American Journal of Biology and Natural Sciences
https://biojournals.us/index.php/AJBNS
ISSN: 2997-7185

Evaluation of Serum SLC30A8 Levels in Patients with Type 2 Diabetes Mellitus-Related Hypertension in a Population from Wasit Province, Iraq

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Received: 2024, 15, May
Accepted: 2025, 21, Jun
Published: 2025, 17, Jul

Annotation: This study aimed to evaluate serum levels of the SLC30A8 protein in patients with type 2 diabetes mellitus (T2DM)-related hypertension. Quantification was performed using an enzyme-linked immunosorbent assay (ELISA). Results demonstrated significantly lower serum SLC30A8 concentrations in diabetic patients (304.577 ± 9.173 ng/mL) compared to healthy controls (364.085 ± 12.899 ng/mL, P = 0.0002). Gender stratification revealed significantly lower levels in female patients (283.886 ± 10.759 ng/mL) than in male patients (326.704 ± 16.267 ng/mL, P = 0.032). Both male and female diabetic patients showed reduced SLC30A8 levels compared to their respective control counterparts, with the decline more prominent in females (P = 0.0009 vs. P = 0.256 in males). No significant difference was found between male and female controls (P = 0.734).

Conclusion: The findings suggest a significant association between reduced serum SLC30A8 levels and T2DM-related hypertension, particularly in females. This reduction may reflect a functional impact of

the SLC30A8 rs13266634 polymorphism on protein expression, which could contribute to β-cell dysfunction and impaired insulin secretion.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder characterized by insulin resistance and impaired insulin secretion, representing a substantial global health challenge (Zimmet et al., 2014). Hypertension is a common comorbidity among individuals with T2DM and significantly increases the risk of cardiovascular disease and mortality (Cheng et al., 2017). Understanding genetic and molecular markers, such as the *SLC30A8* gene, is essential to elucidate disease mechanisms and potential therapeutic targets in patients affected by both conditions.

The objective of this study is to evaluate serum levels of the SLC30A8 protein in patients with T2DM-related hypertension and compare them to healthy controls, with a specific focus on gender-based differences. This aims to clarify the potential role of SLC30A8 expression in the pathophysiology of diabetes-associated hypertension.

2. Materials and Methods

2.1. Study Design

The current study is a case-control study. The study was carried out from

1 st October 2024 to 30th January 2025 in adult patients with type 2 daibetes mullitus-related hypertension compared to control populations living in Wasit. This study was performed

at the Department of biology College of Education for the Pure Sciences University of Wasit.

2.2. Study subjects

A total of 80 participants :45 confirmed patients with diabetes and

35 healthy individuals as controls were selected by using a convenient

sampling method.

1- Type 2 diabetes mellitus –related hypertension patients group: 45 patients with T2DM-related hypertension 22males and 23 females), and their age range was between 40–75 years (58.84 ± 8.20) years, median= 59 years).

2- Control group: the control group which comprised of 35 healthy individuals (18 males and 17 females) and their age range between 40-75 years (54.77 ± 11.63) years, median=50 years).

2.3. Blood Sample Collection

Five ml of venous blood was collected using a vacuum blood collection

Tube. The blood was placed in a pain tube to collect serum through centrifugation at 3000 revolutions per minute (rpm) for15min. Sera were dispensed into Eppendrof tubes and preserved at 20C°.

2.4. Determination of (SLC30A8) concentrations in sera from patients and controls

Human (SLC30A8) was used in the enzyme-linked immunosorbent assay technique (ELISA) to detect the amounts of (SLC30A8 rs13266634) in the serum of patients and controls. (Bioassay Technology Laboratory) in compliance with the guidelines provided by the manufacturer.

3. Results

3.1. Serum *SLC30A8* Protein Levels in Diabetic Patients and Healthy Controls

Serum concentrations of *SLC30A8* were significantly lower in diabetic patients (mean ± SE: 304.577 ± 9.173 ng/mL) compared to healthy controls (364.085 ± 12.899 ng/mL), with a highly significant difference ($P = 0.0002$). This reduction in protein levels may reflect a biological impact of the *rs13266634* polymorphism on gene expression or protein stability.

Table 1: Concentration of *SLC30A8* in patients and controls

Parameters Groups	ng/ml Mean±SE
Control	364.085±12.899
Patients	304.577 ±9.173
P-value	0.0002
Significant	* Sig.

3.2. Serum *SLC30A8* Levels by Gender

When analyzed by gender, serum *SLC30A8* levels were significantly lower in female diabetic patients (283.886 ± 10.759 ng/mL) than in male diabetic patients (326.704 ± 16.267 ng/mL), with $P = 0.032$. Furthermore, both male and female diabetic patients exhibited significantly reduced *SLC30A8* levels compared to their corresponding control groups. In males, levels decreased from 356.107 ± 19.56 ng/mL in controls to 326.704 ± 16.267 ng/mL in patients ($P = 0.256$), while in females, the decrease was more pronounced (from 365.410 ± 18.840 ng/mL in controls to 283.886 ± 10.759 ng/mL in patients; $P = 0.0009$). Notably, no significant difference in serum levels was found between males and females in the control group ($P = 0.734$)

Table 2: Concentration of SLC30A8 among male and females

Parameters Groups	ng/ml Mean± SE			
	Male	**Female**	**P-value**	**Significant**
Control	356.107**±19.56**	365.410±18.840	0.734	Ns.
Diabetic Patients	326.704**±16.267**	283.886±10.759	0.032	Sig.
P-value	0.256	0.0009		
Significance	Ns.	Sig.		

4. Discussion

The significant reduction in serum SLC30A8 protein levels observed in diabetic patients compared to controls supports the functional impact of the rs13266634 polymorphism on ZnT8 expression or stability. Lower ZnT8 levels could impair insulin secretion, contributing to β-cell dysfunction. This finding is consistent with previous research demonstrating decreased ZnT8 protein expression in diabetic subjects and its association with defective glucose-stimulated insulin secretion (Kobayashi *et al.*, 2017). The serum ZnT8 reduction might also reflect a compensatory downregulation in response to chronic hyperglycemia or β-cell stress.

Notably, females with diabetes exhibited significantly lower serum SLC30A8 levels compared to males. This sex difference in protein levels could be due to hormonal regulation, as estrogens have been shown to influence zinc transporter expression and β-cell function (Lefevre *et al.*, 2018). Additionally, sex-specific differences in inflammatory and metabolic profiles in T2DM may further modulate ZnT8 expression or turnover. Similar gender disparities in diabetes-related biomarkers have been documented in other populations, underscoring the importance of considering sex as a biological variable in genetic and biochemical studies (Kautzky-Willer *et al.*, 2016).

In previous studies that have investigated the association of other biomarkers among patients with

type2 DM from Wasit province, (Yousif and Ghali,2021), revealed that IL-10 is a major contributor to the onset of type 2 diabetes mellitus and there may be a correlation between low levels of interleukin-10 and type two diabetes .(Al-Sarray and Ahmed ,2021) found that may be a correlation between high levels of TNF-α and type 2 diabetes mellitus.(Shamkhi and Ahmed ,2021), displayed that levels of SIRT1 may be not associated with type2 diabetes mellitus. Furthermore, the cell free mitochondrial DNA increases significantly in patients with type2 diabetes mellitus (Hussein and Ghali,2022). COX-1 is a major contributor to the onset of type 2 diabetes and there may be an association between low levels of cyclooxygenase-1and type 2 diabetes (Jebil and Ghali,2021). (Mahmood and Ghali,2022), found also that there may be a correlation between high levels of OPG and T2DM.(Thamer etal.,2021) evaluated the serum levels of Interleukin-4 (IL-4) and Interleukin-6 (IL-6) of patients with type 2 diabetes mellitus among cases from Wasit province-Iraq.their results revealed that IL-4 concentrations had a non-significant difference when compared patients with type-2 diabetes mellitus with the control group (154 ± 7.00 versus (vs) 151.49 ± 21, P-value (P) = > 0.05). While patients with T2DM revealed elevated serum levels of IL-6 compared to control group (B 637.1 ± 355.9 versus 266.3 ± 128.8, P = < 0.001).

5. Conclusion

The findings suggest a significant association between reduced serum *SLC30A8* levels and T2DM-related hypertension, particularly in females. This reduction may reflect a functional impact of the *SLC30A8* rs13266634 polymorphism on protein expression, which could contribute to β-cell dysfunction and impaired insulin secretion.

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