International Journal of Nutrology
(Official Journal of the ABRAN - Brazilian Association of Nutrology)

ORIGINAL ARTICLE

DOI: 10.54448/ijn26S312

Evaluation of serum IL-39 levels as a potential risk marker in type 2 diabetic patients: a case-control study

Hussein Dhahir Ayyez Al-Fatlawi[1,*]; Hasan Ali Madhloom[2]; Asia Ali Hamza[3]; Hanaa Addai Ali[4]

[1] Al-Furat Al-Awsat Technical University. Technical Engineering Najaf College. Department of Health Physics and Radiation Therapy Technical Engineering, Al-Najaf, Iraq.
[2] University of Cordoba. Faculty of Health and Medical Techniques. Department of Radiology Techniques, Al-Najaf, Iraq.
[3] University of AlKafeel. College of Pharmacy. Department of Clinical Laboratory Sciences, Al-Najaf, Iraq.
[4] Department of Chemistry, College of Science, University of Kufa, Al-Najaf, Iraq.

*Corresponding author: Hussein Dhahir Ayyez Al-Fatlawi.
Al-Furat Al-Awsat Technical University. Technical Engineering Najaf College. Department of Health Physics and Radiation Therapy Technical Engineering, Al-Najaf, Iraq.
E-mail: hussein.ayzze@atu.edu.iq
DOI: https://doi.org/10.54448/ijn26S312
Received: 03-12-2026; Revised: 05-15-2026; Accepted: 05-20-2026; Published: 07-28-2026; IJN-id: e26S312

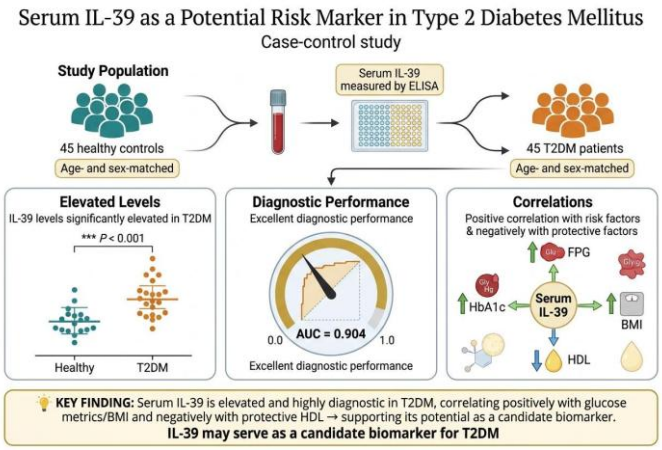
Editor: Dr. Leah D. Whigham, MD, Ph.D., FTOS.

Abstract

Introduction: Type 2 diabetes mellitus (T2DM) is a heterogeneous metabolic disorder characterised by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both, leading to long-term damage of multiple organ systems, including the kidneys, retina, nervous system, heart, and blood vessels. Interleukin-39 (IL-39) is a novel heterodimeric member of the IL-12 cytokine family that may participate in the pathogenesis of human inflammatory disorders. Because T2DM is characterised by chronic low-grade inflammation, IL-39 may be a relevant cytokine whose pathogenic involvement in the disease warrants investigation. **Objective:** The present study aimed to evaluate the role of serum interleukin-39 in patients with type 2 diabetes mellitus. **Materials and Methods:** A case-control study was conducted in which serum IL-39 levels were measured in 45 patients with type 2 diabetes mellitus (T2DM) and 45 age- and sex-matched healthy controls. Biochemical measurements included fasting plasma glucose (FPG), glycosylated haemoglobin (HbA1c), total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL), measured using spectrophotometric enzymatic colorimetric methods. Serum IL-39 was quantified using an enzyme-linked immunosorbent assay (ELISA) kit. **Results:** The mean serum IL-39 level was significantly higher in patients than in controls (11.21 ± 2.38 ng/mL vs. 7.42 ± 1.76 ng/mL; $p < 0.001$). Serum IL-39 showed a significant positive correlation with FPG ($r = 0.298$, $P = 0.005$), HbA1c ($r = 0.499$, $p < 0.001$), and body-mass index, and a significant negative correlation with HDL ($r = –0.367$, $p < 0.001$). Receiver-operating-characteristic (ROC) curve analysis of serum IL-39 yielded a cut-off value of 8.975 ng/mL, an area under the curve of 0.904, sensitivity of 0.844, specificity of 0.820, and $p < 0.001$. **Conclusion:** Serum IL-39 levels were significantly elevated in patients with T2DM and correlated positively with markers of glycaemic control. ROC analysis demonstrated excellent diagnostic performance of IL-39 in distinguishing T2DM patients from healthy controls. These findings suggest that IL-39 may serve as a potential novel biomarker for T2DM.

Keywords: Interleukin-39; Type 2 diabetes mellitus; HbA1c; Inflammation; Biomarker; Case-control study.

Graphical Abstract



Graphical Abstract. Summary of the study design and main findings. Serum IL-39 was measured in 45 patients with type 2 diabetes mellitus (T2DM) and 45 age- and sex-matched healthy controls. IL-39 was significantly elevated in T2DM patients ($P < 0.001$) and showed excellent diagnostic performance (AUC = 0.904), correlating positively with FPG, HbA1c and BMI, and negatively with HDL. Source: Own authorship.

Introduction

Diabetes mellitus is one of the most prevalent non-communicable diseases worldwide and is recognised as a chronic endocrine and metabolic disorder. According to the International Diabetes Federation, an estimated 589 million adults aged 20–79 years were living with diabetes in 2024, with this number projected to rise to 853 million by 2050 **[1]**. Diabetes results from insufficient or ineffective insulin produced by the pancreatic β-cells, and the resulting chronic hyperglycaemia leads to damage of multiple organ systems, particularly the heart, blood vessels, kidneys, eyes, and nerves **[2]**.

Diabetes is classified into several types, including type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). Type 1 diabetes is an autoimmune disorder characterised by a local inflammatory process in the pancreatic islets leading to selective destruction of insulin-producing β-cells, whereas T2DM is characterised by peripheral insulin resistance and relative insulin deficiency due to progressive β-cell dysfunction **[2]**. The pathophysiology of T2DM involves diminished insulin biosynthesis, reduced glucose uptake in liver, muscle, and adipose tissue, increased lipolysis, and hyperglycaemia **[3]**.

Chronic low-grade inflammation has emerged as a key pathogenic feature of T2DM. Hyperglycaemia-induced oxidative stress, dysregulated immune responses, and elevated pro-inflammatory cytokines such as tumour-necrosis-factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) contribute to insulin resistance, β-cell dysfunction, and the development of diabetic complications **[4]**. Investigation of novel inflammatory cytokines may therefore provide further insight into the pathogenesis of T2DM and identify new biomarkers for disease diagnosis and risk stratification.

Interleukin-39 (IL-39) is a recently identified heterodimeric member of the IL-12 cytokine family, consisting of the Ebi3 and IL-23p19 subunits **[5]**. IL-39 is mainly secreted by B cells stimulated with lipopolysaccharide (LPS), and its mRNA has also been detected in other immune cells, including macrophages and dendritic cells **[6]**. The biological functions and the very existence of bioactive IL-39 in humans remain areas of active investigation, with some studies questioning its expression in human immune cells **[7]**, while others have reported measurable levels of IL-39 in human serum across several disease conditions.

Elevated serum IL-39 has been observed in patients with ST-segment-elevation myocardial infarction, in whom IL-39 was suggested as a marker of left-ventricular systolic dysfunction **[8]**, and in patients with neuromyelitis-optica spectrum disorders, in whom IL-39 correlated with disease severity **[9]**. Furthermore, IL-39 has been shown to exacerbate concanavalin-A–induced hepatitis **[10]**. Together, these findings indicate that IL-39 may participate in the pathogenesis of several human inflammatory diseases.

Limited but emerging evidence supports the involvement of IL-39 in T2DM. A recent casecontrol study from Iraq reported that serum IL-39 was significantly elevated in patients with T2DM compared with controls and demonstrated excellent diagnostic performance **[11]**. Increased IL-39 levels have also been detected in the gingival crevicular fluid of diabetic patients with generalised periodontitis **[12]**, suggesting that IL-39 may participate in the inflammatory burden associated with diabetic complications. Nevertheless, the evidence remains scarce, and the role of IL-39 as a circulating biomarker for T2DM requires confirmation in independent populations **[13]**.

Based on the above considerations, the present study aimed to evaluate the levels of serum interleukin-39 in patients with type 2 diabetes mellitus, to compare them with those of age- and sex-matched healthy controls, and to assess the associations of IL-39 with clinical and biochemical parameters of T2DM, as well as its diagnostic performance as a potential biomarker for the disease.

Materials and Methods

Study design and population

A case-control study was conducted from 15 April 2023 to 15 August 2024 at the Diabetes Centre of Al-Sadr Medical City, Al-Najaf Governorate, Iraq. Two groups were enrolled: forty-five patients with type 2 diabetes mellitus (T2DM; mean age 53.49 ± 6.83 years, range 38–64 years) and forty-five age- and sex-matched apparently healthy volunteers (mean age 51.60 ± 5.07 years, range 36–64 years; 25 males, 20 females). The diagnosis of T2DM was established according to the criteria of the American Diabetes Association: FPG ≥ 126 mg/dL and/or HbA1c ≥ 6.5 % **[14]**. Healthy controls were apparently healthy blood donors and hospital staff without symptoms or signs of diabetes, with normal random blood glucose (80 ± 6 mg/dL) and HbA1c (5.4 ± 0.4 %). Exclusion criteria were type 1 diabetes mellitus, gestational diabetes, established diabetic complications, chronic systemic diseases, cardiovascular disease, and malignancy. Written informed consent was obtained from all participants.

Ethical Approval

The study protocol was reviewed and approved by the Research Ethics Committee of the Faculty of Pharmacy, University of Kufa, Al-Najaf, Iraq and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from every participant before enrolment, and all data were anonymised prior to analysis.

Sample size justification

The required sample size was calculated using G*Power version 3.1 software, assuming a two-tailed independent-samples *t*-test with a significance level (α) of 0.05, statistical power (1 − β) of 0.80, and an anticipated medium-to-large effect size (Cohen's *d*) of 0.60, based on previously reported effect sizes for circulating cytokine biomarkers in T2DM **[11,15]**. This calculation indicated that a minimum of 90 participants (45 per group) was required. The observed standardised mean difference for serum IL-39 in the current study (Cohen's $d \approx 1.81$) confirmed that the achieved post-hoc statistical power exceeded 0.99 for the observed between-group difference, thereby supporting the adequacy of the sample size for the present analysis **[15]**.

Anthropometric and biochemical measurements

Body-mass index (BMI) was calculated as body weight in kilograms divided by the square of height in metres (kg/m^2). Participants were classified according to the World Health Organization criteria as normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥ 30 kg/m^2) **[16]**. Biochemical parameters — FPG, HbA1c, total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol — were measured on an automated Cobas c311 analyser (Roche Diagnostics, Mannheim, Germany) using assay-specific reagents and spectrophotometric enzymatic colorimetric methods.

Serum IL-39 concentrations were quantified by an enzyme-linked immunosorbent assay (ELISA) kit (catalogue No. MBS4504; MyBioSource Inc., San Diego, CA, USA) according to the manufacturer's instructions. After an overnight fast of 8–10 hours, 5 mL of venous blood was drawn into plain tubes, allowed to clot at room temperature (20–25 °C) for at least 30 minutes, and centrifuged at 1000 × g for 15 minutes. The separated serum was aliquoted and stored at –20 °C until analysis.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages, and differences were examined using the Pearson chi-square test. The normality of continuous variables was assessed by the Shapiro–Wilk and Kolmogorov–Smirnov tests. Normally distributed data were expressed as mean ± standard deviation (SD), and differences between groups were tested by the independent-samples *t*-test or one-way analysis of variance. Non-normally distributed variables were presented as median and interquartile range and compared by the Mann–Whitney *U*-test or the Kruskal–Wallis test. Correlations between IL-39 and clinical variables were examined using the Pearson correlation coefficient. To evaluate the diagnostic value of serum IL-39 for T2DM, receiver-operating-characteristic (ROC) curve analysis was performed. A two-tailed P-value < 0.05 was considered statistically significant **[15]**.

Results

Baseline clinical and demographic characteristics

The baseline demographic and clinical characteristics of the study participants are summarised in Table 1 and Figure 1. The mean BMI of patients with T2DM was 29.60 ± 5.05 kg/m^2, above the normal-weight range, and the majority of patients were classified as overweight or obese. The mean ages of the patient and control groups were comparable

(53.49 ± 6.83 vs. 51.60 ± 5.07 years; P = 0.140). As expected, the patient group had significantly higher levels of FPG (210.56 ± 90.38 mg/dL vs. 95.89 ± 2.99 mg/dL; P < 0.001) and HbA1c (9.24 ± 2.20 % vs. 5.55 ± 2.27 %; P < 0.001), and significantly lower HDL (31.04 ± 10.72 mg/dL vs. 47.47 ± 11.07 mg/dL; P < 0.001). The mean serum IL-39 concentration was significantly higher in the patient group than in the control group (11.21 ± 2.38 ng/mL vs. 7.42 ± 1.76 ng/mL; P < 0.001) (Figure 2).

Table 1. Baseline clinical and demographic characteristics of the healthy controls and patients with type 2 diabetes mellitus.

Parameter	Healthy controls (n = 45) Mean ± SD	T2DM patients (n = 45) Mean ± SD	p-value
Age (years)	51.60 ± 5.07	53.49 ± 6.83	0.140
BMI (kg/m²)	23.28 ± 0.69	29.60 ± 5.05	< 0.001
FPG (mg/dL)	95.89 ± 2.99	210.56 ± 90.38	< 0.001
HbA1c (%)	5.55 ± 2.27	9.24 ± 2.20	< 0.001
HDL (mg/dL)	47.47 ± 11.07	31.04 ± 10.72	< 0.001
TG (mg/dL)	156.22 ± 99.68	213.38 ± 131.33	0.022
Total cholesterol (mg/dL)	142.98 ± 39.02	153.12 ± 48.43	0.289
LDL (mg/dL)	64.27 ± 40.71	79.46 ± 54.03	0.136
VLDL (mg/dL)	31.24 ± 19.94	42.68 ± 26.27	0.022
IL-39 (ng/mL)	7.42 ± 1.76	11.21 ± 2.38	< 0.001

Abbreviations: BMI, body-mass index; FPG, fasting plasma glucose; HbA1c, glycosylated haemoglobin; HDL, high-density lipoprotein; IL-39, interleukin-39; LDL, low-density lipoprotein; SD, standard deviation; T2DM, type 2 diabetes mellitus; TG, triglycerides; VLDL, very-low-density lipoprotein. P-values were obtained from the independent-samples t-test or the Pearson chi-square test, as appropriate. Source: Own authorship.

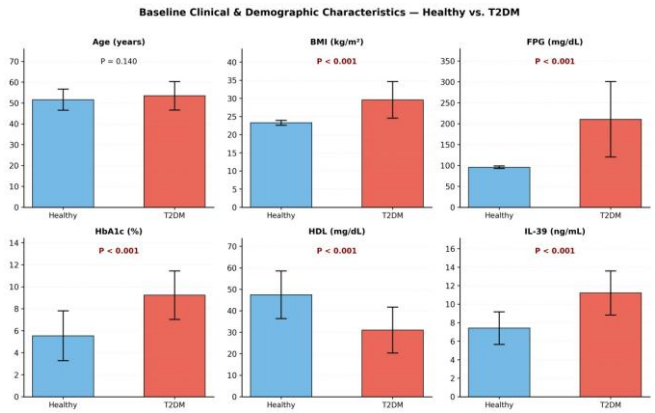


Figure 1. Comparison of baseline clinical and demographic characteristics between healthy controls (n = 45) and patients with T2DM (n = 45). Bars represent mean values; error bars represent the standard deviation. P-values were obtained from the independent-samples t-test. Significant differences (p < 0.001) were observed for BMI, FPG, HbA1c, HDL, and IL-39, while age did not differ significantly between groups (p = 0.140). Source: Own authorship.

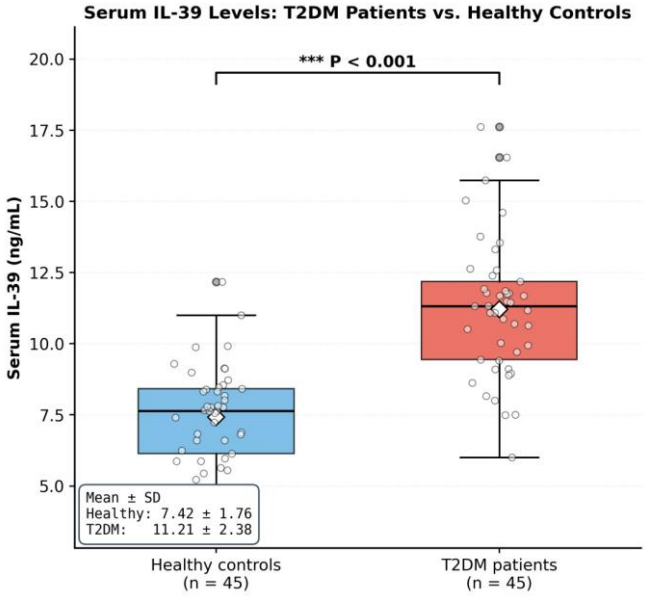


Figure 2. Box-and-whisker plot of serum IL-39 levels in T2DM patients (n = 45) and healthy controls (n = 45). The horizontal line within each box indicates the median; the diamond marker indicates the mean; the whiskers extend to the minimum and maximum values within 1.5 × IQR; open circles represent outliers; individual data points are shown with jitter. Serum IL-39 was significantly elevated in T2DM patients compared with healthy controls (11.21 ± 2.38 vs. 7.42 ± 1.76 ng/mL; *** p < 0.001). Source: Own authorship.

Correlation of serum IL-39 with clinical parameters

Pearson correlation analysis revealed that serum IL-39 was significantly and positively correlated with FPG (r = 0.298, P = 0.005), HbA1c (r = 0.499, p < 0.001), total cholesterol (r = 0.229, p = 0.031), and LDL (r = 0.282, p = 0.007). A significant negative correlation was observed between serum IL-39 and HDL (r = –0.367, p < 0.001). Correlations of serum IL-39 with age, BMI, triglycerides, and VLDL did not reach statistical significance (Table 2 and Figure 3).

Table 2. Pearson correlation coefficients between serum IL-39 and clinical parameters in patients with T2DM.

Parameter	Correlation coefficient (r)	p-value
Age (years)	0.076	0.476
BMI (kg/m²)	0.139	0.192
FPG (mg/dL)	0.298**	0.005
HbA1c (%)	0.499**	< 0.001
HDL (mg/dL)	–0.367**	< 0.001
TG (mg/dL)	0.066	0.542
Total cholesterol (mg/dL)	0.229*	0.031
LDL (mg/dL)	0.282**	0.007
VLDL (mg/dL)	0.066	0.542

* p < 0.05; ** P < 0.01. Abbreviations as in Table 1. Source: Own authorship.

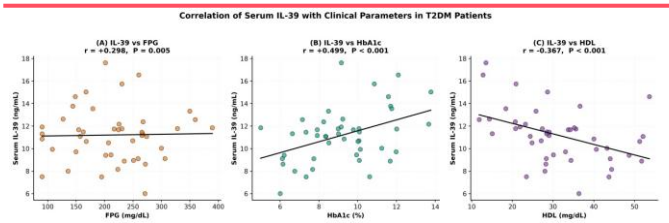


Figure 3. Scatter plots with linear-regression fits showing the correlations of serum IL-39 with (A) fasting plasma glucose (FPG; r = 0.298, P = 0.005), (B) glycosylated haemoglobin (HbA1c; r = 0.499, P < 0.001), and (C) high-density-lipoprotein cholesterol (HDL; r = –0.367, P < 0.001) in patients with T2DM. The solid line in each panel represents the best linear fit. Source: Own authorship.

Diagnostic performance of serum IL-39

Receiver-operating-characteristic (ROC) curve analysis was conducted to assess the diagnostic performance of serum IL-39 in distinguishing patients with T2DM from healthy controls. As shown in Table 3 and Figure 4, the area under the curve (AUC) was 0.904 (95 % CI: 0.845–0.964), with a cut-off value of 8.975 ng/mL, a sensitivity of 0.844, and a specificity of 0.820 (P < 0.001). These results indicate that serum IL-39 has excellent diagnostic accuracy for distinguishing T2DM patients from healthy controls.

Table 3. Diagnostic performance of serum IL-39 by ROC curve analysis (patients vs. controls).

Variable	Cut-off	Sensitivity	Specificity	AUC	95 % CI (Lower – Upper)	P-value
IL-39 (ng/mL)	8.975	0.844	0.820	0.904	0.845 – 0.964	< 0.001

AUC, area under the curve; CI, confidence interval; IL-39, interleukin-39. Source: Own authorship.

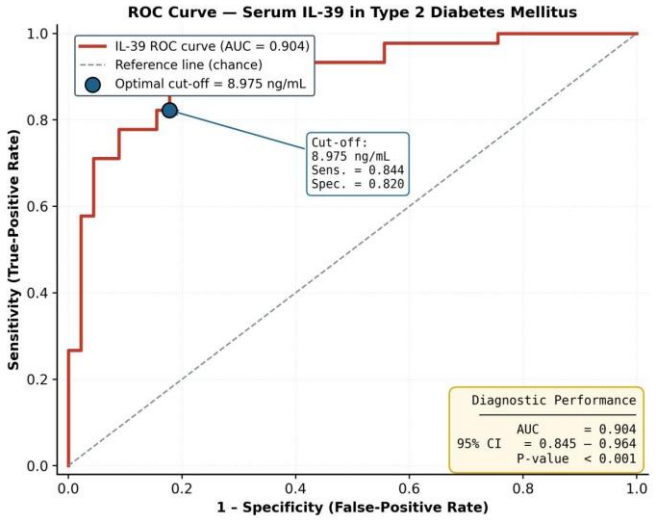


Figure 4. Receiver-operating-characteristic (ROC) curve of serum IL-39 for discriminating patients with T2DM from healthy controls. The area under the curve was 0.904 (95 % CI: 0.845–0.964); the optimal cut-off value of 8.975 ng/mL provided a sensitivity of 0.844 and a specificity of 0.820 (p < 0.001). The blue marker on the curve indicates the position of the optimal cut-off; the dashed grey line represents the reference (chance) line. Source: Own authorship.

Discussion

The present study evaluated serum levels of interleukin-39 in patients with type 2 diabetes mellitus and in age- and sex-matched healthy controls. The majority of the patients enrolled in this study had a fasting blood glucose above 126 mg/dL and HbA1c above 6.5 %, consistent with the diagnostic criteria of the American Diabetes Association **[14]**. Most of the patients were classified as overweight or obese, in agreement with previous reports indicating that obesity is one of the major risk factors for the development of T2DM **[17]**.

Obesity is now recognised as a chronic, low-grade inflammatory state in which adipose-tissue macrophages, predominantly pro-inflammatory M1-polarised cells, secrete elevated levels of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β. These cytokines impair insulin-receptor signalling, reduce GLUT-4 translocation, and promote systemic insulin resistance, providing a mechanistic link between adiposity and T2DM **[18,19]**. Pro-inflammatory cytokines have also been shown to predict the incidence of diabetic peripheral neuropathy and other diabetic complications **[20,21]**, emphasising the central role of inflammation in the natural history of the disease.

In the present study, serum IL-39 was significantly elevated in patients with T2DM compared with healthy controls and showed significant positive correlations with FPG, HbA1c, LDL-cholesterol, and total cholesterol, and a significant negative correlation with HDL-cholesterol. These findings are consistent with those of Nussrat and Ad'hiah, who reported that serum IL-39 was markedly elevated in 106 patients with T2DM compared with 109 controls, and that IL-39 showed excellent diagnostic performance for T2DM (AUC = 0.973) and was positively correlated with body-mass index **[11]**. Hassan and colleagues likewise demonstrated elevated IL-39 levels in the gingival crevicular fluid of diabetic patients with generalised periodontitis, suggesting a role for IL-39 in the inflammatory complications of diabetes **[12]**. Together, these observations support a pathogenic role for IL-39 in the chronic inflammatory environment characteristic of T2DM.

Mechanistically, IL-39 — a heterodimer of Ebi3 and IL-23p19 — signals through the IL-23R/gp130 receptor complex and activates the STAT1/STAT3 pathway **[5,6]**. This pathway has been implicated in T-

cell pathogenicity in graft-versus-host disease [22] and in the regulation of inflammatory responses in lupus-like animal models [6]. The exact source of circulating IL-39 in human T2DM has not yet been established, but it is plausible that activated B cells, macrophages, and adipose-tissue immune cells contribute to its production in the context of metabolic inflammation. The positive correlation between IL-39 and HbA1c observed in the present study supports the hypothesis that IL-39 expression is modulated by chronic glycaemic stress, while the negative correlation with HDL is consistent with the inflammatory-cytokine profile typically observed in dyslipidaemic patients with T2DM [19].

ROC curve analysis demonstrated that serum IL-39 has excellent ability to discriminate patients with T2DM from healthy controls (AUC = 0.904, sensitivity = 0.844, specificity = 0.820 at a cut-off of 8.975 ng/mL). The AUC obtained in this study is somewhat lower than that reported by Nussrat and Ad'hiah (AUC = 0.973) [11], which may reflect differences in study populations, ELISA kits, or analytical calibration. Nevertheless, the consistent direction of effect across two independent Iraqi cohorts reinforces IL-39 as a candidate biomarker for T2DM and warrants further investigation in multi-centre, multi-ethnic studies.

A family history of diabetes is a well-established risk factor for T2DM; individuals with parents or siblings affected by the disease have a markedly increased risk of developing T2DM [23,24]. Whether genetic predisposition modulates IL-39 expression in T2DM remains to be determined, and future studies should also investigate the relationship between IL-39 and other immune-metabolic markers, such as adipokines, TNF-α, and IL-6, in larger, prospectively followed cohorts.

Limitations

Several limitations of the present study should be acknowledged. First, this was a single-centre, case-control study conducted at the Diabetes Centre of Al-Sadr Medical City in Al-Najaf, Iraq, and the relatively limited sample size (45 patients and 45 controls) may restrict the generalisability of the findings to other populations and ethnicities. Second, the cross-sectional design precludes inferences about causality between elevated serum IL-39 levels and the development or progression of T2DM. Third, serum IL-39 was measured at a single time-point, and intra-individual variability over time was not assessed. Fourth, important potential confounders — including the duration of diabetes, specific antidiabetic medications, dietary habits, smoking status, and other circulating inflammatory mediators (e.g., TNF-α, IL-6, hs-CRP) — were not included in the analysis. Fifth, the question of whether bioactive IL-39 is expressed in human immune cells remains an open scientific debate, and the analytical performance of commercial ELISA kits for human IL-39 still requires further independent validation. Finally, follow-up data are not available, and prospective longitudinal studies will be required to clarify whether IL-39 can serve as a prognostic biomarker for T2DM and its complications.

Conclusion

In summary, serum IL-39 levels were significantly elevated in patients with T2DM compared with healthy controls and were significantly correlated with fasting plasma glucose, HbA1c, and lipid parameters. ROC curve analysis demonstrated that serum IL-39 has excellent diagnostic performance in distinguishing T2DM patients from healthy controls (AUC = 0.904). These findings support the inclusion of IL-39 among the panel of inflammatory cytokines under investigation as candidate biomarkers for T2DM. Larger, multi-centre, prospective studies are warranted to confirm these findings and to evaluate the prognostic value of IL-39 for diabetic complications.

CRediT

Author contributions: All authors contributed to the conception and design of the study. Material preparation, data collection, and laboratory analyses were performed by all authors. The first draft of the manuscript was prepared by the corresponding author, and all authors critically reviewed, edited, and approved the final version of the manuscript for submission.

Acknowledgment

The authors express their sincere appreciation to all the staff of the Diabetes Centre at Al-Sadr Teaching Hospital, Al-Najaf, Iraq, for their support during sample collection and patient recruitment, and to all participants who agreed to take part in this study.

Ethical Approval

The study protocol was reviewed and approved by the Institutional Review Board of Al-Nasiriyah General/ Turkish Hospital (approval number 1202; date of approval 22 February 2026), and was conducted in accordance with the Declaration of Helsinki, as revised in 2013. All participants provided written informed consent before any study procedure.

Informed Consent

Not applicable.

Funding

This study was self-funded by the authors and did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data Sharing Statement

The datasets generated and analysed during the current study are not publicly available because of confidentiality of patient information, but are available from the corresponding author on reasonable request, subject to institutional approval and compliance with applicable data-protection regulations.

Conflict of Interest

The authors declare no competing interests.

Similarity Check

It was applied by Ithenticate@.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

About The License©

References

1. International Diabetes Federation. IDF Diabetes Atlas. 11th ed. Brussels: International Diabetes Federation; 2024. Available from: https://diabetesatlas.org
2. Roden M, Shulman GI. The integrative biology of type 2 diabetes. Nature. 2019;576(7785):51–60.
3. Berbudi A, Rahmadika N, Tjahjadi AI, Ruslami R. Interplay between insulin resistance and immune dysregulation in type 2 diabetes mellitus: implications for therapeutic interventions. J Inflamm Res. 2025;18:1413–1437.
4. Weinberg Sibony R, Segev O, Dor S, Raz I. Overview of oxidative stress and inflammation in diabetes. J Diabetes. 2024;16(10):e70014.
5. Lu Z, Xu K, Wang X, Li Y, Li M. Interleukin 39: a new member of interleukin 12 family. Cent Eur J Immunol. 2020;45(2):214–217.
6. Wang X, Wei Y, Xiao H, Liu X, Zhang Y, Han G, et al. A novel IL-23p19/Ebi3 (IL-39) cytokine mediates inflammation in lupus-like mice. Eur J Immunol. 2016;46(6):1343– 1350.
7. Ecoeur F, Weiss J, Schleeger S, Guntermann C. Lack of evidence for expression and function of IL-39 in human immune cells. PLoS One. 2020;15(12):e0242329.
8. Luo Y, Liu F, Liu H, Chen H, Cheng W, Dong S, et al. Elevated serum IL-39 in patients with ST-segment elevation myocardial infarction was related with left ventricular systolic dysfunction. Biomark Med. 2017;11(6):419–426.
9. Yang MG, Tian S, Zhang Q, Wang J, Shang R, Hua R, et al. Elevated serum interleukin-39 levels in patients with neuromyelitis optica spectrum disorders correlated with disease severity. Mult Scler Relat Disord. 2020;46:102430.
10. Li Y, Wang H, Liu R, Chen R. Interleukin-39 exacerbates concanavalin A-induced liver injury. Immunopharmacol Immunotoxicol. 2021;43(1):94–99.
11. Nussrat SW, Ad'hiah AH. Interleukin-39 is a novel cytokine associated with type 2 diabetes mellitus and positively correlated with body mass index. Endocrinol Diabetes Metab. 2023;6(3):e409.
12. Hassan SS, Abdelkawy M, Shaker OG, Tarrad NAF. IL-39 and IL-35 gingival crevicular fluid levels in diabetic patients with generalized periodontitis. Clin Oral Investig. 2024;28(2):124.
13. Ahmadi P, Janzadeh A, Honardoost M, Taherkhani S, Doyle D, Mojarad N. The role of IL-39 in autoimmune diseases: from general to immunopathogenesis. Cytokine. 2025;192:156969.
14. American Diabetes Association Professional Practice Committee. 2. Diagnosis and classification of diabetes: standards of care in diabetes—2024. Diabetes Care. 2024;47(Suppl 1):S20–S42.
15. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods. 2007;39(2):175–191.
16. Weir CB, Jan A. BMI classification percentile and cut off points. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.
17. Aras M, Tchang BG, Pape J. Obesity and diabetes. Nurs Clin North Am. 2021;56(4):527–541.
18. Klein S, Gastaldelli A, Yki-Järvinen H, Scherer PE. Why does obesity cause diabetes? Cell Metab. 2022;34(1):11–20.
19. Khanna D, Khanna S, Khanna P, Kahar P, Patel

BM. Obesity: a chronic low-grade inflammation and its markers. Cureus. 2022;14(2):e22711.

20. Feldman EL, Callaghan BC, Pop-Busui R, Zochodne DW, Wright DE, Bennett DL, et al. Diabetic neuropathy. Nat Rev Dis Primers. 2019;5(1):41.
21. Zheng H, Sun W, Zhang Q, Zhang Y, Ji L, Liu X, et al. Pro-inflammatory cytokines predict the incidence of diabetic peripheral neuropathy over 5 years in Chinese type 2 diabetes patients: a prospective cohort study. EClinicalMedicine. 2021;31:100649.
22. Bastian D, Wu Y, Betts BC, Yu XZ. Interleukin-23 receptor signaling by interleukin-39 potentiates T cell pathogenicity in acute graft-versus-host disease. Am J Transplant. 2021;21(11):3538–3549.
23. Choi J, Choi JY, Shin A, Lee SA, Lee KM, Oh J, et al. Association between family history of diabetes and clusters of adherence to healthy behaviors: cross-sectional results from the Health Examinees-Gem (HEXA-G) study. BMJ Open. 2019;9(4):e025477.
24. Tsenkova VK, Karlamangla AS, Ryff CD. Parental history of diabetes, positive affect, and diabetes risk in adults: findings from MIDUS. Ann Behav Med. 2016;50(6):836–843.