Molecular Biology Research Communications 2026;15(3):165-173 DOI:10.22099/mbrc.2026.55659.2277

Original Article MBRC Open Access

Linking *SIRT1* gene variation and protein levels to the pathophysiology of type 2 diabetes

Hayder Hasan-Idan[1], Leila Kohan[2,*]

1) Department of Biology, Shi.C., Islamic Azad University, Shiraz, Iran
2) Department of Biology, Ars.C., Islamic Azad University, Arsanjan, Iran

ABSTRACT

Sirtuin 1 (*SIRT1*), an NAD^+-dependent deacetylase, is involved in glucose homeostasis, insulin signaling, and inflammatory regulation, making it a potential molecular target in type 2 diabetes mellitus (T2DM). This case–control study investigated the association between serum SIRT1 levels, the *SIRT1* promoter polymorphism rs7895833, and metabolic parameters in 150 patients with T2DM and 150 age- and sex-matched healthy controls. Serum SIRT1 concentrations were measured by ELISA, and rs7895833 genotyping was performed using allele-specific PCR. Clinical and biochemical variables were also assessed. Serum SIRT1 levels were significantly lower in patients with T2DM than in controls ($p < 0.001$) and showed significant inverse correlations with fasting plasma glucose ($p = 0.001$) and HbA1c ($p < 0.001$). Genotypic analysis revealed a significant difference in the distribution of the rs7895833 AG genotype between the two groups ($p = 0.03$), and under the overdominant model (AG vs. AA + GG), the heterozygous AG genotype was significantly associated with T2DM risk (OR = 1.81, $p = 0.011$), whereas no significant association was found between *SIRT1* genotypes and circulating SIRT1 levels. These findings suggest that reduced SIRT1 is associated with hyperglycemia and poor glycemic control in T2DM. Overall, SIRT1 may serve as a potential biomarker and molecular mediator in T2DM pathogenesis. This study provides original data from a Middle Eastern population and may help inform future mechanistic and comparative studies.

Keywords: Type 2 Diabetes Mellitus; SIRT1; Serum Biomarker; Genetic Association Study

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disease characterized by persistent hyperglycemia due to defects in insulin secretion, impaired insulin action, or a combination of both. Its global burden has risen dramatically, and estimates suggest that the number of affected individuals may exceed 640 million by 2040, largely as a consequence of physical inactivity, obesity, and population aging [1, 2]. In addition to disrupting glucose homeostasis, T2DM markedly elevates the risk of both microvascular and macrovascular complications, thereby increasing morbidity and premature mortality [3].

Recent developments in molecular endocrinology have highlighted the contribution of epigenetic regulators to T2DM pathogenesis. Among these, Sirtuin 1 (SIRT1)—a nicotinamide

*Corresponding Author: Department of Biology, Ars.C., Islamic Azad University, Arsanjan, Iran. P.O. Box: 73761/168; Tel: +98 9177193094; Email: leila.kohan@iau.ac.ir

pISSN 2322-181X eISSN 2345-2005

adenine dinucleotide (NAD^+)-dependent class III histone deacetylase—has attracted considerable attention as an important regulator of energy balance, insulin responsiveness, and inflammatory processes [4]. SIRT1 influences metabolic regulation across multiple tissues: it supports pancreatic β-cell viability and function, facilitates insulin signaling, suppresses hepatic glucose output, enhances fatty acid oxidation in skeletal muscle and liver, and dampens inflammatory pathways [5, 6]. Owing to these broad metabolic effects, SIRT1 has emerged as a promising target for the treatment of insulin resistance and T2DM.

Genetic variation within the *SIRT1* gene may alter its expression or biological activity, thereby affecting susceptibility to metabolic disorders. The rs7895833 single-nucleotide polymorphism (SNP), situated in the promoter region of SIRT1 on chromosome 10q21.3, has received particular attention because of its potential regulatory significance. Previous studies have linked this variant to metabolic traits, including body mass index (BMI), lipid profile, and insulin sensitivity, and have also suggested associations with cardiovascular disease, polycystic ovary syndrome, and T2DM [7, 8].

Nevertheless, the functional significance of rs7895833 in relation to circulating SIRT1 levels and its clinical relevance in T2DM remains incompletely understood. Accordingly, the present study was designed to examine the association of rs7895833 with T2DM risk and to assess its relationship with serum SIRT1 levels. In addition, we evaluated the correlation between *SIRT1* expression and key anthropometric and biochemical indicators of metabolic health, with the aim of clarifying its potential utility as a biomarker and therapeutic target in T2DM.

MATERIALS AND METHODS

Study Design and Ethical Approval: This cross-sectional case–control study was performed between November 1, 2022, and January 20, 2023, as a component of postgraduate research affiliated with an academic institution in Iran. The practical elements of the research, encompassing participant recruitment, biological sample collection, and laboratory investigations, were executed in Babylon, Iraq, under the guidance of local authorities. The study's protocol received ethical approval from the Research Committee of the Training and Human Development Center, Babylon Health Directorate, Ministry of Health, Iraq, under approval number 22, issued on November 14, 2022.

Data acquisition entailed a thorough review of existing patient records, supplemented by the administration of standardized questionnaires to both individuals diagnosed with type 2 diabetes and healthy control subjects. Access to the collected data was granted from November 2022 through January 2023. To uphold participant confidentiality, researchers were precluded from accessing any directly identifiable personal information during or subsequent to data collection; all records were anonymized prior to analysis.

The research adhered strictly to the ethical tenets outlined in the Declaration of Helsinki. Prior to their enrollment, all participants provided written informed consent. Furthermore, stringent measures were implemented to anonymize all personal details, ensuring unwavering confidentiality throughout the research process.

Study Population and Selection Criteria: A total of 300 participants were enrolled, comprising 150 patients with newly diagnosed T2DM and 150 age- and sex-matched healthy controls. To ensure the integrity of the metabolic and biochemical data, rigorous inclusion and exclusion criteria were applied. Inclusion criteria for the case group were: (1) Age between 30 and 65 years; (2) Recent diagnosis of T2DM based on ADA criteria (FPG ≥ 126 mg/dL or HbA1c ≥ 6.5%); (3) Being drug-naive, having received no prior pharmacological treatment for diabetes (including metformin, sulfonylureas, or insulin therapy).

Exclusion criteria for both groups included: (1) Use of lipid-lowering agents (e.g., statins), anti-inflammatory drugs (corticosteroids or NSAIDs), or any antioxidant supplements within the

three months prior to the study; (2) Presence of chronic inflammatory diseases, autoimmune disorders, or advanced diabetic complications (nephropathy or retinopathy); (3) History of malignancy or hepatic dysfunction; (4) Pregnancy or lactation.

By excluding individuals on medication, we minimized potential confounding effects on the SIRT1 signaling pathway and metabolic homeostasis.

Sample Collection: Five milliliters of venous blood were collected from each participant using sterile technique. The samples were then divided into two aliquots: 2 mL was placed into EDTA-containing tubes for genomic DNA extraction, whereas the remaining 3 mL was transferred to plain gel tubes for serum separation. The gel tubes were centrifuged at 3,000 rpm for 10 minutes, after which the separated serum was aliquoted and stored at −20◦C until subsequent biochemical and molecular analyses.

Biochemical and Hormonal Assessments: Serum concentrations of SIRT1 were determined using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (SunLong Biotech, China) according to the manufacturer's instructions. Fasting insulin levels were quantified via ELISA (Monobind Inc., USA). Glycated hemoglobin (HbA1c) was measured using an automated analyzer (Clover A1c Plus, Osang Healthcare, Korea).

Standard biochemical parameters, encompassing fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), blood urea, and serum creatinine, were assessed utilizing colorimetric assay kits (Linear Chemicals, Spain). Insulin resistance was estimated using the following formula: HOMA-IR = [Fasting Insulin (µIU/mL) × FPG (mg/dL)] / 405.

Genotyping of *SIRT1* rs7895833: Genomic DNA was isolated from whole blood using the AddBio extraction kit (Sweden). Genotyping of the *SIRT1* rs7895833 polymorphism was performed using the tetra-primer amplification refractory mutation system-polymerase chain reaction (T-ARMS PCR) method.

The T-ARMS PCR primers for the *SIRT1* rs7895833 polymorphism were designed and optimized using Oligo 7 software (Molecular Biology Insights, Inc., USA). To ensure high specificity for the target alleles and to avoid cross-reactivity or primer-dimer formation, the sequences were further cross-validated using AlleleID software and screened against the human genome using the NCBI Primer-BLAST tool. The finalized primer sequences, which produce distinct fragments for the A and G alleles as well as an internal control (outer primers), are detailed in Table S1 of the supplementary file.

The PCR amplification was performed in a 25 µL total reaction volume. Each reaction mixture comprised 12.5 µL of 2× Master Mix (Promega, USA), 0.5 µL of each outer forward and reverse primer, 2 µL of each allele-specific inner primer, 1 µL of genomic DNA template, and 6.5 µL of nuclease-free water.

Thermal cycling conditions were as follows: initial denaturation at 95°C for 5 min; 30 cycles consisting of denaturation at 95°C for 45 s, annealing at 57°C for 45 s, and extension at 72°C for 45 s; followed by a final extension step at 72°C for 7 min. Subsequent to amplification, the PCR products were separated on 2% agarose gels stained with ethidium bromide and visualized using UV transillumination.

Statistical Analysis: Data analysis was conducted using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA). Genotype distributions were evaluated for Hardy–Weinberg equilibrium using the chi-square ($\chi 2$) test. Continuous variables were compared between groups using the independent sample t-test or one-way ANOVA, as appropriate.

The association between the *SIRT1* polymorphism and T2DM risk was assessed by calculating odds ratios (ORs) and 95% confidence intervals (CIs) via logistic regression analysis. Genetic associations were examined under codominant, dominant, recessive, codominant and allelic inheritance models, following the strategic framework established by

Saadat [9]. Furthermore, Pearson correlation coefficients were employed to analyze the relationships between serum SIRT1 concentrations and clinical or biochemical parameters. Statistical significance was defined as a two-tailed p-value < 0.05.

RESULTS

No statistically significant differences in age (p = 0.069) or sex distribution (p = 0.489) were observed between the case and control groups, confirming that the demographic matching was appropriate for subsequent analyses. Conversely, patients with T2DM demonstrated significantly higher levels of body mass index (BMI), fasting plasma glucose (FPG), HbA1c, fasting insulin, HOMA-IR, triglycerides (TG), and very-low-density lipoprotein (VLDL) compared to the healthy controls (p < 0.001 for all). No significant differences were detected between the groups regarding total cholesterol (TC), HDL, LDL, or creatinine levels (Supplementary Table S2).

As depicted in Figure 1, the mean serum SIRT1 concentration was significantly lower in the T2DM group (6.01 ± 1.29 ng/mL) compared to the healthy controls (8.70 ± 1.64 ng/mL; p < 0.001). This marked discrepancy highlights a potential inverse correlation between circulating SIRT1 levels and the diagnosis of T2DM.

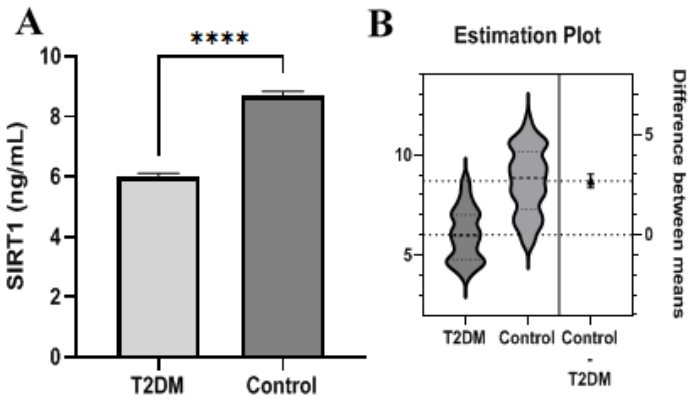

Figure 1: (A) Comparison of mean serum SIRT1 levels between individuals with type 2 diabetes mellitus (T2DM) and healthy controls, showing a markedly lower concentration in the T2DM group (****p < 0.001). **(B)** Estimation plot further illustrating the significant reduction in circulating SIRT1 levels among diabetic patients, reinforcing its potential as a disease-related biomarker.

Figure 2 demonstrates the agarose gel electrophoresis results of the T-ARMS PCR used for genotyping the *SIRT1* rs7895833 polymorphism. Distinct banding patterns corresponding to the AA, AG, and GG genotypes are clearly visible, confirming successful amplification and reliable differentiation between alleles.

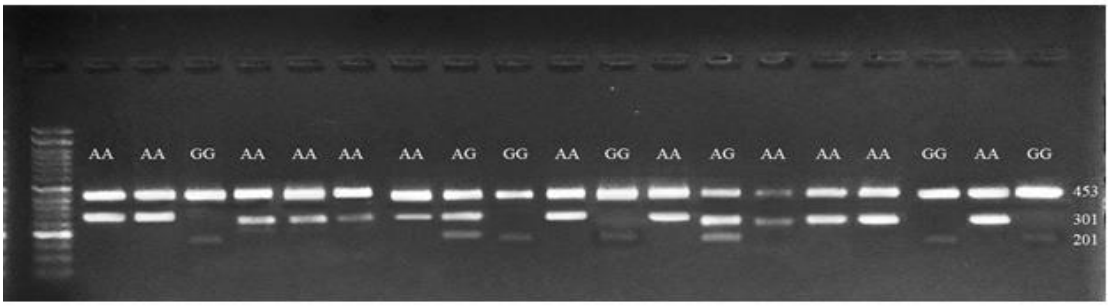

Figure 2: Agarose gel electrophoresis of SIRT1 rs7895833 genotypes amplified by T-ARMS PCR. Clear banding patterns corresponding to AA (453 bp), AG (453, 301, and 201 bp), and GG (453 and 201 bp) genotypes are shown, confirming successful discrimination of alleles and genotypic profiles.

The distribution of genotype and allele frequencies for the *SIRT1* rs7895833 variant is presented in Table 1. Genotype distribution in the control group conformed to Hardy–Weinberg equilibrium ($\chi^2 = 2.97$, df=1, $p = 0.227$). The AG genotype was the most frequently observed in the T2DM group (52.7%), whereas the AA genotype was predominant among healthy controls (48.0%). Logistic regression analysis indicated that carriers of the AG genotype were at a significantly higher risk of T2DM compared to those with the AA genotype (OR = 1.69; p=0.033). Furthermore, we evaluated the association of the *SIRT1* rs7895833 polymorphism with T2DM risk under various inheritance models, including codominant and overdominant models. The logistic regression analysis revealed that the overdominant model—comparing the AG genotype against the combined AA and GG genotypes—was significantly associated with an increased risk of T2DM (OR = 1.815, p = 0.011).

Table 1: Distribution of *SIRT1* rs7895833 genotypes and genetic model analysis in the study groups.

Genotype/allele	Control (%) n=150	T2DM (%) n=150	OR (95% CI)	*p*-value
Co-dominant				
AA	72 (48.0)	59 (39.3)	1.0	
AG	57 (38)	79 (52.7)	1.69 (1.04-2.74)	0.033
GG	21 (14.0)	12 (8.0)	0.69 (0.31-1.53)	0.370
Overdominant				
AA+GG	93 (62)	71 (47.3)	1.0	
AG	57 (38)	79 (52.7)	1.81 (1.14-2.87)	0.011

Subgroup analysis of serum SIRT1 concentrations stratified by rs7895833 genotypes showed no significant differences in either the T2DM or control group (Fig. 3). Within the diabetic group, mean SIRT1 levels across AA, AG, and GG genotypes were 6.13 ± 1.30, 5.97 ± 1.32, and 5.74 ± 1.12 ng/mL, respectively (p = 0.593). Similar non-significant trends were observed in the control group (p = 0.872), Serum SIRT1 levels did not differ significantly across rs7895833 genotypes in either the diabetic or control group, as assessed by subgroup analysis.

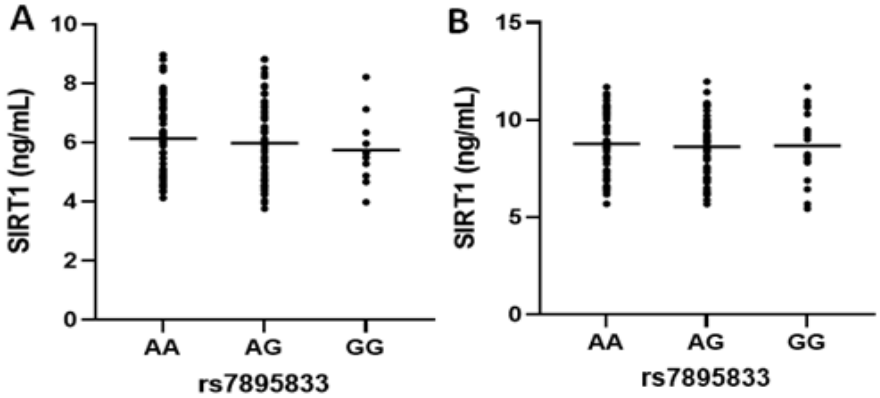

Figure 3: (A) Mean serum SIRT1 level in T2DM group according to rs7895833 polymorphism. (B) Mean serum SIRT1 level in control group according to rs7895833 polymorphism.

Pearson correlation analysis revealed significant inverse correlations between serum SIRT1 levels and several key clinical and metabolic parameters. Within the T2DM group, lower SIRT1 concentrations were significantly associated with increased BMI, age, fasting insulin, HbA1c, FPG, and HOMA-IR. These associations were consistent with findings in the control group for BMI and age, although correlations with insulin, HbA1c, and FPG were not statistically significant (Table 2).

Notably, no significant correlations were detected between SIRT1 levels and lipid profile components, including TG, TC, HDL, LDL, or VLDL, in either study group. This suggests that the regulatory role of SIRT1, within the context of our population, may be more pronounced in glucose metabolism and insulin signaling pathways rather than in lipid homeostasis.

Table 2: Pearson correlation analysis of serum SIRT1 concentrations with anthropometric and biochemical variables in diabetic and non-diabetic groups.

SIRT1/Parameters	Groups	Pearson correlation	*p*-value
Body Mass Index (BMI)	T2DM (n=150)	-.263-**	.001
	Control (n=150)	-.394-**	.000
Age	T2DM (n=150)	-.199-*	.015
	Control (n=150)	-.173-*	.035
Insulin	T2DM (n=150)	-.288-**	.000
	Control (n=150)	-.115-	.163
HbA_{1c}	T2DM (n=150)	-.303-**	.000
	Control (n=150)	-.059-	.476
Fasting plasma glucose (FPG)	T2DM (n=150)	-.285-**	.000
	Control (n=150)	-.006-	.939
Homeostatic Model Assessment for Insulin Resistance (HOMA-IR)	T2DM (n=150)	-.270-**	.001
	Control (n=150)	-.116-	.158
Triglycerides (TG)	T2DM (n=150)	-.145-	.077
	Control (n=150)	-.066-	.422
Total cholesterol (TC)	T2DM (n=150)	-.099-	.228
	Control (n=150)	.072	.383
High density lipoprotein (HDL)	T2DM (n=150)	.003	.975
	Control (n=150)	-.076-	.354
High density lipoprotein (LDL)	T2DM (n=150)	-.063-	.445
	Control (n=150)	.097	.240
very low density lipoprotein (VLDL)	T2DM (n=150)	-.145-	.077
	Control (n=150)	-.066-	.422

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

Type 2 diabetes mellitus (T2DM) emerges from a complex interplay of insulin resistance, β-cell failure, and persistent systemic inflammation. Central to this metabolic stability is SIRT1, an NAD^+-dependent deacetylase, which functions as a key orchestrator of insulin signaling, energy homeostasis, and mitochondrial biogenesis across metabolically active tissues, including the liver, adipose tissue, and skeletal muscle [10, 11].

Our data, revealing markedly lower serum SIRT1 levels in patients with T2DM, corroborate earlier findings that link diminished SIRT1 expression to progressive metabolic decline [12]. Beyond this reduction, the significant inverse associations between circulating SIRT1 and markers such as BMI, FPG, HbA1c, fasting insulin, and HOMA-IR further characterize SIRT1 as a potential indicator of metabolic health, a stance echoed by previous studies in various glycemic cohorts [13]. These findings point toward a probable deficit in glucose homeostasis driven by systemic *SIRT1* downregulation. Interestingly, the absence of significant correlations between SIRT1 and lipid profile components in our study suggests that the regulatory influence of SIRT1 in this cohort is perhaps more deeply embedded in glucose metabolism rather than lipid homeostasis. This functional hierarchy is consistent with existing evidence demonstrating that pharmacological or metabolic activation of the AMPK/SIRT1/PGC-1α signaling axis can effectively attenuate diabetic complications, such as nephropathy, through the rectification of oxidative stress and inflammatory signaling [14, 15].

A primary finding of this research is the significant correlation between the rs7895833 AG genotype and T2DM susceptibility. Despite the absence of a statistically significant difference in allele frequencies between groups, employing an overdominant model—in accordance with established guidelines for genetic association studies [9]—revealed that the heterozygous (AG) state confers a notably higher risk (OR = 1.815; p=0.011) compared to the homozygous counterparts (AA and GG). This pattern, suggestive of a 'heterozygote disadvantage' or 'negative heterosis,' aligns with earlier evidence linking this specific locus to diabetic susceptibility, particularly under conditions of environmental or prenatal stress [16].

Furthermore, our observations corroborate data from Chinese Han cohorts and other populations, where rs7895833 has been tied to metabolic syndrome and various glycemic traits [17]. The lack of a direct correlation between this genotype and circulating SIRT1 levels implies that the variant may exert its influence through post-transcriptional or tissue-specific regulatory pathways rather than by modulating systemic protein concentration.

The existing literature regarding *SIRT1* polymorphisms exhibits considerable heterogeneity. While the rs3758391 variant, for example, has been associated with T2DM in both Iranian and Bangladeshi populations, such findings are not universally consistent across ethnic groups [13]. Similarly, other SIRT1 polymorphisms have recently emerged as potential markers for diabetic nephropathy in European Caucasian cohorts [18, 19]. This variability is likely rooted in differences regarding ethnicity, environmental exposures, sample size, and the selection of analytical models [20]. Significantly, our findings contribute a novel perspective to this field by offering data from a Middle Eastern population, a demographic that has remained underrepresented in prior genetic studies.

SIRT1 exerts a profound influence on metabolic homeostasis through multifaceted molecular pathways. By activating PGC-1α, it drives mitochondrial biogenesis; concurrently, it tempers NF-κB-mediated inflammatory responses and modulates gluconeogenesis through the deacetylation of FOXO1. Furthermore, SIRT1 potentiates insulin signaling within hepatic and muscular tissues via the PI3K/Akt axis [11, 21, 22]. The metabolic profile observed in T2DM patients may, therefore, be a direct consequence of the disruption of these critical regulatory circuits. Recent evidence further suggests that nutrient-sensitive modifications, particularly O-GlcNAcylation, modulate SIRT1 functionality, thereby providing a dynamic link between shifting metabolic states and hyperglycemia [23, 24].

This study acknowledges several limitations. Given our cross-sectional design, establishing definitive causal relationships between SIRT1 concentrations, genetic polymorphisms, and T2DM pathogenesis remains constrained. Furthermore, the geographic specificity of our recruitment may affect the broader generalizability of these findings. It is also important to note that certain confounding variables—including dietary patterns, physical activity levels, and broader systemic inflammation—were not within the scope of this investigation. Similarly, the study did not explore tissue-specific expression patterns or complex gene-gene interactions.

Nevertheless, these findings offer distinct strengths. By integrating biochemical profiling with genetic analysis, this research provides a comprehensive view of SIRT1's role in T2DM. The application of robust methodologies, such as T-ARMS PCR for genotyping and standardized biochemical assays, ensures a high degree of analytical reliability. Critically, our data fill a significant gap in genetic epidemiology by providing original evidence from a Middle Eastern cohort, a population historically underrepresented in this field.

In conclusion, this study identifies both decreased circulating SIRT1 levels and the rs7895833 AG genotype as independent correlates of heightened T2DM risk. These significant inverse correlations between SIRT1 and clinical metabolic markers emphasize its potential utility as a biomarker for metabolic health. Moving forward, large-scale, multiethnic longitudinal studies and functional genomic assessments are essential to elucidate the causal dynamics and potential therapeutic avenues for SIRT1 modulation in diabetes care.

Acknowledgements: We thank all patients and healthy subjects for participating in this study. No financial support in any form has been or received from any commercial party related directly or indirectly to the subject of this article.

Conflict of Interest: The authors declare that they have no conflict of interest.

Authors' Contribution: HHI, did all experiments, figures, and table preparation, and prepared the first draft of the manuscript. LK co-correspond to the project, made the initial plan of the project, supervised the direction of the project, and did a final proof of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate: The study protocol was reviewed and approved by the Research Committee of the Training and Human Development Center, Babylon Health Directorate, Ministry of Health, Iraq (Approval No. 22, dated 14 November 2022).

REFERENCES

1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018;14:88-98.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37(Suppl 1):S81-S90.
3. Lawrence JM, Divers J, Isom S, Saydah S, Imperatore G, Pihoker C, Marcovina SM, Mayer-Davis EJ, Hamman RF, Dolan L, Dabelea D, Pettitt DJ, Liese AD; SEARCH for diabetes in youth study group. Trends in prevalence of type 1 and type 2 diabetes in children and adolescents in the US, 2001-2017. JAMA 2021;326:717-727.
4. Kume S, Uzu T, Kashiwagi A, Koya D. SIRT1, a calorie restriction mimetic, in a new therapeutic approach for type 2 diabetes mellitus and diabetic vascular complications. Endocr Metab Immune Disord Drug Targets 2010;10:16-24.
5. Lee DH. Sirt1 as a new therapeutic target in metabolic and age-related diseases. Chonn Med J 2010;46:67-73.
6. Albiero M, Avogaro A, Fadini GP. A perspective on sirtuins in the metabolic syndrome. Metab Syndr Relat Disord 2015;13:161-164.
7. Han J, Wei M, Wang Q, Li X, Zhu C, Mao Y, Wei L, Sun Y, Jia W. Association of genetic variants of SIRT1 with type 2 diabetes mellitus. Gene Expr 2015;16:177-185.
8. Ramkaran P, Phulukdaree A, Khan S, Moodley D, Chuturgoon AA. Sirtuin 1 rs1467568 and rs7895833 in South African Indians with early-onset coronary artery disease. Cardiovasc J Afr 2016;27:213-217.
9. Saadat M. A strategic approach to genetic model selection in association studies: A practical guide. Mol Biol Res Commun 2026;15:81-83.
10. Kitada M, Ogura Y, Monno I, Koya D. Sirtuins and type 2 diabetes: Role in inflammation, oxidative stress, and mitochondrial function. Front Endocrinol (Lausanne) 2019;10:187.
11. Kitada M, Koya D. SIRT1 in type 2 diabetes: Mechanisms and therapeutic potential. Diabetes Metab J 2013;37:315-325.
12. Mihanfar A, Akbarzadeh M, Ghazizadeh Darband S, Sadighparvar S, Majidinia M. SIRT1: a promising therapeutic target in type 2 diabetes mellitus. Arch Physiol Biochem 2024;130:13-28.
13. Ahmed R, Safa MR, Zahid ZI, Chowdhury MMI, Hasan ABMK, Mostaid MS, Reza HM. Association of SIRT1 rs3758391 polymorphism with T2DM in Bangladeshi population: Evidence from a case-control study and meta-analysis. Health Sci Rep 2025 19;8:e70495.
14. Hou S, Zhang T, Li Y, Guo F, Jin X. Glycyrrhizic acid prevents diabetic nephropathy by activating AMPK/SIRT1/PGC-1α signaling in db/db mice. J Diabetes Res 2017;2017: 2865912.
15. Dong YJ, Liu N, Xiao Z, Sun T, Wu SH, Sun WX, Xu ZG, Yuan H. Renal protective effect of sirtuin 1. J Diabetes Res 2014;2014:843786.
16. Botden IP, Zillikens MC, de Rooij SR, Langendonk JG, Danser AH, Sijbrands EJ, Roseboom TJ. Variants in the SIRT1 gene may affect diabetes risk in interaction with prenatal exposure to famine. Diabetes Care 2012;35:424-426.
17. Tao TT, Lin XH, Tang S, Gui WW, Zhu WF, Li H. Association of genetic variants in the Sirt1 and Nrf2 genes with the risk of metabolic syndrome in a Chinese Han population. BMC Endocr Disord 2022;22:84.

18. Letonja J, Završnik M, Makuc J, Šeruga M, Peterlin A, Cilenšek I, Petrovič D. Sirtuin 1 rs7069102 polymorphism is associated with diabetic nephropathy in patients with type 2 diabetes mellitus. Bosn J Basic Med Sci 2021;21:642-646.
19. Naseri R, Khalili F, Rahimi Z, Yari K, Rezaei M. Protective role of SIRT1 (rs3758391 T > C) polymorphism against T2DM and its complications: Influence on GPx activity. Health Sci Rep 2024;7:e70106.
20. Wei L, Xiao Y, Li L, Xiong X, Han Y, Zhu X, Sun L. The susceptibility genes in diabetic nephropathy. Kidney Dis (Basel) 2018;4:226-237.
21. Palomer X, Salvadó L, Barroso E, Vázquez-Carrera M. An overview of the crosstalk between inflammatory processes and metabolic dysregulation during diabetic cardiomyopathy. Int J Cardiol 2013;168:3160-3172.
22. Ren BC, Zhang YF, Liu SS, Cheng XJ, Yang X, Cui XG, Zhao XR, Zhao H, Hao MF, Li MD, Tie YY, Qu L, Li XY. Curcumin alleviates oxidative stress and inhibits apoptosis in diabetic cardiomyopathy via Sirt1-Foxo1 and PI3K-Akt signalling pathways. J Cell Mol Med 2020;24:12355-12367.
23. DiNicolantonio JJ, McCarty MF, O'Keefe JH. Nutraceutical activation of Sirt1: a review. Open Heart 2022;9:e002171.
24. Chattopadhyay T, Maniyadath B, Bagul HP, Chakraborty A, Shukla N, Budnar S, Rajendran A, Shukla A, Kamat SS, Kolthur-Seetharam U. Spatiotemporal gating of SIRT1 functions by O-GlcNAcylation is essential for liver metabolic switching and prevents hyperglycemia. Proc Natl Acad Sci U S A 2020;117:6890-6900.