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Association between serum adenosine deaminase activity and insulin resistance in adults with type 2 diabetes

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Abstract

Purpose

Routine markers such as HbA1c incompletely reflect metabolic dysfunction in type 2 diabetes mellitus (T2DM) patients. Adenosine deaminase (ADA) is a purine metabolism enzyme that depletes adenosine and promotes inflammation; however, its role in insulin resistance in T2DM patients is poorly characterized. This study evaluated the serum ADA concentration and its association with insulin resistance in T2DM patients and controls.

Methods

This cross-sectional case–control study involved 90 adults with type 2 diabetes mellitus (T2DM) and 40 age- and sex-matched controls. Serum ADA, insulin, fasting glucose, HbA1c, and uric acid were measured in overnight fasting blood samples. Insulin resistance was quantified via the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). Spearman's rank correlation, log-linear regression adjusted for age, sex and body mass index (BMI), and receiver operating characteristic (ROC) curve analysis were performed.

Results

Serum ADA was significantly greater in T2DM patients than in controls (median 28.3vs8.2 U/L; $p < 0.001$; $r = 0.79$). ADA was strongly correlated with HOMA-IR ($\rho = 0.799$; 95%CI 0.71–0.87), HbA1c ($\rho = 0.606$) and fasting glucose ($\rho = 0.735$). Regression identified ADA as the strongest independent predictor of HOMA-IR ($\beta = 0.735$; $p < 0.001$; $R^2=0.576$). ROC analysis yielded an AUC = 0.887; an optimal cutoff of ≥ 13.1 U/L provided 87.0% sensitivity and 81.6% specificity.

Conclusion

Serum ADA is markedly elevated in T2DM patients and shows a strong, independent association with insulin resistance alongside promising discriminatory ability. These findings are consistent with the role of ADA in adenosine depletion and impaired glucose disposal, supporting its potential as a cost-effective surrogate biomarker following prospective external validation.

1. Introduction

Type 2 diabetes mellitus is a chronic metabolic disorder associated with beta-cell dysfunction and persistent hyperglycemia. It is an increasing public health concern, with an estimated 589 million adults affected globally in 2024, and projections suggest that this number may reach approximately 853 million by 2050 [1]. In India, recent national estimates indicate that more than 100 million adults are currently

living with diabetes, reflecting a substantial and growing health burden [2]. Diabetes is strongly linked to insulin resistance, which appears early in the disease process and contributes to long-term microvascular and macrovascular complications [3]. This finding reinforces the need for simple and reliable metabolic markers that can help identify individuals at greater risk at an earlier stage.

A potential candidate for such metabolic monitoring is adenosine deaminase (ADA). ADA is a crucial enzyme in the purine metabolism pathway, catalyzing the deamination of adenosine to inosine and regulating extracellular adenosine levels [4]. Adenosine signals via four distinct G-protein coupled receptors, namely, A1, A2A, A2B and A3, thereby influencing immune modulation and other inflammatory processes [5]. Elevated ADA activity increases the breakdown of adenosine and alters receptor signaling in a manner that favors a proinflammatory state [6]. Experimental evidence in mice shows that dysregulated adenosine signaling, particularly through A2B receptor activation, leads to the release of inflammatory mediators such as IL-6 and CRP, along with impaired glucose disposal, contributing to insulin resistance [7]. As ADA functions within the purine-degradation pathway, alterations in this pathway can influence uric acid production, which has been associated with oxidative stress and metabolic dysfunction [8]. These observations provide a biological basis for considering ADA as a marker of metabolic dysfunction.

Elevated levels of ADA have been documented in type 2 diabetes mellitus patients across few studies [9]. The role of ADA in the context of metabolic syndrome and other inflammatory conditions has been investigated; however, findings remain inconsistent across studies [10]. Most previous work has focused on ADA levels in individuals with established diabetes, with less emphasis on how ADA activity correlates with specific markers of insulin resistance that may contribute to long-term complications [11]. There is also limited evidence describing how ADA varies within Indian diabetic populations across different levels of glycemic control, even though genetic, dietary and environmental factors may influence such variation [12]. Accordingly, evaluating ADA within a diabetic cohort may help clarify how this enzyme reflects underlying metabolic variation.

Routine markers such as fasting glucose and HbA1c do not always fully reflect the underlying metabolic variability in individuals with type 2 diabetes, supporting the need to investigate additional biochemical indicators [13]. The present observational study was undertaken to address the gaps described. The primary objective of this study was to evaluate the association between serum adenosine deaminase (ADA) activity and insulin resistance via the homeostatic model assessment for insulin resistance (HOMA-IR). The secondary objectives were to compare ADA levels between T2DM patients and healthy controls; examine the correlations of ADA with HbA1c, fasting glucose and serum uric acid; and describe BMI differences between cases and controls.

2. Subjects, Materials and Methods

2.1 Study design and setting

An observational case–control study was conducted in the Department of Biochemistry in association with the Department of Medicine at Ballari Medical College and Research Centre, India, over a period of five months between May and September 2025.

2.2 Ethical considerations

The study protocol was approved by the Institutional Ethics Committee of Ballari Medical College and Research Centre (IEC approval no. 12/2025). The study procedures complied with established ethical standards, and written informed consent was obtained from all participants before sample collection.

2.3 Study population

The participants included adults aged 18 years or older who attended the outpatient department and had a clinical diagnosis of type 2 diabetes mellitus according to the American Diabetes Association criteria. To assess the specificity of serum ADA as a metabolic marker, we implemented rigorous exclusion criteria. Participants were excluded if they presented with conditions known to independently influence ADA activity, including (i) systemic inflammatory conditions, acute infections, tuberculosis, or other chronic infectious diseases; (ii) altered purine metabolism or excretion (gout, hematological malignancies, or eGFR < 30 mL/min/1.73 m^2); and (iii) hepatic dysfunction (including chronic liver disease and elevated transaminases). Furthermore, to isolate endogenous ADA levels, we excluded individuals on insulin therapy or medications with known immunomodulatory effects, such as corticosteroids and immunosuppressants. A standardized clinical history was obtained from all participants to ensure proper screening for these conditions before enrollment. These exclusions were applied specifically because ADA is a nonspecific enzyme whose activity may be elevated in conditions beyond diabetes. Hence, rigorous exclusion of such confounders was considered essential to the integrity of the case–control comparison.

The sample size was determined in advance on the basis of parameters reported by Niraula et al. [9], who reported a mean serum ADA activity of 35.74 ± 16.78 U/L in T2DM patients and 10.55 ± 2.20 U/L in healthy controls. Using a two-sample comparison of means at 80% power and a two-tailed alpha of 0.05, a minimum of 12 cases and 6 controls were estimated to be required to detect the anticipated between-group difference in ADA at the planned allocation ratio. This minimum was further informed by the requirements of the secondary analyses: multivariable regression with four predictor variables necessitated a minimum of 40 participants at the recommended threshold of 10 subjects per predictor, whereas stable AUC estimation by ROC analysis required a minimum of 80 participants with the condition of interest [29]. Accordingly, a target of 90 T2DM patients and 40 age- and sex-matched healthy controls was set, and this enrollment was achieved in full. The final sample of 130 participants provided greater than 99% power for the primary between-group comparison and 32.5 subjects per regression predictor variable, exceeding standard adequacy thresholds for all planned analyses.

2.4 Clinical and anthropometric data

The clinical information recorded for each participant included age, sex, duration of diabetes and past medical history. Anthropometric measurements included height and weight, which were obtained with participants wearing light clothing and without footwear; body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2).

2.5 Sample collection and handling

After an overnight fast of 8–10 hours, 5 mL of venous blood was collected from each participant under aseptic conditions. Blood samples were distributed into appropriate collection tubes: EDTA (ethylenediaminetetraacetic acid) tubes for HbA1c estimation, plain tubes for serum assays (adenosine deaminase, insulin and uric acid), and sodium fluoride tubes for fasting plasma glucose. The plain tubes were allowed to warm at room temperature for approximately 30 minutes and then centrifuged at 3000 rpm for 10 minutes to obtain the serum. The processed samples were analyzed immediately or stored at − 20°C until testing. Routine internal quality-control procedures were followed throughout sample handling.

2.6 Biochemical analysis

Serum ADA activity was measured via a colorimetric enzymatic assay via the Erba Mannheim ADA Kit (TransAsia Biomedicals Ltd., India) following the manufacturer's protocol; the results are expressed in U/L. Fasting plasma glucose was estimated via the glucose oxidase–peroxidase method on an XL-1000 analyzer. HbA1c was measured in EDTA whole blood via the immunoturbidimetric method via the Erba Mannheim HbA1c Kit (TransAsia Bio-Medicals Ltd., India). Serum insulin was quantified by electrochemiluminescence (Insulin CalSet, Roche Diagnostics, Germany), and serum uric acid was determined by a urease-based enzymatic assay. For all the assays, the intra- and interassay coefficients of variation were within acceptable limits (< 10%). The laboratory reference ranges used were those routinely used by the institutional clinical laboratory.

2.7 Calculation of insulin resistance

Insulin resistance was calculated via the homeostatic model assessment for insulin resistance (HOMA-IR), a validated index derived from fasting insulin and fasting glucose concentrations [14]. The HOMA-IR score was calculated as follows:

HOMA-IR = [Fasting Insulin (μU/mL) × Fasting Glucose (mg/dL)]/405

A value of ≥ 2.5 was considered indicative of insulin resistance for analytical purposes [15].

2.8 Statistical analysis

The data were analyzed via descriptive and inferential statistics with IBM SPSS v27.0. Normality was assessed by the Shapiro–Wilk test. Continuous variables are expressed as medians (IQRs) or means ± SDs as appropriate. Group comparisons were performed via independent-samples t tests or Mann–Whitney U tests. Associations were evaluated via Spearman's rank correlation. Multivariable linear regression on natural log-transformed variables identified independent predictors of HOMA-IR while

adjusting for age, sex and BMI. Diagnostic performance was assessed by receiver operating characteristic (ROC) curve analysis, and the optimal cutoff was determined by the Youden index. Statistical significance was set at $p < 0.05$. Figures were generated via Python (version 3.11) with the matplotlib (v3.x) and seaborn (v0.x) libraries.

3. Results

3.1 Study population and baseline characteristics

The study enrolled 130 participants: 90 patients with type 2 diabetes mellitus and 40 age- and sex-matched healthy controls. No missing data were recorded. Baseline characteristics are summarized in Table 1. The mean age was 57.6 ± 11.4 years in the cases and 52.9 ± 9.6 years in the controls. BMI was significantly greater in the T2DM group (median 26.0 kg/m²) than in the control group (median 22.6 kg/m²; $p < 0.001$). Glycemic marker levels were markedly elevated in the cases: the median HbA1c level was 7.4% versus 5.4% in the controls, and the median fasting blood sugar level was 143.5 mg/dL versus 100.5 mg/dL. Similarly, fasting insulin and HOMA-IR were significantly greater, with median HOMA-IR values of 4.91 in T2DM patients and 1.84 in controls. The median serum ADA concentration differed markedly: 28.3 U/L in patients and 8.2 U/L in controls (all $p < 0.001$; Table 1). Box-and-whisker plots highlighting the significant separation between groups are presented in Online Resource 1.

Table 1
Baseline characteristics of T2DM patients and healthy controls.

Variable	Cases (n = 90)	Controls (n = 40)	p value
Age (years)	58.0 (15.0); 57.6 ± 11.4	52.5 (13.8); 52.9 ± 9.6	0.022
Sex (Male/Female)	58/32	24/16	—
BMI (kg/m²)	26.0 (6.0); 26.3 ± 3.9	22.6 (2.6); 22.6 ± 1.9	< 0.001
HbA1c (%)	7.4 (2.4); 8.1 ± 1.8	5.4 (0.8); 5.4 ± 0.5	< 0.001
Fasting blood sugar (mg/dL)	143.5 (84.0); 159.9 ± 60.9	100.5 (26.3); 103.5 ± 15.3	< 0.001
HOMA-IR	4.91 (4.96); 6.10 ± 3.88	1.84 (0.76); 1.97 ± 0.66	< 0.001
Uric acid (mg/dL)	5.2 (2.4); 5.6 ± 2.1	4.6 (2.0); 4.4 ± 1.3	0.001
ADA (U/L)	28.3 (11.1); 28.1 ± 8.9	8.2 (2.7); 8.4 ± 2.0	< 0.001

Data are expressed as the median (IQR); the mean ± SD is provided for descriptive reference. The reported p values reflect between-group comparisons (cases vs *controls) via the Mann–Whitney U test for skewed variables and the independent-samples t test for approximately normally distributed variables.*

3.2 ADA distribution and comparison between groups

The primary outcome of interest, serum ADA levels, displayed a nonnormal distribution (Shapiro–Wilk W = 0.967; p = 0.022). Detailed normality tests and distribution plots are provided in Online Resource 2 and Online Resource 3. Consequently, the Mann–Whitney U test was used for between-group comparisons. Serum ADA levels were significantly elevated in T2DM patients compared with controls, with a median of 28.3 U/L (IQR 11.1) in cases, whereas the control group had a median of 8.2 U/L (IQR 2.7). The difference was statistically significant (Mann–Whitney U = 8.00; Z = − 9.04; p < 0.001).

The effect size for this difference was large (r = 0.79; 95% CI 0.72–0.85), indicating substantial group separation. The range of ADA values in the T2DM group (11.0–64.2 U/L) was broader than the tighter clustering observed in the control group (4.4–13.0 U/L). This clear separation indicates that higher ADA levels are characteristic of the diabetic cohort in this study.

3.3 Primary association: ADA versus HOMA-IR

The associations between the serum ADA concentration and the HOMA-IR score were evaluated via Spearman's rank correlation. A strong, positive and statistically significant correlation was observed (ρ = 0.799; p < 0.001). Bootstrap resampling with 1,000 iterations yielded a 95% confidence interval of 0.71–0.87, confirming the robustness of the estimate. Fisher z-transformation of the correlation coefficient produced a similar 95% CI of 0.72–0.86 for the population parameter. The squared correlation ($\rho^2 = 0.64$) reflects a substantial shared association between ADA and insulin resistance.

The scatterplot of ADA versus HOMA-IR (Fig. 1) visualizes this positive linear trend. Sensitivity analysis via Pearson correlation was performed on natural log-transformed variables (ln_ADA and ln_HOMA-IR) to account for skewness, yielding a robust coefficient of r = 0.76 (p < 0.001).

3.4 Secondary correlations: ADA with glycemic and metabolic parameters

Secondary analyses explored pairwise associations between ADA and other biochemical and anthropometric parameters (Table 2). ADA was strongly positively correlated with fasting blood sugar (ρ = 0.735; 95% CI 0.64–0.82; p < 0.001) and moderately to strongly correlated with HbA1c (ρ = 0.606; 95% CI 0.45–0.72; p < 0.001), indicating that ADA activity closely tracks both short- and long-term glycemic deregulation. A moderate positive correlation was observed with BMI (ρ = 0.399; 95% CI 0.24–0.53; p < 0.001). Serum uric acid showed a weaker but statistically significant positive correlation (ρ = 0.290; 95% CI 0.12–0.44; p = 0.001). The magnitude of the correlation of ADA with HOMA-IR exceeded all other pairwise associations, supporting its primary role as a marker of insulin resistance rather than a simple surrogate for hyperglycemia or adiposity.

Table 2
Spearman's rank correlation coefficients between the serum ADA concentration and key parameters (n = 130).

Variable pair	Spearman ρ	95% CI	p value
ADA vs HOMA-IR	0.799	0.705–0.870	< 0.001
ADA vs Fasting blood sugar	0.735	0.637–0.819	< 0.001
ADA vs HbA1c	0.606	0.451–0.722	< 0.001
ADA vs BMI	0.399	0.245–0.535	< 0.001
ADA vs Uric acid	0.290	0.103–0.441	0.001

The 95% confidence intervals were computed via Fisher z-transformation and verified via the bootstrap percentile method (1000 samples).

3.5 Multivariable regression analysis

To determine whether serum ADA serves as an independent predictor of insulin resistance, a multivariable linear regression was performed on natural log-transformed HOMA-IR. The overall model, which included ln ADA, age, sex and BMI as predictors, was statistically significant ($F[4,125] = 42.50$; $p < 0.001$; Durbin–Watson = 1.784) and explained 57.6% of the variance in insulin resistance ($R^2 = 0.576$; adjusted $R^2 = 0.563$). Complete regression diagnostics, including collinearity checks and residual plots, are presented in Online Resource 4 and Online Resource 5. Serum ADA was the strongest independent predictor (B = 0.854; β = 0.735; $p < 0.001$), indicating that a 1% increase in serum ADA was associated with an approximately 0.85% increase in HOMA-IR after adjusting for covariates (Table 3). Among the covariates, sex was significantly related (B = 0.212; $p = 0.019$), whereas age ($p = 0.215$) and BMI ($p = 0.391$) were not significant. The variance inflation factors were less than 1.3 for all the predictors, confirming the absence of multicollinearity. One observation exceeded 3 standard deviations for the standardized residuals; however, Cook's distance values (maximum 0.140) indicated no undue influence. Visual inspection of residual plots revealed random dispersion, supporting homoscedasticity.

Table 3
Multivariable linear regression predicting ln(HOMA-IR)

Variable	B (SE)	β	t	p	VIF
ln ADA	**0.854 (0.075)**	**0.735**	**11.43**	**< 0.001**	**1.22**
Age	−0.005 (0.004)	−0.073	−1.25	0.215	1.02
BMI	0.011 (0.012)	0.055	0.86	0.391	1.19
Sex (male)	0.212 (0.089)	0.139	2.39	0.019	1.00
Model: R^2 = 0.576, Adj R^2 = 0.563, F(4,125) = 42.50, p < 0.001, Durbin-Watson = 1.784					

Dependent variable: natural log-transformed HOMA-IR. B = unstandardized coefficient; SE = standard error; β = standardized beta; VIF = variance inflation factor. n = 130. The residuals ranged from − 4.04 to + 2.06 SD; Cook's D max = 0.140.

3.6 ROC analysis: Diagnostic performance of ADA

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of serum ADA for identifying insulin resistance (defined as HOMA-IR ≥ 2.5). The area under the curve (AUC) was 0.887 (SE = 0.036, 95% CI 0.816–0.957, p < 0.001), indicating promising discriminatory ability within this dataset (Fig. 2).

The optimal cutoff value for ADA was determined via the Youden index (sensitivity + specificity − 1). The maximum Youden index of 0.685 was achieved at a cutoff of ADA ≥ 13.1 U/L. At this threshold, the sensitivity was 87.0% (95% CI 78.9%–92.7%), and the specificity was 81.6% (95% CI 65.2%–92.0%). A comprehensive list of sensitivity and specificity coordinates for all observed cutoff values is available in Online Resource 6.

4. Discussion

The present study demonstrated a strong, positive and statistically significant correlation between serum ADA levels and HOMA-IR (Spearman's ρ = 0.799; p < 0.001; 95% CI 0.71–0.87), indicating that ADA activity increases proportionally with increasing insulin resistance. Patients with type 2 diabetes had markedly elevated ADA levels relative to healthy controls (median 28.3 U/L vs 8.2 U/L; p < 0.001), with a large effect size (r = 0.79) reflecting substantial group separation. The control group median of 8.2 U/L was consistent with the institutional laboratory reference range of 4–21 U/L for healthy adults, confirming assay calibration and supporting the validity of the observed group contrast. Multivariable regression confirmed ADA as the strongest independent predictor of HOMA-IR after adjusting for age, sex and BMI (β = 0.735; R^2 = 0.576), and ROC analysis revealed promising apparent diagnostic performance internally (AUC = 0.887; cutoff ≥ 13.1 U/L), pending prospective external validation.

The elevated ADA levels observed in T2DM patients are consistent with previously reported findings [16, 17]. The consistency across multiple established indices of insulin resistance further strengthens the

evidence supporting the link between elevated serum ADA and insulin resistance [17]. Serum ADA also demonstrated a significant positive correlation with HbA1c ($\rho = 0.606$; $p < 0.001$), confirming that ADA levels increase as long-term glycemic control deteriorates [18]. The greater group separation observed compared with that reported in some prior studies is likely due to the rigorous exclusion of participants whose conditions are independently known to increase ADA levels, which reduced nondiabetic variation in the control group. A moderate positive correlation between ADA and BMI was observed, in agreement with studies indicating that increased adiposity is associated with increased ADA activity in T2DM patients [19]. Serum uric acid also showed a significant positive correlation with ADA, which is consistent with the known relationship between purine metabolism and metabolic dysfunction [20]. Importantly, the magnitude of the correlation of ADA with HOMA-IR exceeded all other pairwise associations, supporting its primary role as a marker of insulin resistance rather than a simple surrogate for hyperglycemia or adiposity.

Adenosine plays a critical role in the upregulation of GLUT4 receptors on the surface of adipose cells, thereby increasing insulin sensitivity [21]. Elevated serum ADA in type 2 diabetes patients depletes available adenosine, impairing this regulatory mechanism. Furthermore, adenosine mimics insulin action in adipose tissue by enhancing insulin-induced activation of phosphatidylinositol-3-kinase (PI3K) and protein kinase B (PKB) [22], promoting glucose uptake and inhibiting lipolysis [23]. Increased ADA activity, therefore, compromises this insulin-mimicking effect of adenosine.

Adenosine also acts as an anti-inflammatory mediator by inhibiting T-cell activation and proliferation. The progression of T2DM is accompanied by low-grade chronic inflammation [9, 24]; chronic hyperglycemia induces oxidative stress through enediol and superoxide formation, which further elevates ADA levels. Cytokines produced by Th1 cells promote ADA expression [25], and the resulting cytokine imbalance may in turn modulate ADA activity. On the other hand, some researchers have proposed that elevated ADA in T2DM patients represents a compensatory response to the gluconeogenic activity of adenosine via the hepatic A2a receptor rather than a primary causative factor [26, 27]. Taken together, these mechanisms indicate that high ADA activity is associated with reduced glucose uptake in insulin-sensitive tissues, including skeletal muscle, which is consistent with the findings of the present study.

The study employed a well-defined case—control design with age- and sex-matched groups and internal quality control for all biochemical assays. Robust statistical methods, including bootstrap confidence intervals, Fisher z-transformation, log-transformation to satisfy regression assumptions and assessment of multicollinearity, were used throughout. The evaluation of diagnostic performance by ROC analysis and the derivation of a discriminatory cutoff value represent important contributions that were largely unexplored in previous studies of ADA in patients with T2DM.

The cross-sectional design prevents the establishment of a causal relationship between serum ADA levels and insulin resistance. Hence, a prospective or longitudinal study is needed to determine temporality. The study was conducted at a single center with a relatively modest sample size, which

limits the generalizability of the findings. While the rigorous exclusion approach strengthened the internal validity of the case–control comparison, it reduced the available recruitment pool and extended the enrollment period. The euglycemic hyperinsulinemic clamp technique remains the gold standard for quantifying insulin resistance [28] and would provide a more definitive characterization of the ADA–insulin resistance relationship. However, the clamp is resource intensive and technically demanding, thereby making it unsuitable for the outpatient setting in which the present study was conducted. HOMA-IR, which has a validated and documented correlation with clamp-derived estimates and is widely used in clinical and epidemiological research [14, 15], was therefore the appropriate index in our resource-limited context. Oxidative stress markers such as glutathione peroxidase and catalase, as well as circulating inflammatory markers such as CRP and IL-6, were not measured, which would have strengthened the biological plausibility assessment. Furthermore, the ROC-based cutoff of ≥ 13.1 U/L was both derived and evaluated within the same population, which constitutes internal validation only and is a recognized source of optimism bias. The apparent AUC of 0.887, sensitivity of 87.0% and specificity of 81.6% may overestimate the performance in independent populations. Finally, dietary intake and physical activity were not recorded and could represent residual confounders.

The present findings raise several questions that require future investigation, particularly whether ADA levels decline or normalize following treatment intensification and glycemic improvement. Additionally, if the derived cutoff of ≥ 13.1 U/L retains validity across diverse Indian subpopulations with varying genetic and dietary patterns? Furthermore, determining whether elevation in ADA precedes detectable insulin resistance in high-risk individuals or correlates with specific microvascular complications should be a priority for prospective cohort designs.

From a clinical perspective, incorporating serum ADA measurement alongside routine glycemic markers could provide additional metabolic information at a minimal cost, especially in resource-limited settings where insulin assays required for measuring insulin resistance are not routinely available. However, as these results stem from a single-center cross-sectional population, external validation is necessary. In conclusion, serum ADA is markedly elevated in type 2 diabetes patients and has a strong, independent association with insulin resistance. While its promising discriminatory ability (AUC = 0.887) supports its potential as a simple, cost-effective surrogate biomarker, future multicenter studies incorporating gold-standard insulin resistance measurements and rigorous confounder adjustments are necessary to confirm causality and facilitate clinical implementation.

Declarations

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author Contribution

S.M. conceptualized the study, developed the research methodology, performed the formal analysis, and managed the project administration. I.V. provided senior supervision and conducted the final critical review and editing. P.K. was responsible for the original draft preparation, data visualization, and statistical results interpretation. N.I. performed the primary data collection and assisted with the technical proofreading. All authors have read and agreed to the published version of the manuscript.

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Data Availability

The data supporting this study and the deidentified individual patient data are available upon reasonable request from the corresponding author.

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Figures

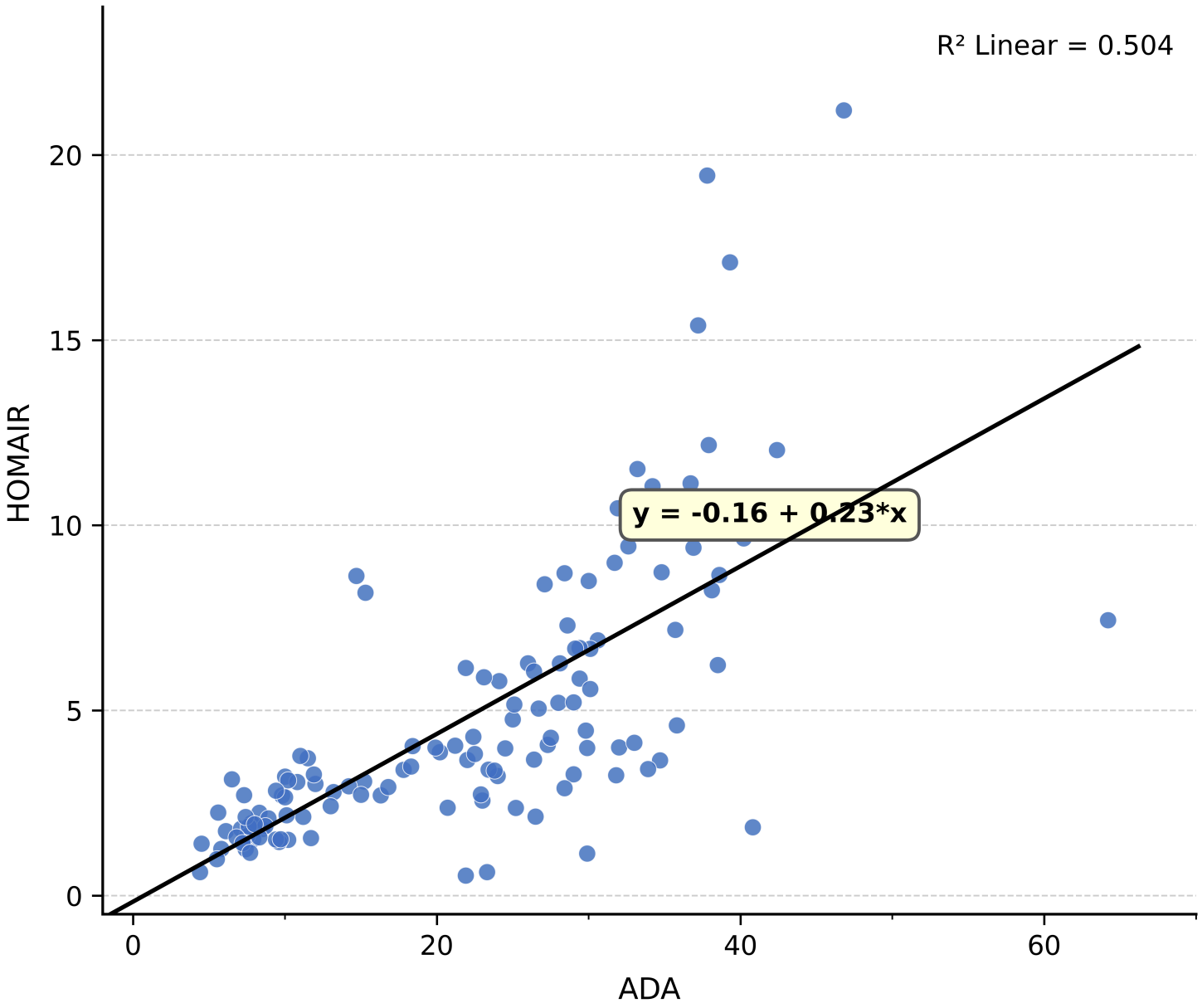


Figure 1

Scatterplot of serum ADA activity versus HOMA-IR in the total study population (n = 130). The regression line illustrates the strong positive linear association between ADA and insulin resistance.

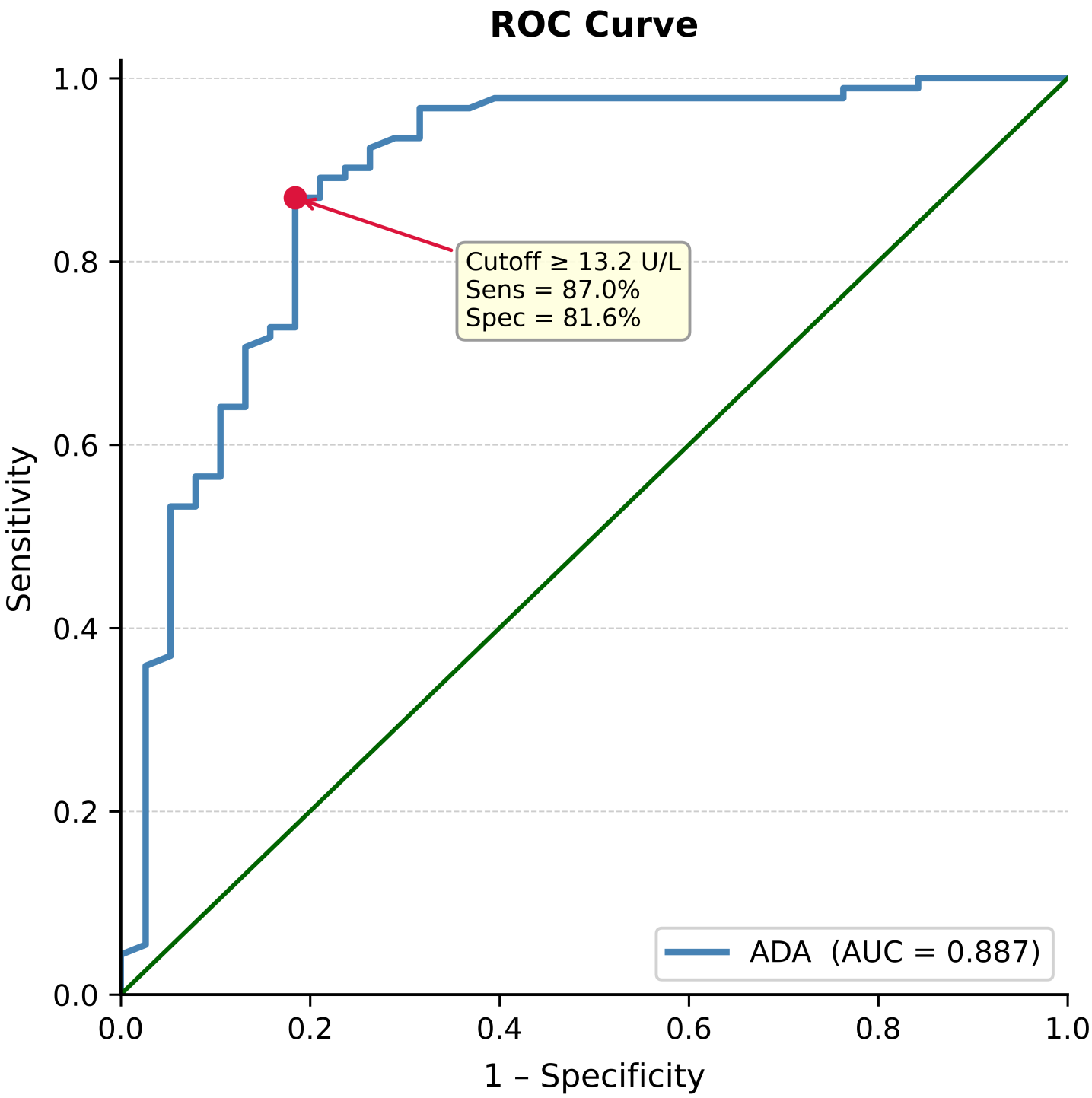


Figure 2

Receiver operating characteristic (ROC) curve for evaluating the utility of serum adenosine deaminase (ADA) for identifying insulin resistance (HOMA-IR ≥ 2.5). AUC = 0.887; optimal cutoff ≥ 13.1 U/L.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- ESM1.tiff
- ESM2.csv
- ESM3.tiff
- ESM4.csv
- ESM5.tiff
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