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# Evaluation of the association between HbA1c and the Atherosclerosis Index of Plasma (AIP) in diabetic patients in Benghazi, Libya

Abdalruof S. Mabrouk<sup>1,\*</sup> , Albashir M. Yhmed<sup>1</sup>

<sup>1</sup>Medical Laboratory Department, Faculty of Medical Technology, Wadi Alshatti University, Brack, Libya

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#### KEYWORDS

HbA1c; Atherogenic index of plasma; Type 2 Diabetes; Cardiovascular Risk; Benghazi; Libya.

#### ABSTRACT

Type 2 diabetes mellitus (T2DM) is a major metabolic disorder associated with an increased risk of atherosclerosis and cardiovascular diseases. Hemoglobin A1c (HbA1c) and the Atherogenic Index of Plasma (AIP) are key biomarkers linked to the progression of cardiovascular complications in diabetic patients. This study aims to evaluate the association between HbA1c and AIP in T2DM patients in Benghazi, Libya. A cross-sectional study was conducted at Al-Tariq Hospital in city of Benghazi in the period between February and June 2024, involving 292 T2DM patients. Blood sample were collected form the patients and analyzed for Fasting blood sugar(FBS), HbA1c, total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL), low-density lipoproteins (LDL) and AIP was calculated (AIP = log10(TG/HDL-C). Data were analyzed using descriptive statistics, independent t-test, correlation analysis, and linear regression to assess the relationship between HbA1c and AIP. The findings revealed a moderate positive correlation between HbA1c and AIP (r=0.51, P<0.001), indicating that higher HbA1c levels are associated with an increased risk of atherosclerosis. Significant gender differences were observed, with male patients exhibiting higher AIP values than females. Additionally, a positive correlation was found between HbA1c and TG as well very low-density lipoproteins (VLDL), while an inverse correlationwas observed with HDL. This study demonstrates the critical role of optimal glycemic control in reducing cardiovascular risk among type 2 diabetes patients. Routine assessment of HbA1c and AIP is recommended as an essential component of comprehensive cardiovascular risk evaluation and prevention strategies.

### تقييم العلاقة بين الهيموغلوبين السكري HbA1c ومؤشر تصلب الشر ايين AIP لدى مرضى السكرى في بنغازي

 $^{2}$ عبدالرؤوف سالم مبروك  $^{1*}$ البشير محمد بن يحمد

الملخص

#### الكلمات المفتاحية

الهيموجلوبين السكري مؤشر تصلب الشرايين مرض السكري من النوع 2 مخاطر القلب والأوعية الدموية بنغازي ليبيا داء السكري من النوع الثاني (T2DM) هو أحد الاضطرابات الايضية الشائعة المرتبطة بزيادة خطر تصلب الشرايين وأمراض القلب والأوعية الدموية.. الهيموغلوبين السكري (HbA1c) ومؤشر تصلب الشرايين في البلازما (AIP) هما علامتان حيويتان ترتبطان بتطور المضاعفات القلبية الوعائية لدى مرضى السكري من الجنسين. تهدف هذه الدراسة إلى تقييم العلاقة بين HbA1c و AIP في مرضى السكري من النوع الثاني في بنغازي- ليبيا. أُجريت هذه الدراسة المقطعية في مستشفى الطارق بمدينة بنغازي خلال الفترة من فبراير إلى يونيو 2024، وشملت 292 مريضًا مصابًا بداء السكري من النوع الثاني. تم تحليل عينات دم صائم لقياس كل من AIP ، ThbA1c ، TG ،TC إلى يونيو 2024، وشملت 292 مريضًا مصابًا بداء السكري من النوع الثاني. تم تحليل البيانات باستخدام الإحصاءات الوصفية، اختبار T للعينة المستقلة، تحليل الارتباط، والانحدار الخطي لتقييم العلاقة بين AIP وAIP ، أظهرت النتائج وجود ارتباط إيجابي بين AIP المحادات الوصفية، اختبار بين المخلوب الشرايين. لوحظت الخلافات كبيرة بين الجنسين، حيث أظهر المرضى الذكور قيم AIP أعلى من الإناث بالإضافة إلى ذلك، وُجدت علاقة إيجابية بين AIP المكري من النوع الثاني. يوصى بتقييم VLDL ، LDL ، AIP وفيعة الدموية بين مرضى السكري من النوع الثاني. يوصى بتقييم المخاطر القلب والأوعية الدموية بين مرضى السكري من النوع الثاني. يوصى بتقييم المخاطر القلبية الوعائية الشامل واستراتيجيات الوقاية.

#### Introduction

Diabetes mellitus(DM),is a group of disorders characterized by chronic hyperglycemia due to defects in insulin secretion, insulin action, or both, significantly impacts carbohydrate metabolism. Insulin, a vital anabolic hormone, when deficient, leads to various metabolic abnormalities in proteins, lipids, and carbohydrates [1].

A rapidly expanding worldwide public health issue, T2DM has a substantial impact on healthcare systems, economic stability, human health, and quality of life. Approximately 425 million persons worldwide today have DM, according to

the International Diabetes Federation (IDF). This number is expected to increase to 629 million by 2045, with an additional 352 million people at risk of having DM [2].

Hyperglycemia, hyperinsulinemia, protein glycation, and oxidative stress are characteristics of uncontrolled diabetic patients that lead to the early development of diabetes complications. Long-term harm, malfunction, and failure of many organs, including the heart, blood vessels, kidneys, eyes, and nerves, are linked to chronic hyperglycemia [3-7]. Because DMcauses dyslipidemia, which leads to an atherogenic lipid profile, it raises the risk of atherosclerotic vascular disease. Compared to people without diabetes, this profile considerably increases their risk of cardiovascular disease CVD [8].

Atherosclerosis is characterized by abnormal lipid metabolism, which is a significant risk factor and clinical characteristic. Numerous researches have looked to the possible links between diabetes and atherosclerosis, focusing on altered metabolic pathways. Both kinds of DMcan cause or accelerate the progression of atherosclerosis. Elevated glucose levels, dyslipidemia, and other metabolic associated changes play an important role in the development of atherosclerosis at almost every stage of the disease. Aside from these factors, DMand atherosclerosis share pathological pathways, such as chronic inflammation and endothelial activation caused by disrupted blood flow, mitochondrial oxidative stress, changes in extracellular matrix components, and disruptions in cellular defense systems. These shared pathways highlight the complex interplay between these two chronic disorders, emphasizing the need for comprehensive management strategies to mitigate their combined impact on cardiovascular health [9,10].

The World Health Organization (WHO) and the American Diabetes Association (ADA) defineHbA1c, as an average blood glucose concentration during the previous 2-3 months. It is generated when glucose in the blood interacts with hemoglobin in red blood cells. HbA1c is a reliable test for diagnosing diabetes and tracking long-term blood glucose control [11, 12]. In recent years, AIP has received increasing attention as a reliable indicator of cardiovascular risk, particularly in diabetic populations. Studies have shown a strong correlation between AIP and coronary artery disease, and some evidence suggests that it may outperform conventional lipid parameters in predicting cardiovascular events [13-15].

Several investigations have explored the relationship between HbA1c and dyslipidemia in individuals with T2DM [3,7] reported significant associations between poor glycemic control and elevated lipid parameters. Likewise, previous studies highlighted HbA1c as a predictor of dyslipidemia [16,17]. Whileother studies further support this correlation in diverse populations [18-19].

Given the pathophysiological links and clinical relevance of both HbA1c and AIP in diabetic patients, this study aims to investigate the association between these two markers among individuals with T2DM attending Al-Tariq Hospital in Benghazi, Libya.

#### **Materials and Methods**

#### **Study Design**

This study was conducted at Al-Tariq Hospital in Benghazi, Libya, from February to June 2024, and included 292 patients with T2DM, aged between 39 and 80 years, of whom 91 were females and 201 were males. All participants were selected based on the criteria that they did not have any other chronic diseases or diabetes-related complications.

Blood samples were collected after a fasting period of at least 10 hours using plain tubes and EDTA tubes. Serum was separated from the blood cells collected in the plain tubes using a centrifuge at 3000 RPM for 10 minutes. The concentrations of FBS, TG, TC, HDL and LDL were measured using an automated method with the XL-200ERBA analyzer. VLDL were calculated using the formula (VLDL = TG/5). HbA1c levels were measured in the EDTA tubes using high-performance liquid chromatography (HPLC) on the HLC-723(GX) analyzer from TOSOH.TheAIP was subsequently calculated using the formula:AIP = log10(TG / HDL-C).Additionally, the LDL/HDL ratio was calculated (LDL/HDL ratio = LDL / HDL).

#### **Statistical Analysis**

Data were entered and analyzed using SPSS version 29. Participants were divided into two groups based on glycated hemoglobin (HbA1c) levels: one group with good glycemic control (HbA1c < 7%) and other with poor glycemic control (HbA1c > 7%). Results were reported as percentages, means, and standard deviations to compare variables between groups. Pearson's correlation test was conducted to assess the relationship between the AIP, HbA1c, lipid profile, and FBS, linear regression between AIP with HbA1c. Additionally, an independent sample t-Test was performed. Statistical significance was determined at P-values below 0.05, with a confidence interval of 95%.

#### Results

Participants were classified into two groups based on their HbA1c levels. The first group, which included 148 participants (50.7%), had good glycemic control (HbA1c <7%), while the second group, comprising 144 participants (49.3%), had poor glycemic control (HbA1c>7%). Statistically significant differences were observed between the two groups in terms of AIP, HDL, VLDL, TG, and FBS, indicating that these variables have a significant impact on HbA1c levels. Conversely, no statistically significant differences were found for TC and LDL(Table1).

**Table 1:** Comparison basic characteristics of T2DM patients according to their glycemic control (HbA1c)

	HbA1c < 7% (148n)	HbA1c >7% (144n)	
Parameter	Mean±Std. Deviation		P - Value
FBS(mg/dl)	120.38±25.032	192.97±65.620	< 0.001*
TC(mg/dl)	$177.99 \pm 40.055$	174.43±41.456	< 0.456
TG(mg/dl)	119.67±36.61	$185.16 \pm 78.72$	< 0.001*
HDL(mg/dl)	$48.91 \pm 12.476$	$41.12 \pm 10.292$	< 0.001*
LDL(mg/dl)	109.20±34.429	$105.53\pm37.605$	< 0.386
VLDL(mg/dl)	23.93±7.324	$37.03\pm15.744$	< 0.001*
AIP(mg/dl)	$0.229 \pm 0.196$	$0.278 \pm 0.205$	< 0.001*

\* P < 0.001- highly significant

The basic characteristics of the participants were analyzed and compared according to gender. Results indicated that females had significantly higher values for TC and HDL compared to males. Conversely, males exhibited significantly higher values for age, FBS, AIP and the LDL/HDL ratio as shown in Table 2.

The study demonstrated a moderate positive correlation between HbA1c and AIP,TG,VLDL, and FBS. Additionally, it showed an inverse correlation between HbA1c and HDL as illustrated in Table 3.

The linear regression analysis results indicate a positive association between HbA1c values and the AIP (Figure 1).

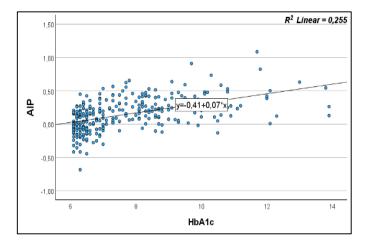
**Table 2:** Gender-wise comparison of basic characteristics of type 2 diabetes mellitus patients.

	Females (N=91)	Males (N=201)	
Parameters	Mean ± SD		p-value
Age (yrs)	67.49±7.54	71.20±7.45	<0.001*
HbA1c (%)	$7.59\pm1.52$	$7.77 \pm 1.74$	0.380
FBS (mg\dl)	145.03±52.58	161.43±64.39	0.034*
TC (mg\dl)	$183.88 \pm 41.10$	$172.78\pm40.18$	0.031*
TG (mg\dl)	151.89±60.21	152.0±73.15	0.990
HDL (mg\dl)	50.58±12.03	42.57±11.27	<0.001*
LDL (mg\dl)	110.34±38.24	106.07±34.89	0.348
$VLDL\ (mg\backslash dl)$	30.38±12.04	30.40±14.63	0.990
LDL/HDL	$2.29\pm0.90$	$2.62\pm0.98$	0.007*
AIP	0.1026±0.222	$0.1698 \pm 0.243$	0.025*

<sup>\*</sup> Significant P-value < 0.05

**Table 3:** Correlation of HbA1c with AIP FBS and lipid profile.

		r r
Parameters	r- value	P- value
FBS(mg/dl)	0.74	< 0.001
TG(mg/dl)	0.49	< 0.001
HDL(mg/dl)	-0.30	< 0.001
VLDL(mg/dl)	0.50	< 0.001
AIP	0.51	< 0.001



**Fig. 1:** Relationship between HbA1c levels and AIP with linear regression line and confidence intervals.

#### **Discussion**

The current study showed clear differences between patients with good HbA1c control (<7%) and those with elevated HbA1c levels (>7%). The results indicated that the poorly controlled group had significantly higher AIP, TG, and VLDL levels, along with lower HDL levels. This is consistent with several studies which demonstrated that poor glycemic control is associated with increased lipid profileimbalance and cardiovascular disease risk [18-19,21-23]. Chronic hyperglycemia, as reflected by elevated HbA1c levels, triggers several pathophysiological mechanisms contributing to atherosclerosis, including non-enzymatic glycation of proteins, oxidative stress, chronic inflammation, and endothelial dysfunction. Additionally, hyperglycemia enhances hepatic synthesis of atherogenic lipoproteins such as TG and VLDL and reduces HDL production, collectively aggravating atherosclerotic progression. Studies have confirmed a strong correlation between HbA1c control and improved lipid ratios [16,18].

The findings of the present study reveal significant gender-based differences in baseline biochemical parameters among patients with T2DM. Female participants exhibited significantly higher levels of TC andHDL, whereas male patients had elevated levels of FBS, AIP, and LDL/HDL ratio. These outcomes are consistent with those reported by Nnakenyi et al. [24], suggesting that women may have a physiological advantage due to higher HDL levels, which are known to exert protective effects against atherosclerosis. From a physiological perspective, these differences can be attributed to hormonal influences, particularly the role of estrogen, which has been shown to increase HDL concentrations and improve lipid metabolism, thus reducing the risk of atherogenesis [10].

The study results also indicated a moderate positive correlation between HbA1c andAIP, along with its association with TG and VLDL, and an inverse relationship with HDLThese findings suggest that HbA1c can serve as a valuable predictor for atherosclerotic risk in patients with T2DM, supporting previous research [3,8,19,21,22, 25,26].

Moreover, previous studies highlighted the role of HbA1c as a robust biomarker for lipid abnormalities, demonstrating significant associations with elevated TG and reduced HDL levels [22,27]. These results reinforce the role of HbA1c in modulating metabolic parameters closely related to atherosclerosis. Other studies shown that diabetic patients have dense atherosclerotic plaques compared to non-diabetic, further emphasizing the connection between poor glycemic control and vascular pathology [16, 28].

Additionally, chronic inflammatory processes and oxidative stress are closely associated with elevated HbA1c, lead to increased oxidation of LDL, exacerbating vascular damage and atherosclerosis development. This correlation reflects the physiological mechanisms linking inadequate glucose control and arterial disorders [1,10].

Finally, the study showed a moderate linear correlation between the AIP and HbA1c levels, with the regression equation indicating that each unit increase in HbA1c is associated with a 0.07 increase in AIP value (AIP = 0.41 +  $0.07 \times \text{HbA1c}$ ). This correlation suggests that elevated HbA1c directly impacts increasing atherosclerosis risks by affecting the balance between atherogenic and antiatherogenic factors. Moreover, the coefficient determination (R<sup>2</sup>) of 0.255 suggests that approximately 25.5% of the variability in AIP can be explained by HbA1c levels. While this underscores the pivotal role of HbA1c in influencing lipid-related atherogenic risk, it also highlights the contribution of other factors such as inflammation, oxidative stress, and disturbances in lipid metabolism. These findings are consistent with Verma [21], who conducted a similar analysis to determine the relationship between HbA1c and AIP in T2DM. The study found a positive relationship between HbA1c and AIP. The study emphasized the importance of HbA1c as a crucial marker in assessing vascular risk, showing that patients with higher HbA1c levels were more likely to have elevated AIP values.

#### Conclusion

This study concludes that patients with poorglycemic control have an atherogenic lipid profile. Indicatingthat HbA1c is a predictive tool for dyslipidemia and atherosclerosis in T2DMpatients.AIP is an independent marker significantly associated with cardiovascular risk. The study emphasizes the importance of AIP as a complementary tool for cardiovascular riskassessment, providing valuable insights for developing therapeutic strategies aimed at improving

diabetesmanagement and reducing associated cardiovascular complications.

#### Recommendations

- 1. Enhancing good HbA1c control.
- 2. Implementing routine monitoring of AIP.
- 3. Enhancing patient health education.
- Encouraging Early Screening for patients at risk of atherosclerosis and cardiovascular diseases.

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