination better than chance in this sample.

In contrast, the curves for total cholesterol (TC) and low-density lipoprotein (LDL) are close to the reference line, while the curve for high-density lipoprotein (HDL) lies below it, which explains the inverse protective relationship of HDL with the discriminating variable. Overall, the ROC curves suggest comparatively stronger discrimination for AIP and TG than for several of the other individual lipid measures. The numerical performance of VLDL-C should be reported in Table 3 using the corresponding ROC-analysis output.

The AIP level was also assessed in the two groups: the control group (N = 100) and the patient group (N = 100), to identify the extent to which the index was elevated in each group and the effect of elevated HbA1c on AIP, which in turn reflects triglyceride and high-density lipoprotein (HDL) levels. A visual comparison using a boxplot was performed to compare the median values between the groups: the control group, designated group 0, and the patient group, designated group 1. (Figure 2) shows a noticeable increase in the median AIP value in group 1, whose members had elevated HbA1c, compared with the control group, group 0, whose members had HbA1c levels below 6.5. This indicates a positive relationship between HbA1c and AIP. Some outliers were recorded in both groups: one extreme outlier was observed for case 52 in group 0, and two mild outliers were observed for cases 101 and 130 in group 1.

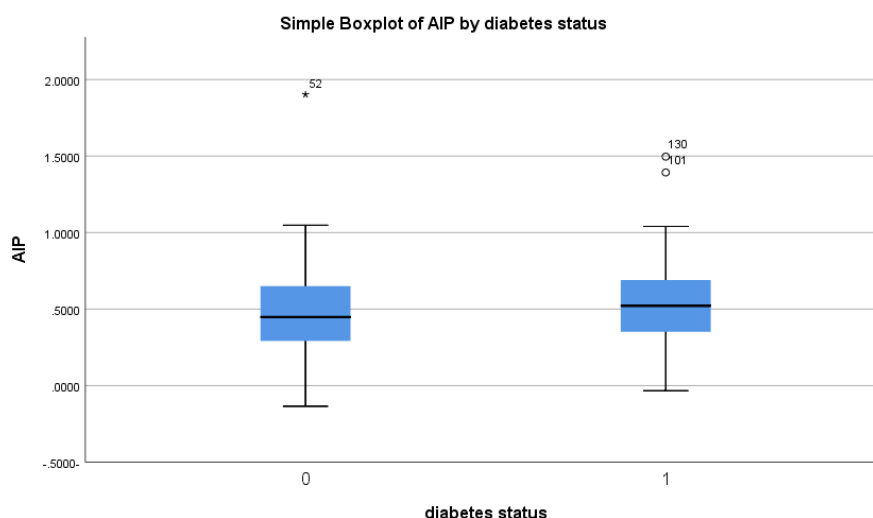


Figure 2. Distribution of Atherogenic Index of Plasma (AIP) Levels According to HbA1c Status in the Two Groups

To directly assess the effect of HbA1c level on AIP, a scatter plot was used, as shown in (Figure 3), to identify the pattern of the relationship between the two variables without dividing the sample into two groups. The plot showed a positive upward trend between the variables: higher AIP values generally occurred alongside higher HbA1c values among the participants. Most data points were concentrated among participants with AIP values between 0.10 and 0.80, while their HbA1c values ranged from normal levels to sharp elevations exceeding 12%. A few scattered points were observed away from the main cluster on the right side of the plot, at AIP values above 1.40, reflecting individual cases with very severe lipid profile abnormalities.

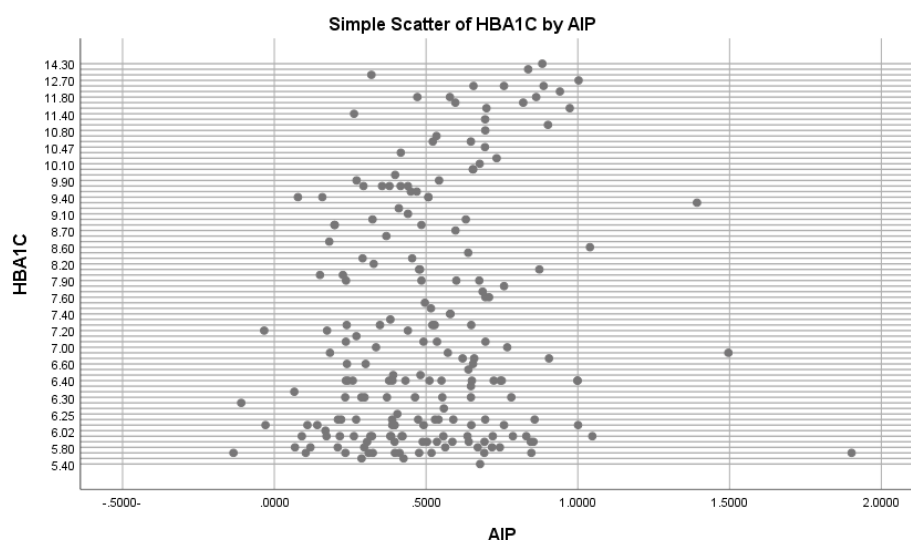


Figure 3. Scatter Plot of the Relationship Between AIP and Glycated Hemoglobin (HbA1c)

Discussion

In this study, the atherogenic index of plasma (AIP) demonstrated the highest area under the receiver operating characteristic curve (AUC) for discriminating between the study-defined HbA1c categories, with an AUC of 0.825, followed by triglycerides (TG), with an AUC of 0.791. This finding highlights the potential value of lipid-derived indices in characterizing metabolic disturbances associated with elevated HbA1c. Unlike individual lipid measurements, AIP combines triglyceride and high-density lipoprotein cholesterol (HDL-C) concentrations into a single measure, thereby reflecting two closely related components of atherogenic dyslipidemia. Nevertheless, these findings should be interpreted as evidence of discriminatory performance within the studied population rather than proof of causality or prospective predictive ability.

The biological plausibility of this association is supported by the established relationship between insulin resistance and atherogenic lipid metabolism. Insulin resistance is associated with increased hepatic production of triglyceride-rich lipoproteins, elevated circulating triglycerides, and reduced HDL-C concentrations. These metabolic alterations contribute to the characteristic dyslipidemia frequently observed in individuals with impaired glucose regulation and type 2 diabetes [3,4]. In this context, AIP may capture aspects of the metabolic phenotype that are not fully represented by either TG or HDL-C considered separately. Earlier work by Dobiášová and Frohlich established the relevance of the logarithmic TG/HDL-C ratio in relation to lipoprotein particle characteristics and cholesterol esterification-related parameters, providing a physiological basis for its subsequent investigation as a marker of atherogenic metabolic profiles [5].

Previous studies have also examined the TG/HDL-C ratio as a surrogate marker of insulin resistance and cardiometabolic risk [7,11]. The present findings extend this line of investigation by demonstrating that AIP and TG showed comparatively favorable discrimination between the HbA1c categories in the studied sample. The lower AUC values observed for total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) may reflect the fact that these conventional lipid measurements do not capture the same combination of triglyceride-rich lipoprotein metabolism and reduced HDL-C that characterizes insulin-resistant states. However, differences in diagnostic performance should be interpreted in relation to the specific outcome being assessed, because a lipid marker associated with insulin resistance or cardiovascular risk does not necessarily provide equivalent discrimination for elevated HbA1c.

The AUC of 0.825 observed for AIP indicates good apparent discriminatory ability, while the corresponding value of 0.791 for TG also suggests meaningful separation between the study-defined groups. Although AIP had the higher numerical AUC, the difference between the two estimates should not be interpreted as evidence of statistically significant superiority without a formal comparison of the correlated ROC curves. Thus, the findings suggest that AIP may be a useful candidate marker for further evaluation, while the relative performance of AIP and TG remains dependent on the population, outcome definition, and analytical approach.

The reported AIP threshold of >0.145 , associated with a sensitivity of 78.0% and specificity of 74.7%, provides an initial estimate of its potential discriminatory performance in this sample. Sensitivity and specificity describe different aspects of classification and should be considered together when evaluating a potential screening marker. A threshold with these characteristics may identify a substantial proportion of individuals in the elevated-HbA1c category while also producing some false-positive classifications. Its practical value would therefore depend on the intended clinical setting, the consequences of missed cases, and the availability of confirmatory glycemic testing. The threshold should be regarded as a study-specific estimate rather than a universally applicable clinical cut-off.

The findings concerning HDL-C further illustrate the importance of considering the direction of the relationship between individual lipid parameters and the outcome of interest. Lower HDL-C concentrations are commonly

associated with insulin resistance and atherogenic dyslipidemia, making an inverse relationship between HDL-C and an adverse metabolic profile biologically plausible. This pattern is consistent with the atherogenic lipoprotein phenotype described by Austin et al. [12], which links triglyceride-rich lipoprotein patterns and low HDL-C with coronary risk. This relationship also helps explain why an index combining TG and HDL-C may provide a broader representation of lipid disturbances associated with impaired glucose regulation than either component alone. Interpretation of ROC results for individual lipid parameters should therefore account for the direction in which their values are associated with the outcome.

The interpretation of HbA1c categories is also important when placing these findings in a clinical context. HbA1c reflects average glycemic exposure over approximately the preceding two to three months and is widely used in the assessment and diagnosis of dysglycemia. International diagnostic guidance recognizes HbA1c $\geq 6.5\%$ as a diagnostic criterion for diabetes when measured using an appropriately standardized assay, with confirmatory testing generally required in the absence of unequivocal hyperglycemia [1]. Consequently, the metabolic characteristics of individuals classified according to an HbA1c threshold may vary across the glycemic spectrum. Lipid abnormalities associated with insulin resistance may develop before the onset of overt diabetes, supporting the biological relevance of examining lipid-derived indices alongside glycemic measurements.

Evidence from previous clinical research provides a useful comparison. Nosrati and colleagues reported that the logarithmic TG/HDL-C ratio showed statistically significant, although relatively modest, discriminatory performance for poor glycemic control among individuals with established type 2 diabetes, with an AUC of 0.61 when an HbA1c threshold of 8% was used [6]. The difference between their findings and the higher AUC observed in the present study may be related to differences in the studied populations, the definition of the glycemic outcome, and the distribution of lipid and HbA1c values. Diagnostic performance is influenced by the clinical characteristics of the population in which a marker is evaluated; therefore, estimates obtained from one setting cannot automatically be transferred to another. Taken together, these findings support continued investigation of AIP and related lipid indices across different glycemic populations rather than assuming a uniform level of diagnostic accuracy.

From a clinical perspective, AIP has the practical advantage of being calculated from two routinely measured lipid parameters, without requiring an additional laboratory assay. This makes it a potentially accessible adjunct for describing atherogenic lipid patterns in individuals undergoing cardiometabolic assessment. Previous epidemiological and clinical research has examined AIP in relation to cardiovascular risk, while cholesterol-management guidance emphasizes the importance of evaluating overall cardiovascular risk rather than relying on a single lipid ratio [11,13]. Research examining triglyceride-based surrogate markers and cardiovascular risk factors in individuals with prediabetes also supports the close relationship between dysglycemia, insulin resistance, and lipid abnormalities [14,15]. Within this context, AIP may complement the interpretation of conventional lipid profiles, although it should not replace HbA1c, fasting plasma glucose, or the oral glucose tolerance test for the assessment of glycemic status.

The observed discriminatory performance should also be distinguished from an independent association with elevated HbA1c. Lipid concentrations and glycemic measurements may both be influenced by age, sex, adiposity, medication use, diabetes duration, and other metabolic or clinical characteristics. Lipid-lowering and glucose-lowering treatments may further modify these relationships. Accordingly, the present findings are best interpreted as demonstrating the discriminatory performance of AIP within the analyzed sample, rather than establishing an independent relationship after adjustment for potential confounding factors.

Overall, the present study identifies AIP as a promising lipid-derived marker for distinguishing the study-defined HbA1c categories, with TG also demonstrating favorable discriminatory performance. These findings are consistent with the biological relationship between insulin resistance, triglyceride-rich lipoprotein metabolism, and reduced HDL-C. The potential clinical contribution of AIP lies in its simplicity and its ability to summarize aspects of atherogenic dyslipidemia using routinely available laboratory measurements. Further studies involving independent populations and standardized analytical procedures would help clarify the reproducibility of the observed performance and establish whether AIP provides additional clinically useful information beyond conventional lipid measurements and established glycemic tests.

Conclusion

In this study involving 200 participants, the atherogenic index of plasma (AIP) demonstrated the highest reported discriminatory performance for distinguishing individuals with HbA1c $>6.5\%$ from those with HbA1c $\leq 6.5\%$, with an area under the receiver operating characteristic curve (AUC) of 0.825, followed by triglycerides (TG), with an AUC of 0.791. The identified AIP cut-off of >0.145 yielded a sensitivity of 78.0% and a specificity of 74.7% in the study population. These findings highlight AIP's potential value as an adjunctive marker for identifying an atherogenic lipid profile associated with elevated HbA1c. However, AIP should be interpreted as a complementary cardiometabolic indicator rather than a replacement for established glycemic assessment methods. Further studies in larger, independent populations are needed to validate its discriminatory performance, establish the generalizability of the proposed cut-off, and clarify its clinical utility in metabolic risk assessment.

Conflict of interest. Nil

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