

## Original Article

## Association of the Atherogenic Index of Plasma with Glomerular Filtration Rate and Albuminuria: A Discriminatory Biomarker for Diabetic Nephropathy

Iqra Sarwar<sup>1</sup>, Palvasha Waheed<sup>2</sup>, Ayesha Sanam<sup>3</sup>, Amir Rashid<sup>4</sup>, Zunaira Ali Baiq<sup>5</sup>

**Contributions:**

IS PW AS - Conception, Design  
IS PW AR ZAB - Acquisition, Analysis, Interpretation  
IS PW - Drafting  
IS PW AS AR ZAB - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

**Conflicts of Interest:** None

**Financial Support:** None to report

**Potential Competing Interests:**

None to report

**Disclaimer:** This study has not been published or submitted elsewhere for publication.

**AI Disclosure:** Artificial intelligence tools were used solely for language refinement and formatting. No AI tools were used for data analysis, interpretation, or result generation. All scientific content, analyses, and conclusions were developed and verified by the authors, who took full responsibility for the integrity and accuracy of the work.

**Data Availability Statement:** The data supporting the findings of this study are available from the corresponding author upon reasonable request.

**Institutional Review Board****Approval**

05/2025/454

04-06-2025

Army Medical College, Rawalpindi

Review began 06/01/2026

Review ended 04/06/2026

Published 30/06/2026

© Copyright 2026

Sarwar et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY-SA 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



**How to cite this article:** Sarwar I, Waheed P, Sanam A, Rashid A, Baig ZA. Association of the Atherogenic Index of Plasma with Glomerular Filtration Rate and Albuminuria: A Discriminatory Biomarker for Diabetic Nephropathy. JRMC. 2026 Jun. 30;30(2).

<https://doi.org/10.37939/jrmc.v30i2.3157>

**Abstract**

**Objective:** To assess AIP as an independent predictor of eGFR and a discriminating biomarker for DN, this study compared AIP and other measures among patients with nephropathy (DN), those without nephropathy (DM), and healthy controls (HC).

**Methods:** Following ethical approval, a comparative cross-sectional study was conducted at a tertiary care hospital in Rawalpindi, Pakistan. The study enrolled 309 participants (103 DN, 103 DM, and 103 HC subjects). ANOVA/Kruskal-Wallis tests were used to evaluate anthropometric, metabolic (HbA1c, lipid profile, AIP), and renal parameters (urea, creatinine, eGFR, UACR). Spearman's rank test was used to evaluate the correlations. Multivariate linear regression models were constructed to identify the independent variables of eGFR and UACR. Receiver Operating Characteristic (ROC) curve analysis was used to assess the discriminating capacity of AIP for DN.

**Results:** The mean AIP was substantially greater in the DN group [mean (SD): 0.339 (0.358)] than in the DM [-0.03 (0.25)] and HC [-0.11 (0.021)] groups ( $P < 0.001$ ). AIP was significantly positively correlated with UACR ( $\rho = 0.370$ ,  $p < 0.001$ ) and negatively correlated with eGFR ( $\rho = -0.491$ ,  $p < 0.001$ ). After controlling covariates, AIP was a significant independent negative predictor of eGFR in the multivariate analysis ( $\beta = -0.091$ ,  $P = 0.008$ ). With an ideal threshold of -0.01 (sensitivity, 86.4% (89/103); specificity, 62.1% (128/206)), the ROC curve showed that AIP effectively distinguished DN from non-nephropathy participants (AUC = 0.828,  $P < 0.001$ ).

**Conclusions:** AIP is an independent inverse predictor of renal function and markedly increased in diabetic nephropathy. It has a high degree of discriminating capacity for recognising DN, indicating that it may be useful as an easy-to-use, reasonably priced biomarker for risk assessment in patients with diabetes.

**Keywords:** Diabetic Nephropathies; Dyslipidemias; Glomerular Filtration Rate; Albuminuria; Biomarkers; Diabetes Mellitus Type 2

**Introduction**

Diabetic nephropathy (DN) is one of the most common and severe microvascular consequences of type 2 Diabetes Mellitus (T2DM) and a major global cause of end-stage renal disease (ESRD).<sup>1</sup> Chronic hyperglycaemia, haemodynamic abnormalities, and genetic susceptibility are all part of its complex aetiology.<sup>2</sup> The variation in the course of renal illness among adults with diabetes remains only partially explained by conventional risk factors.<sup>3</sup>

Dyslipidaemia significantly contributes to the onset and advancement of diabetic nephropathy, in addition to glycaemic management.<sup>4</sup> High triglyceride (TG) levels, low high-density lipoprotein cholesterol (HDL-C) levels, and dense LDL particles are characteristics of the "atherogenic dyslipidemia" phenotype, which is prevalent in type 2 diabetes and is closely associated with renal and cardiovascular impairment.<sup>5</sup> A composite and powerful indicator of this atherogenic lipid profile is the Atherogenic Index of Plasma (AIP), which is defined as the base-10 logarithm of the ratio of triglyceride to HDL-C ( $\log_{10}(\text{TG}/\text{HDL-C})$ ).<sup>6</sup> It is a powerful indicator of cardiovascular events and represents the equilibrium between proatherogenic and anti-atherogenic lipid particles.<sup>7</sup>

As an integrated metric, AIP may offer a better evaluation of cardiovascular and renal risks, even if the relationship between separate lipid fractions and renal illness has been investigated. AIP's function of AIP as an independent predictor and a diagnostic discriminator for established DN versus simple diabetes requires further confirmation, notwithstanding recent data linking it to microalbuminuria or decreased eGFR in diabetic populations.<sup>8</sup>

The objectives of this study were to, compare AIP with other metabolic and renal indices among patients with DN, T2DM without nephropathy, and healthy controls; and examine the relationship between AIP and important renal function markers (eGFR and UACR); and ascertain whether AIP is an independent predictor of eGFR and UACR after controlling for confounding variables; and assess the diagnostic utility of AIP in differentiating DN from non-nephropathy states.

## Materials And Methods

Between March and August 2025, a comparative cross-sectional case-control study was conducted at a tertiary care hospital in Rawalpindi, Pakistan. Biochemical data from a parent cohort that was previously examined for renal metabolic characteristics were used in this investigation. The institute's Ethical Review Committee (ERC ID No:05/2025/454) granted ethical approval, guaranteeing adherence to both institutional policies and the tenets of the Declaration of Helsinki. Before the collection of data and samples, each participant provided written informed consent using bilingual consent forms in both Urdu and English that had been authorised by the ethics committee.<sup>9</sup>

Using predetermined inclusion and exclusion criteria, a non-probability purposive selection technique was used to identify participants. The final sample comprised 309 participants, split equally into three groups: 103 patients with T2DM, 103 patients with diabetic nephropathy, and 103 healthy controls with no known renal or metabolic conditions. The sample size was calculated using OpenEpi version 2.3, based on a 95% confidence interval, a margin of error of 5%, and a population proportion of 27%.<sup>10</sup> Participants were recruited into three groups, with 103 participants in each group.

The patients included in the study are,

Group IA – Type 2 Diabetes Mellitus Patients:

Diagnosed T2DM per ADA criteria (HbA1c  $\geq 6.5\%$  [ $\geq 48$  mmol/mol]), age 40–90 years, normal renal function (urea 1.8–7.3 mmol/L; creatinine: men 61.9–114.9  $\mu\text{mol/L}$ , women 53–97.2  $\mu\text{mol/L}$ ).

Group IB – Diabetic Nephropathy Patients:

Diagnosed T2DM per ADA criteria (HbA1c  $\geq 6.5\%$ ); age 40–90 years; normal-sized, bilaterally equal kidneys; diabetic nephropathy confirmed by a nephrologist (CKD stages 3a–5 per KDIGO criteria: persistent UACR  $>30$  mg/g and/or eGFR  $<60$  mL/min/1.73 m<sup>2</sup>).

Group II – Healthy Controls:

Healthy individuals aged 40–90 years; HbA1c  $\leq 5.7\%$  (ADA criteria); normal fasting blood glucose; normal urea (1.8–7.3 mmol/L) and creatinine (men 61.9–114.9  $\mu\text{mol/L}$ ; women 53–97.2  $\mu\text{mol/L}$ ); no known diabetes or renal disease.

The patients excluded from the study are:

Groups IA and IB (T2DM and DN patients):

Hypertensive retinopathy, ischaemic heart disease (IHD) leading to cardiorenal syndrome (CRS), type 1 diabetes mellitus, autoimmune disorders, and liver disorders. Additionally, Group IB included small-sized kidneys, solitary kidneys or solitary functioning kidneys, and nephrolithiasis.

Group II (Healthy controls):

Diagnosed type 1 or type 2 diabetes mellitus; any malignancy.

Anthropometric and demographic information, including age, sex, height, and weight, was documented. Weight (kg) divided by height (m<sup>2</sup>) yields the Body Mass Index (BMI). Fasting venous blood samples were collected for analysis.

- Glycaemic Control: High-Performance Liquid Chromatography (HPLC) was used to quantify glycated haemoglobin (HbA1c) (Roche Cobas 501).
- Lipid Profile: Enzymatic colorimetric techniques were used to assess HDL-C, total cholesterol, and triglyceride (TG) levels (Roche Cobas c311). The Friedewald formula was used to determine the LDL-C level.
- The Atherogenic Index of Plasma (AIP) was computed as  $\log_{10}(\text{TG} [\text{mmol/L}] / \text{HDL-C} [\text{mmol/L}])$ .
- Renal Function Tests: Blood Urea Nitrogen (BUN), creatinine, and serum urea levels were assessed. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI 2021) equation was used to determine the estimated glomerular filtration rate (eGFR). The Urinary Albumin-to-Creatinine Ratio (UACR) was calculated using a spot urine sample.

IBM SPSS Statistics version 25 was used for data analysis. Continuous variables with a normal distribution are expressed as mean (SD); non-normally distributed variables are reported as median [IQR]. The Shapiro-Wilk test and

Q-Q plots were used to assess the normality of continuous variables prior to statistical test selection. To compare the three groups:

- For regularly distributed data, one-way ANOVA was employed
- For non-normally distributed variables, the Kruskal-Wallis H test was employed

To find intergroup differences, post-hoc analyses (Bonferroni-adjusted pairwise comparisons for Kruskal-Wallis; Tukey HSD for ANOVA) were carried out. The Chi-square test was used to compare categorical data, such as sex. The association between AIP, eGFR, and UACR was evaluated using Spearman's rank correlation coefficient ( $\rho$ ). AIP, age, sex, BMI, HbA1c, serum creatinine, and UACR (in the eGFR model) were all identified as independent predictors of UACR and eGFR using multivariable linear regression analysis. The absence of multicollinearity was verified by ensuring that the Variance Inflation Factor (VIF) was  $< 5$ . Receiver Operating Characteristic (ROC) curve analysis was used to assess AIP's diagnostic performance in detecting DN, and the Youden Index (J) was used to determine the optimal cutoff. Statistical significance was defined as a p-value of less than 0.05.

## Results

### Demographic and clinical parameters

A total of 309 participants were included in the study and divided into three groups: Diabetic Nephropathy (DN, n = 103), Diabetes Mellitus without nephropathy (DM, n = 103), and Healthy Control (HC, n = 103). Table 1 summarises the baseline characteristics of the study participants.

**Table No 1: Demographic and Clinical Parameters Characteristics**

| Variable                         | DN, n = 103            | DM, n = 103             | HC, n = 103              | P value      |
|----------------------------------|------------------------|-------------------------|--------------------------|--------------|
| Female, n (%)                    | 13 (12.6)              | 49 (47.6)               | 91 (88.3)                | $P < 0.001$  |
| Male, n (%)                      | 90 (87.4)              | 54 (52.4)               | 12 (11.7)                |              |
| Age, years                       | 65.00 [60.00 to 73.00] | 56.00 [48.00 to 63.00]  | 48.00 [43.00 to 57.50]   | $P < 0.001$  |
| BMI, kg/m <sup>2</sup>           | 26.84 (4.06)           | 26.22 (3.36)            | 26.63 (2.64)             | $P = 0.4157$ |
| HbA1c, %                         | 7.53 [6.82 to 8.87]    | 8.81 [7.24 to 10.55]    | 5.65 [5.38 to 5.95]      | $P < 0.001$  |
| Triglycerides, mmol/L            | 2.35 [1.67 to 3.50]    | 2.30 [1.77 to 3.75]     | 2.01 [1.44 to 2.76]      | $P = 0.0300$ |
| Total cholesterol, mol/L         | 3.62 [2.94 to 4.38]    | 4.53 [3.91 to 5.19]     | 4.67 [3.74 to 5.42]      | $P < 0.001$  |
| LDL, mmol/L                      | 1.21 [0.91 to 1.93]    | 1.07 [0.90 to 1.23]     | 1.23 [1.04 to 1.46]      | $P = 0.0019$ |
| HDL, mmol/L                      | 0.98 [0.83 to 1.56]    | 2.80 [2.09 to 3.45]     | 2.83 [2.34 to 3.46]      | $P < 0.001$  |
| Urea, mmol/L                     | 10.60 [7.76 to 14.10]  | 4.33 [3.69 to 5.20]     | 3.55 [2.88 to 4.51]      | $P < 0.001$  |
| Creatinine, $\mu$ mol/L          | 199.0 [145.0 to 291.0] | 79.90 [65.20 to 90.50]  | 62.00 [54.15 to 77.25]   | $P < 0.001$  |
| UACR, mg/g                       | 4.00 [1.00 to 43.00]   | 1.00 [1.00 to 1.50]     | 1.00 [1.00 to 1.00]      | $P < 0.001$  |
| BUN, mmol/L                      | 4.95 [3.62 to 6.58]    | 2.01 [1.68 to 2.43]     | 1.65 [1.33 to 2.10]      | $P < 0.001$  |
| eGFR, mL/min/1.73 m <sup>2</sup> | 30.00 [19.00 to 46.50] | 89.0 [73.5 to 100.0]    | 101.0 [88.0 to 111.0]    | $P < 0.001$  |
| AIP                              | 0.301 [0.112 to 0.577] | -0.024 [-0.25 to 0.116] | -0.163 [-0.276 to 0.015] | $P < 0.001$  |

Abbreviations: DN, diabetic nephropathy; DM, diabetes mellitus without nephropathy; HC, healthy control; BMI, body mass index; HbA1c, glycated haemoglobin; TG, triglycerides; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; AIP, Atherogenic Index of Plasma [ $\log_{10}(\text{TG}/\text{HDL-C})$ ]; UACR, urinary albumin-to-creatinine ratio; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate (CKD-EPI 2021 equation). Data are presented as median (Q1–Q3) for non-normally distributed variables and mean  $\pm$  standard deviation for normally distributed variables. Categorical variables are expressed as frequency (percentage). The Mann–Whitney U test was used to compare continuous variables, and the chi-square test was used to compare categorical variables. A p-value  $< 0.05$  was considered statistically significant.

Using the chi-square test, a significant difference in sex distribution was found ( $P < 0.001$ ), with a female preponderance in the HC group and male predominance in the DN group. The DN group was the oldest (65.28 (8.99) years), followed by the DM group (56.06 (9.87) years) and the HC group (51.30 (10.34) years). The mean age also varied substantially ( $P < 0.001$ ). The body mass index (BMI) was similar across all three groups ( $P = 0.416$ ). no significant pairwise differences in BMI were found by post-hoc comparisons (DN vs. DM,  $P = 0.394$ ; DN vs. HC,  $P = 0.898$ ; DM vs. HC,  $P = 0.665$ ).

Table 2 displays the metabolic characteristics of the three groups. As expected, glycaemic control was poorer in both diabetes groups than in the controls ( $P < 0.001$ ). The DN group exhibited considerable dyslipidaemia, as indicated by the lipid profile. The DN group had the highest triglyceride (TG) levels (2.95 (2.07) mmol/L;  $p < 0.001$ ). Compared with the DM and HC groups, the DN group had considerably lower HDL (1.37 (0.98) mmol/L) and significantly

higher LDL (1.49 (0.81) mmol/L) ( $P < 0.001$ ). The Atherogenic Index of Plasma (AIP) was substantially higher in the DN group [mean (SD): 0.339 (0.358)] than in the DM [-0.03 (0.25)] and HC [-0.11 (0.021)] groups ( $P < 0.001$ ).

The DN group showed substantial deterioration in renal function, as shown in Table 3. The DN group had significantly higher amounts of urea and serum creatinine (12.06 (7.04) mmol/L and 252.6 (158.03)  $\mu\text{mol/L}$ , respectively) than the DM and HC groups ( $P < 0.001$ ). The DN group had the highest values of the Urinary Albumin-to-Creatinine Ratio (UACR), which showed a steep gradient (39.16 (66.52) mg/g). The estimated Glomerular Filtration Rate (eGFR) was significantly decreased in the DN group (31.48 (15.01) mL/min/1.73 m<sup>2</sup>), suggesting stage 3-4 chronic kidney disease, but it was maintained in the DM (87.56 (16.00) mL/min/1.73 m<sup>2</sup>) and HC groups (98.84 (16.71) mL/min/1.73 m<sup>2</sup>) ( $P < 0.001$ ).

The association between the Atherogenic Index of Plasma (AIP), estimated glomerular filtration rate (eGFR), and urine albumin-to-creatinine ratio (UACR) across all study participants ( $n = 309$ ) was assessed using Spearman's rank correlation analysis. According to Spearman's correlation analysis, higher atherogenicity was linked to lower renal function (Table 4), which showed a strong negative connection between AIP and eGFR ( $\rho = -0.491$ ,  $P < 0.001$ ). AIP was strongly positive correlated with UACR ( $\rho = 0.370$ ,  $P < 0.001$ ), indicating that elevated albuminuria is associated with higher AIP levels. An inverse correlation was also observed between eGFR and UACR ( $\rho = -0.427$ ,  $P < 0.001$ ), supporting the idea that deteriorating metabolic dysregulation is linked to progressive renal impairment.

**Table 2: Spearman's correlation between Atherogenic Index of Plasma (AIP) and renal parameters**

| Variables                         | AIP    | eGFR (mL/min/1.73m <sup>2</sup> ) | UACR (mg/g) |
|-----------------------------------|--------|-----------------------------------|-------------|
| AIP                               | 1.000  | -0.491                            | 0.370       |
| eGFR (mL/min/1.73m <sup>2</sup> ) | -0.491 | 1.000                             | -0.427      |
| UACR (mg/g)                       | 0.370  | -0.427                            | 1.000       |
| p value                           | —      | $P < 0.001$                       | $P < 0.001$ |

To identify independent predictors, two multivariable linear regression models were constructed.

To find independent predictors of the Urinary Albumin-to-Creatinine Ratio (UACR), a multivariable linear regression was used. The model identified several significant independent variables after controlling for AIP, serum creatinine, HbA1c, BMI, age, body weight, and eGFR (Table 5). In particular, greater serum creatinine ( $\beta = 0.176$ , 95% CI: 0.001 to 0.119,  $P = 0.048$ ) and lower eGFR ( $\beta = -0.333$ , 95% CI: -0.687 to -0.157,  $P = 0.002$ ) were linked to higher UACR levels. Male sex ( $\beta = 0.155$ , 95% CI: 2.426 to 23.864,  $P = 0.016$ ) was also a significant predictor, meaning that being male was linked to a greater UACR than being female. In this model, the Atherogenic Index of Plasma (AIP) was not a statistically significant independent predictor of UACR ( $\beta = 0.066$ , 95% CI: -7.515 to 23.655,  $P = 0.309$ ). All Variance Inflation Factor (VIF) values were less than 5, indicating no multicollinearity.

**Table 3: Multivariable Linear Regression Analysis for Predictors of Urinary Albumin-to-Creatinine Ratio (UACR)**

| Predictor Variable                     | B (Unstandardized Coefficient) | SE     | $\beta$ (Standardized) | t      | p value     | 95% CI for B      | VIF   |
|--|--------------------------------|--------|------------------------|--------|-------------|-------------------|-------|
| Constant                               | 25.127                         | 30.469 | —                      | 0.825  | $p = 0.410$ | -34.833 to 85.086 | —     |
| Atherogenic Index of Plasma (AIP)      | 8.070                          | 7.919  | 0.066                  | 1.019  | $p = 0.309$ | -7.515 to 23.655  | 1.569 |
| Serum Creatinine ( $\mu\text{mol/L}$ ) | 0.060                          | 0.030  | 0.176                  | 1.988  | $p = 0.047$ | 0.001 to 0.119    | 2.929 |
| HbA1c (%)                              | 1.713                          | 1.128  | 0.085                  | 1.518  | $p = 0.130$ | -0.507 to 3.932   | 1.168 |
| BMI (kg/m <sup>2</sup> )               | 0.129                          | 1.173  | 0.010                  | 0.110  | $p = 0.912$ | -2.180 to 2.438   | 3.297 |
| Age (years)                            | -0.358                         | 0.242  | -0.096                 | -1.479 | $p = 0.140$ | -0.835 to 0.118   | 1.555 |
| Body Weight (kg)                       | -0.043                         | 0.393  | -0.011                 | -0.109 | $p = 0.913$ | -0.816 to 0.730   | 3.533 |
| eGFR (mL/min/1.73 m <sup>2</sup> )     | -0.422                         | 0.135  | -0.333                 | -3.134 | $p = 0.001$ | -0.687 to -0.157  | 4.218 |
| Sex (male = 1, female = 0)             | 13.145                         | 5.447  | 0.155                  | 2.413  | $p = 0.016$ | 2.426 to 23.864   | 1.541 |

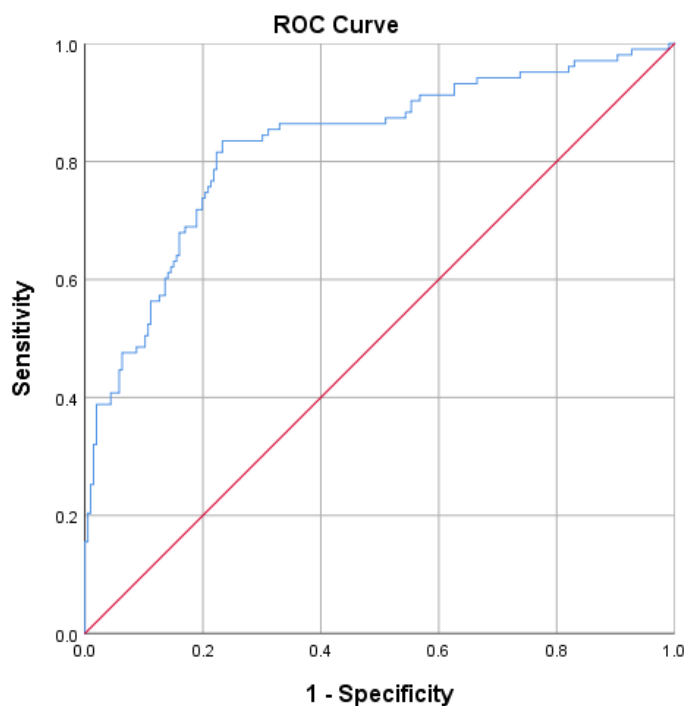
After controlling for creatinine, HbA1c, BMI, age, weight, sex, and UACR, the Atherogenic Index of Plasma (AIP) emerged as a significant independent negative predictor ( $\beta = -0.091$ , 95% CI:  $-15.273$  to  $-2.257$ ,  $p = 0.008$ ) in a different multivariable linear regression model with eGFR as the dependent variable (Table 6). This suggests that a lower eGFR, which indicates poorer renal function, is independently correlated with a higher AIP score. Higher serum creatinine ( $\beta = -0.529$ , 95% CI:  $-0.160$  to  $-0.122$ ,  $P < 0.001$ ), older age ( $\beta = -0.277$ , 95% CI:  $-1.000$  to  $-0.642$ ,  $P < 0.001$ ), higher UACR ( $\beta = -0.095$ , 95% CI:  $-0.122$  to  $-0.028$ ,  $P = 0.002$ ), and female sex ( $\beta = 0.187$ , 95% CI:  $8.180$  to  $16.854$ ,  $P < 0.001$ ), which was linked to a lower eGFR, were additional strong independent predictors. In this model, body weight, BMI, and HbA1c were not significant predictors of mortality. There were no multicollinearity issues because all the VIF values were less than 5.

**Table No 4: Multivariable Linear Regression Analysis for Predictors of eGFR**

| Predictor                | B       | Std. Error | Beta   | t       | p           | 95% CI for B       | Tolerance | VIF   |
|--------------------------|---------|------------|--------|---------|-------------|--------------------|-----------|-------|
| Constant                 | 124.004 | 10.687     | —      | 11.603  | $P < 0.001$ | 102.973<br>145.036 | —         | —     |
| AIP                      | -8.765  | 3.307      | -0.091 | -2.650  | $p = 0.008$ | -15.273 – -2.257   | 0.650     | 1.538 |
| Creatinine (mmol/L)      | -0.141  | 0.010      | -0.529 | -14.446 | $P < 0.001$ | -0.160 – -0.122    | 0.571     | 1.750 |
| HbA1c                    | -0.891  | 0.475      | -0.056 | -1.877  | $p = 0.061$ | -1.825 – 0.043     | 0.860     | 1.163 |
| BMI (kg/m <sup>2</sup> ) | 0.061   | 0.495      | 0.006  | 0.122   | $p = 0.903$ | -0.913 – 1.034     | 0.303     | 3.297 |
| Age (years)              | -0.821  | 0.091      | -0.277 | -9.030  | $P < 0.001$ | -1.000 – -0.642    | 0.812     | 1.232 |
| Weight (kg)              | 0.037   | 0.166      | 0.011  | 0.220   | $p = 0.826$ | -0.290 – 0.363     | 0.283     | 3.532 |
| Sex (Male=1)             | 12.517  | 2.204      | 0.187  | 5.680   | $P < 0.001$ | 8.180 – 16.854     | 0.705     | 1.418 |
| UACR (mg/g)              | -0.075  | 0.024      | -0.095 | -3.134  | $p = 0.001$ | -0.122 – -0.028    | 0.831     | 1.203 |

**Discriminatory Power of AIP for Diabetic Nephropathy**

Receiver Operating Characteristic (ROC) curve analysis was used to evaluate the capacity of the Atherogenic Index of Plasma (AIP) to discriminate between individuals with diabetic nephropathy (DN) and those without (DM and HC combined). With an Area Under the Curve (AUC) of 0.828 (95% CI: 0.777–0.880;  $P < 0.001$ ), the study showed that AIP had outstanding discriminating power (Figure 1). With a sensitivity of 86.4% (89/103) and a specificity of 62.1% (128/206), the ideal AIP cutoff value was -0.01 (Youden Index,  $J = 0.48$ ).



**Figure: ROC Curve**

These findings demonstrate that AIP is a potent and statistically significant biomarker for distinguishing DN from non-nephropathic conditions. An AIP  $\geq -0.01$  is a potentially useful technique for screening and risk stratification because of its high sensitivity, which indicates that it can accurately detect most DN cases.

## Discussion

In comparison to the DM and HC groups, the DN group had a much higher AIP, highlighting a severe atherogenic dyslipidaemia status in patients with nephropathy. This is consistent with the well-known "lipid nephrotoxicity" theory, which holds that glomerular and tubular damage is directly caused by lipid imbalances.<sup>11</sup> Our results align with the increasing amount of research conducted over the last five years. For example, a cross-sectional study conducted in 2021 by Li et al. found that in a large Chinese population with type 2 diabetes, AIP was independently linked to the prevalence of chronic renal disease.<sup>5</sup>

More recently, Wang et al. (2023) showed that AIP is a better predictor of renal insufficiency than specific lipid markers.<sup>12</sup> Our findings demonstrate the universality of this link by strongly confirming this trend in a well-phenotyped Pakistani cohort. Our DN group exhibited a unique lipid profile, characterised by high TG and LDL levels and low HDL levels, which is a characteristic pattern of diabetic dyslipidaemia that is exacerbated by renal impairment. By combining these conflicting risk variables into a single, powerful score, the AIP computation appears to be more sensitive than its constituent parts in capturing renal risk.

The study included only participants with complete clinical, biochemical, lipid, and renal function data. Although this ensured the consistency of the analysis and avoided the imputation of missing values, it may have introduced selection bias because individuals with incomplete records were excluded. These excluded individuals may have differed systematically from the included sample in terms of disease severity, treatment history, access to care, or follow-up completeness. Therefore, the findings should be interpreted as applicable primarily to hospital-based patients with complete records and may not be fully generalisable to all adults with type 2 diabetes or diabetic nephropathy.

The multivariable linear regression models, which were created to separate the independent impact of AIP on renal parameters after adjusting for important confounders such as age, sex, BMI, HbA1c, and other renal indicators, form the basis of our research. AIP was not significant ( $P = 0.309$ ), whereas eGFR, serum creatinine, and sex were independent predictors in the UACR model. This implies that AIP's main impact is not on podocyte damage and albumin leakage, which UACR predominantly represents, or that the association between AIP and albuminuria may be mediated through alternative mechanisms, such as total renal function loss (eGFR).<sup>13</sup>

In contrast, the eGFR model produced a crucial result: AIP was a significant independent negative predictor ( $\beta = -0.091$ ,  $p = 0.008$ ). When all other variables were held constant, the negative  $\beta$  coefficient showed an independent decline in eGFR for every unit rise in AIP. This result may be understood in light of Zhao et al.'s (2025) study, which found a similar longitudinal connection in which a greater baseline AIP predicted a quicker fall in eGFR over a two-year follow-up in patients with diabetes.<sup>14</sup>

One important translational result of our study is the remarkable discriminatory power of AIP, with an AUC of 0.828. In clinical epidemiology, an AUC greater than 0.80 is regarded as excellent. With a high sensitivity of 86.4% and an ideal cutoff of  $-0.01$ , the AIP is a powerful screening technique. In this case, a patient with an AIP below  $-0.01$  is highly unlikely to have DN, which might assist in saving needless further testing in a primary care environment. A test with high sensitivity is good for ruling out a diagnosis.

Although the specificity of 62.1% is moderate, it is appropriate for a screening biomarker, particularly one that is easy and affordable to compute as AIP. This performance is comparable to and occasionally better than other suggested biomarkers for DN.

We must acknowledge a few shortcomings of our study. It is possible to determine a connection but not causation due to its cross-sectional nature. Dietary habits, exact duration of diabetes, use of lipid-lowering agents, and physical activity levels were not captured, all of which represent potential unmeasured confounders that may have influenced the observed association. Future longitudinal multicentre studies should account for these variables. To evaluate our suggested AIP cutoff and determine its prognostic significance for the future development of DN, further multicentre prospective cohort studies are required.

In individuals with type 2 diabetes mellitus, this study found that the Atherogenic Index of Plasma (AIP) is a useful and affordable diagnostic tool for the early diagnosis of diabetic nephropathy (DN). AIP may represent both lipid and renal impairment, as evidenced by the strong associations between AIP, eGFR, and UACR. This study highlights the significance of metabolic regulation in maintaining kidney function by connecting dyslipidaemia to renal impairment. AIP might improve early detection, facilitate preventative measures, and eventually lessen the burden of chronic kidney disease in diabetic populations by being included in routine diabetes examinations.

## Conclusions

This study offers strong evidence that AIP is a reliable, independent predictor of declining renal function and is markedly elevated in diabetic nephropathy (DN). The following is a summary of our main findings: First, AIP showed a significant graded increase in individuals with established DN, diabetics without nephropathy, and healthy controls. Second, multivariate analysis showed that AIP was an independent predictor of eGFR but not of UACR, despite its association with both eGFR and UACR. Third, and perhaps most significantly, AIP demonstrated a high-sensitivity cutoff value and outstanding discriminating ability for recognising DN. These findings imply that, rather than being a passive risk factor, AIP may play an active role in the pathophysiology of diabetic kidney disease. The Atherogenic Index of Plasma is a clinically important biomarker for diabetic nephropathy, as concluded in this study. It is an independent predictor of glomerular filtration rate and has a substantial correlation with the existence of DN. Its high sensitivity and outstanding discriminatory power highlight its promise as a straightforward, affordable, and noninvasive method for risk assessment and early nephropathy screening in patients with diabetes. By incorporating AIP into the routine treatment of type 2 diabetes, we may be better able to recognize high-risk individuals and take early action.

## Author Information

1,3. Student, Army Medical College, NUMS 2,4. Professor, Army Medical College, NUMS 5. Research Associate, Army Medical College, NUMS

**Corresponding author:** Dr. Palvasha Waheed  p\_waheed@hotmail.com

## References

1. Rout P, Jialal I, Doerr C. Diabetic nephropathy (nursing). StatPearls [Internet]: StatPearls Publishing; 2025.
2. Zhang H, Zhao H, Wang K, Qin B, Cai X, Wu M, et al. Diabetic kidney disease: from pathogenesis to multimodal therapy-current evidence and future directions. *Frontiers in Medicine*. 2025;12:1631053. <https://doi.org/10.3389/fmed.2025.1631053>
3. Mohandes S, Doke T, Hu H, Mukhi D, Dhillon P, Susztak K. Molecular pathways that drive diabetic kidney disease. *The Journal of clinical investigation*. 2023;133(4). <https://doi.org/10.1172/JCI165654>
4. Cui M, Xiao X, Zhao X, Wang Y, Gang X, Wang G. Association between the atherogenic index of plasma and chronic kidney disease: an evaluation of an adult population of American patients with diabetes mellitus. *Renal Failure*. 2025;47(1):2556495. <https://doi.org/10.1080/0886022X.2025.2556495>
5. Li H, Miao X, Zhong J, Zhu Z. Atherogenic index of plasma as an early marker of chronic kidney disease and liver injury in type 2 diabetes. *Clinical Medicine Insights: Endocrinology and Diabetes*. 2024;17:11795514241259741. <https://doi.org/10.1177/11795514241259741>
6. Wang Z, Lu B, Zhang L, Tang F, Pan Y, Zhong S. Association between the atherogenic index of plasma and kidney stones: a nationally representative study. *BMC urology*. 2024;24(1):179. <https://doi.org/10.1186/s12894-024-01567-9>
7. Zhao M, Xiao M, Zhang H, Tan Q, Ji J, Cheng Y, et al. Relationship between plasma atherogenic index and incidence of cardiovascular diseases in Chinese middle-aged and elderly people. *Scientific Reports*. 2025;15(1):8775. <https://doi.org/10.1038/s41598-025-86213-6>
8. Şener G, Kahvecioğlu ED. Diagnostic Value of Plasma Atherogenicity Index for Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus. *Eastern Journal of Medicine*. 2025;30(3):403-410. <https://doi.org/10.5505/ejm.2025.93457>
9. Association WM. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human participants. *Jama*. 2025;333(1):71-4.
10. Dean AG. OpenEpi: open source epidemiologic statistics for public health, version 2.3. 1.
11. Mitrofanova A, Merscher S, Fornoni A. Kidney lipid dysmetabolism and lipid droplet accumulation in chronic kidney disease. *Nature Reviews Nephrology*. 2023;19(10):629-45. <https://doi.org/10.1038/s41581-023-00741-w>
12. Wang B, Jiang C, Qu Y, Wang J, Yan C, Zhang X. Nonlinear association between atherogenic index of plasma and chronic kidney disease: a nationwide cross-sectional study. *Lipids in Health and Disease*. 2024;23(1):312. <https://doi.org/10.1186/s12944-024-02288-6>

13. Zhu L, Lv T, Song S, Tan Y, She Y, Zhou X, et al. Association of atherogenic index of plasma with kidney dysfunction in diabetic individuals: findings from two national population-based studies. *BMC Endocrine Disorders*. 2025;25(1):105. <https://doi.org/10.1186/s12902-025-01925-0>
14. Zhou Q, Wu Y, Li M. Association between the atherogenic index of plasma and long-term risk of type 2 diabetes: a 12-year cohort study based on the Japanese population. *Cardiovascular Diabetology*. 2025;24(1):50. <https://doi.org/10.1186/s12933-025-02605-y>.