Research Article

The Relationship Between Spexin With Antioxidants And Lipid Levels In Patients With Type 2 Diabetes And Obesity

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Abstract:

Type 2 diabetes mellitus (T2DM) is a chronic metabolic condition marked by sustained elevations in blood glucose levels and is frequently associated with dyslipidemia, obesity, and increased oxidative stress. This investigation aimed to determine serum spexin levels and to explore their relationships with selected biochemical parameters and antioxidant indicators among patients diagnosed with T2DM. Analysis of the collected data revealed a significant decrease in serum spexin levels in the patient group (156.72 ± 26.88 pg/mL) compared with healthy controls (205.5 ± 89.81 pg/mL). Spexin concentrations were also significantly lower across most body mass index (BMI) categories, while no statistically significant difference was identified in the ≥30 BMI category. Furthermore, patients showed significantly elevated fasting blood glucose, total cholesterol, triglycerides, LDL-C, VLDL-C, and peroxidase activity. In contrast, HDL-C levels, as well as catalase and aryl esterase activities, were significantly lower than those observed in the control group. Overall, the results indicate that reduced serum spexin is closely linked to impaired lipid metabolism, obesity, and inadequate glycemic control, supporting its potential value as a biomarker of oxidative stress among patients with T2DM.

Keywords: BMI, Dyslipidemia, Diabetes, Oxidative Stress, Spexin.

Introduction

Diabetes mellitus comprises a group of metabolic disorders defined by persistent elevation of blood glucose levels caused by inadequate insulin secretion, reduced insulin sensitivity, or the combined effect of both abnormalities [1], Among the different forms of diabetes, type 2 diabetes mellitus (T2DM) accounts for the largest proportion of cases and remains one of the most common chronic non-communicable diseases worldwide [2].

T2DM has a close association with metabolic syndrome, a condition commonly characterized by obesity, dyslipidemia, and excessive fat accumulation in the liver [3], Among these factors, obesity is recognized as one of the principal clinical contributors to the onset and progression of metabolic abnormalities that predispose individuals to T2DM [4]. of diabetes mellitus. Reactive oxygen species (ROS) together with other free radicals are produced during normal cellular metabolism, while additional oxidative molecules may arise following exposure to environmental factors such as cigarette smoking, radiation, and air pollution. These reactive molecules can damage cellular structures and are considered important contributors to the onset of several metabolic disorders, including diabetes mellitus [5,6], Spexin (SPX) is a peptide consisting of 14 amino acids that was first identified through bioinformatic approaches [7 It has been reported to participate in the regulation of glucose balance, lipid metabolism, and skeletal muscle physiology [8].

The peptide is widely distributed in several endocrine organs, including the pancreas, thyroid gland, and visceral adipose tissue [10]. Increasing evidence suggests that oxidative stress represents an important factor underlying the metabolic alterations associated with T2DM. Excessive production of reactive oxygen species (ROS) disrupts cellular homeostasis, promotes insulin resistance, and accelerates the progression of metabolic dysfunction [11].

Subjects and Methods

Venous blood specimens were obtained from individuals diagnosed with diabetes mellitus who attended Al-Wafaa Center in Mosul city. The study included 35 blood samples obtained from healthy individuals aged 30–65 years (15 females and 20 males), as well as 55 blood specimens collected from individuals diagnosed with type 2 diabetes

mellitus (T2DM) within the same age range (29 females and 26 males), collected during the period from 15/11/2025 to 15/1/2026.

Serum Preparation:

A volume of 5 mL of venous blood was obtained from both individuals with diabetes mellitus and healthy controls. The collected blood was transferred into gel tubes, maintained in a 37°C water bath for 10 minutes, after which serum was separated by centrifugation at 3000 × g for 10 minutes [12].

The concentration of spexin was determined using a commercial kit from Sunlong Biotech (China) based on the enzyme-linked immunosorbent assay (ELISA) technique. Body mass index (BMI) for both patients and control subjects was determined by dividing each participant's body weight (kg) by the square of their height (m^2) [13]. Serum glucose levels and glycated hemoglobin (HbA1c) were assessed using an automated clinical chemistry analyzer (Respons®920, DiaSys Diagnostic Systems, Germany). Glucose concentration was determined using an enzymatic colorimetric method based on the glucose oxidase–phenol aminophenazone (GOD-PAP) principle [14], while HbA1c levels were directly quantified in whole blood samples using a latex-enhanced immunoturbidimetric method [15]. Urea, creatinine, triglycerides, total cholesterol, together with high-density lipoprotein cholesterol (HDL-C), were analyzed using the FUJIFILM DRI-CHEM NX500i automated biochemical analyzer (Japan), which employs dry chemistry technology and measures analytes through reflectance spectrophotometry [16]. LDL-C and VLDL-C concentrations were calculated using the Friedewald equation, according to the following formula:

LDL-C (mmol/L) = Total cholesterol − HDL-C − (Triglycerides / 2.2) [17]

VLDL-C (mmol/L) = (Triglycerides) / 2.2 [18]

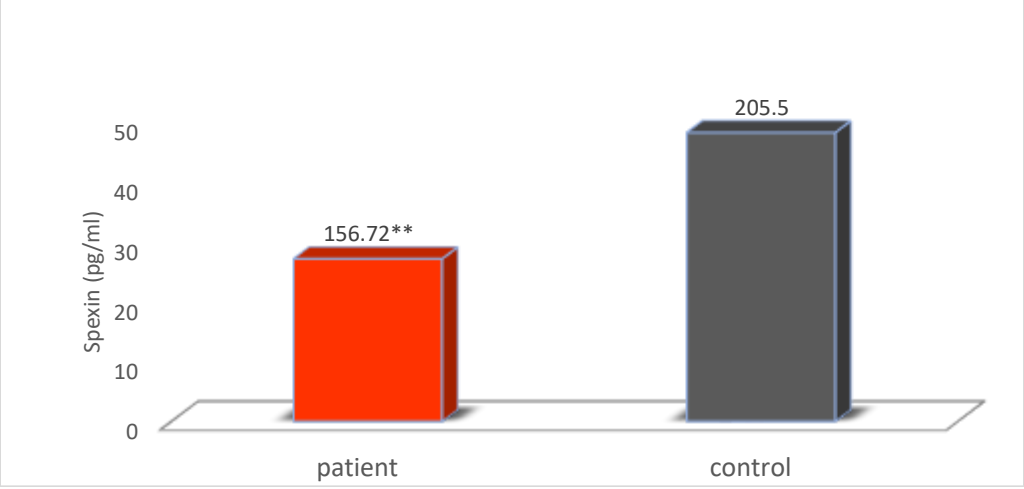
Peroxidase activity was determined through the enzymatic oxidation of hydrogen peroxide [19], while catalase activity was assessed by measuring the color produced by the reaction with hydrogen peroxide [20]. Aryl esterase activity was estimated using a modified method based on the enzymatic hydrolysis of phenyl acetate to produce acetic acid and phenol [21].

Statistical analysis

The data obtained in this study were analyzed using the Statistical Package for the Social Sciences (SPSS). Means and standard deviations were calculated using standard statistical methods. One-way analysis of variance (ANOVA) was applied to compare more than two groups, while the independent samples t-test was used for comparisons between two groups. The Pearson correlation coefficient (r) was employed to assess the relationship between the different parameters. A p-value of ≤ 0.05 was considered statistically significant.

Results and Discussion

Study the effect of Spexin hormone in Type 2 Diabetes patients compared to a control group:



**significant difference between patients and control at p≤0.01

Figure 1: Spexin levels in type 2 diabetes patients compared to the control group.

Figure 1. shows a decrease in spexin levels in patients with type 2 diabetes (156.72 ± 26.88 pg/mL) compared with the control group (205.5 ± 89.81 pg/mL). Several studies have similarly reported lower spexin levels among individuals diagnosed with type 2 diabetes than among healthy controls. This reduction in spexin levels reflects a disruption in metabolic processes and is often associated with increased insulin resistance, indicating the impact of the disease on this hormone and its role in regulating blood glucose levels [22,23,24].

Study of the effect of body mass index (BMI) on spexin concentration in Type 2 Diabetes patients compared to the control group:

Table 1 shows a significant decrease in spexin concentration in patients compared with the control group within the BMI categories of 18–24.9 and 25–29.9, whereas no significant difference was observed in the ≥30 category. The decrease in spexin levels was also significant across age categories within both the patient and control groups.

These results are consistent with previous studies reporting an inverse relationship between spexin levels and body mass index (BMI), whereby spexin levels decrease with increasing adiposity [25,26]. The absence of a statistically significant difference in the ≥30 category may be attributed to obesity-related hormonal alterations that result in hormonal dysregulation [27].

Table 1: Effect of body mass index on spexin in type 2diabetes patients compared with control group

BMI (kg/m2)	Spexin level (pg/ml) Mean ±S.D.	
	Patients	Control
18–24.9	**175.40 ±15.51 bc	276.41 ±32.98 a
25–29.9	**138.75±29.39 c	181.41±27.62 b
≥30	166.68±14.36 bc	158.34±14.89 bc

****significant difference between patients and control at p≤0.01 Vertically different letters indicate a significant difference**

Study of some clinical parameter's concentration in type 2 diabetes patients compared to the control group:

Table 2 shows a significant increase in fasting glucose levels in patients with type 2 diabetes compared with the control group, indicating poor glycemic control and its association with insulin resistance [28]. The results also demonstrated a significant increase in total cholesterol, triglycerides, LDL-C, and VLDL-C levels, accompanied by a significant decrease in HDL-C levels in patients with type 2 diabetes mellitus compared with the control group. These alterations may be associated with decreased spexin levels, given the important role of spexin in regulating lipid and energy metabolism. Spexin contributes to the stimulation of lipolysis through activation of hormone-sensitive lipase, leading to reduced lipid accumulation in adipocytes, and is also involved in enhancing fatty acid oxidation, increasing energy expenditure, and suppressing appetite. Therefore, decreased spexin levels may contribute to lipid imbalance and increased lipid accumulation, which could explain the elevation of atherogenic lipids and the reduction of protective HDL-C observed in patients with type 2 diabetes mellitus [29–31].

Table 2: Some of clinical parameters in type 2 diabetes patients and control group

Parameters	(Mean ± SD.)	
	Patients	Control
Fasting Blood Glucose (mg/dl)	**194.56±38.61	92.68±17.24
HbA1c (%)	**8.83±1.04	4.81 ±0.37
Total Cholesterol (mg/dl)	200.39 ± 30.94 **	118.37 ± 25.54
Triglycerides (mg/dl)	172.36 ± 25.50 **	99.08 ± 15.90

LDL-C (mg/dl)	118.36 ± 21.12 **	52.64 ± 12.73
VLDL-C (mg/dl)	35.85 ± 5.10 **	19.79 ± 3.18
HDL-C (mg/dl)	43.43 ± 12.19 *	48.23 ± 10.62
Atherogenic Index	0.4096 ± 0.306 *	0.3077 ± 0.137

*** Significant difference between patients and control at p≤0.05, ** at p≤0.01**

Study of some indicators of oxidative Stress in type 2 diabetes patients compared with control groups:

The results in Table 3 showed a significant decrease in aryl esterase activity among diabetic participants relative to the control group, consistent with previous studies. This decrease reflects impaired antioxidant defenses and reduced protection against low-density lipoprotein (LDL) oxidation. Chronic hyperglycemia may also lead to glycation of the PON1 enzyme and alterations in HDL structure, resulting in decreased enzyme activity and increased oxidative stress, which in turn may promote the progression of diabetes-related atherosclerosis [32].

Table 3 further demonstrated a significant reduction in catalase activity among individuals with type 2 diabetes relative to the control group, indicating impaired antioxidant enzyme defense systems and increased oxidative stress in diabetic patient [33]. In contrast, peroxidase activity was significantly increased in diabetic patients, an elevation that reflects increased oxidative stress associated with chronic hyperglycemia. This increase in peroxidase activity may represent a compensatory response aimed at eliminating hydrogen peroxide and reactive oxygen species [34].

The observed decrease in spexin levels may be associated with increased oxidative stress and impaired antioxidant defense systems. This could be attributed to the role of spexin in regulating glucose and lipid metabolism, as well as its anti-inflammatory effects, both of which collectively influence the balance between oxidants and antioxidants [35].

Table 3: Indicators of oxidative stress in type2 diabetes patients and control

Antioxidants and Oxidants	Spexin level (pg/ml) Mean ±S.D.	
	Control	Patients
Aryl esterase U/ml	103.48 ± 32.96	63.68 ± 10.37 **
Catalase KU/L	6.38 ± 1.45	4.23 ± 0.89**
Peroxidase U/ml	49.22 ± 9.98	75.74 ± 10.19**

**** significant difference between patients and control at p≤0.01**

Study of the linear correlation coefficient between spexin and some clinical variables in type2 patients and control group:

Table 4 showed a significant negative correlation between spexin levels and lipid profile parameters, specifically total cholesterol and triglycerides, in the control group. This association may be explained by the physiological functions of spexin in regulating lipid metabolism, as the peptide is known to limit the intestinal uptake of long-chain fatty acids and reduce their accumulation in the circulation. Additionally, spexin acts as a satiety-inducing peptide, which may contribute to preserving lipid profile parameters within normal physiological limits among healthy individuals. [36].

Table 4: Linear Correlation Coefficients Between Spexin and Measured Biometric Variables

Measured Variables	r- value	
	control group	Patients Group
Fasting Blood Glucose	-0.177	-0.086
HbA1c (%)	0.136	-0.251
Total Cholesterol	-0.359*	-0.028

Triglycerides	-0.346*	-0.022
HDL-C	-0.254	0.11
LDL-C	-0.304	-0.047
VLDL-C	-0.349*	-0.077
Aryl Esterase	-0.159	0.166
Peroxidase	-0.187	-0.115
Catalase	0.2	0.189
Atherogenic index	-0.158	-0.052

***significant difference at p≤0.05**

Conclusion:

In conclusion, reduced circulating spexin concentrations among individuals diagnosed with type 2 diabetes mellitus were associated with adverse metabolic alterations, including elevated lipid levels, increased body mass index, obesity, and impaired antioxidant defense mechanisms. These findings suggest that spexin may have potential clinical value as a biomarker of oxidative stress and metabolic disturbances among individuals diagnosed with type 2 diabetes mellitus.

Acknowledgement

I would like to thank the University of Mosul, College of Education for Women, for their support during my studies. I also thank all the teachers at the college for their help and guidance.

References

[1] Schleicher,E., Gerdes,G.,Petersmann,A., Müller-Wieland6,D.,Mann,G.F., Heinemann,L., Nauck,M., Landgrafe,R.Definition, classification and diagnosis of diabetes mellitus. Experimental and Clinical Endocrinology & Diabetes. 2022 Dec;127(S 01):S1-S7.

[2] Lu X, Xie Q, Pan X, Zhang R, Zhang X, Peng G, Zhang Y, Shen S, Tong N. Type 2 diabetes mellitus in adults: pathogenesis, prevention and therapy. Signal transduction and targeted therapy. 2024 Oct 2;9(1):262.3.

[3] Afriyanti U. Relationship between food intake on diabetes type 2 mellitus. Journal of Health. 2023 Feb 15;2(1).

[4] Barazzoni R, Gortan Cappellari G, Ragni M, Nisoli E. Insulin resistance in obesity: an overview of fundamental alterations. Eating and Weight disorders-studies on Anorexia, Bulimia and Obesity. 2018 Apr;23(2):149-57.

[5] Debebe E, Dessalegn T, Melaku Y.. Chemical constituents and antioxidant activities of the fruits extracts of Piper capense. Bull. Chem. Soc. Ethiop.2018; 32: 167-174.

[6] Al-Sehemi A.G, Irfan A, al Fahad A, Alfaifi M. Radical scavenging activity of some natural tropolones by density functional theory. Bull. Chem. Soc. Ethiop.2017; 31: 149-157.

[7] Türkel İ, Memi G, Yazgan B. Impact of spexin on metabolic diseases and inflammation: An updated minireview. Experimental Biology and Medicine. 2022 Apr;247(7):567-73.

[8] Sun X, Yu Z, Xu Y, Pu S, Gao X. The role of spexin in energy metabolism. Peptides. 2023 Jun 1;164:170991.

[9] Karaca A, Bakar-Ates F, Ersoz-Gulcelik N. Decreased spexin levels in patients with type 1 and type 2 diabetes. Medical Principles and Practice. 2019 Mar 1;27(6):549-54.

[10] Yu M, Wang M, Han S, Han L, Kan Y, Zhao J, Yu X, Yan J, Jin Y, Zhang Z, Shang W. Spexin ameliorates skeletal muscle insulin resistance through activation of GAL2 receptor. European Journal of Pharmacology. 2022 Feb 15;917:174731.

[11] Almoraie NM, Shatwan IM. The potential effects of dietary antioxidants in obesity: a comprehensive review of the literature. InHealthcare 2024 Jan (Vol. 12, No. 4, p. 416). Multidisciplinary Digital Publishing Institute.

[12] Haque T, Rahman S, Islam S, Molla NH, Ali N. Assessment of the relationship between serum uric acid and glucose levels in healthy, prediabetic and diabetic individuals. Diabetology & metabolic syndrome. 2019 Jun 21;11(1):49.

[13] Liu DM, Jiang LD, Gan L, Su Y, Li F. Association between serum uric acid level and body mass index in sex-and age-specific groups in southwestern China. Endocrine Practice. 2019 May 1;25(5):438-45.
[14] Trinder P. Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor. Annals of clinical Biochemistry. 1969 Jan;6(1):24-7.
[15] Zhou L, Xie D, Xu S, Wang J, Chen S, Huang J. Latex-enhanced Immunoturbidimetric Assay of Human HbA1c Using a Highly Specific Mouse Anti-human Monoclonal Antibody (HbA1c-6C2). Analytical Biochemistry. 2026 Mar 24:116117.
[16] Burtis CA, Bruns DE. Tietz fundamentals of clinical chemistry and molecular diagnostics-E-book: Tietz fundamentals of clinical chemistry and molecular diagnostics-E-book. Elsevier Health Sciences; 2014 Feb 26.
[17] Mundal LJ, Hovland A, Igland J, Veierød MB, Holven KB, Bogsrud MP, Tell GS, Leren TP, Retterstøl K. Association of low-density lipoprotein cholesterol with risk of aortic valve stenosis in familial hypercholesterolemia. JAMA cardiology. 2019 Nov;4(11):1156-9.
[18] Hwang S, Gwon C, Seo DM, Cho J, Kim JY, Uh Y. A deep neural network for estimating low-density lipoprotein cholesterol from electronic health records: Real-time routine clinical application. JMIR Medical Informatics. 2021 Aug 3;9(8):e29331.
[19] Nelson JL, Kulkarni AP. Partial purification and characterization of a peroxidase activity from human placenta. Biochemical Journal. 1990 Jun 15;268(3):739-43.
[20] Hadwan MH, Abed HN. Data supporting the spectrophotometric method for the estimation of catalase activity. Data in brief. 2016 Mar 1;6:194-9.
[21] Allwsh TA, Jasim RF. Study of arylesterase and it's relationship with some clinical variables in atherosclerotic patients in Mosul (Part I).
[22] Tejaswi G, Dayanand CD, Prabhakar K. Insulin resistance and decreased spexin in Indian patients with type 2 diabetes mellitus. Bioinformation. 2021 Sep 30;17(9):790.
[23] Gu L, Yan S, Huang Y, Yang J, Peng Y, Wang Y. Serum spexin differed in newly diagnosed type 2 diabetes patients according to body mass index and increased with the improvement of metabolic status. Frontiers in Endocrinology. 2022 Dec 14;13:1086497.
[24] Atoum MF, Almehsen AS, Alowaisy DA. Evaluation of Spexin Level in Patients with Type 2 Diabetes: A Meta-analysis.
[25] Mashaal YS, Bakr AM, El-Baiomy AA, Abbas NE. Study of serum spexin level in obese and non-obese type 2 diabetic patient. Suez Canal University Medical Journal. 2022 Mar 1;25(1):92-9.
[26] Albeltagy ES, Abd Elbaky NM. Association of lower circulating Spexin levels with higher body mass indices and glucose metabolic profiles in adult subjects in Egypt. Human Nutrition & Metabolism. 2022 Mar 1;27:200137.
[27] Álvarez-Castro P, Sangiao-Alvarellos S, Brandón-Sandá I, Cordido F. Endocrine function in obesity. Endocrinología y Nutrición (English Edition). 2011 Oct 1;58(8):422-32.
[28] Sesti G. Pathophysiology of insulin resistance. Best practice & research Clinical endocrinology & metabolism. 2006 Dec 1;20(4):665-79.
[29] Rasool M, Farooq S, Malik A, Shaukat A, Manan A, Asif M, Sani S, Qazi MH, Kamal MA, Iqbal Z, Hussain A. Assessment of circulating biochemical markers and antioxidative status in acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) patients. Saudi journal of biological sciences. 2015 Jan 1;22(1):106-11.
[30] Artha IM, Bhargah A, Dharmawan NK, Pande UW, Triyana KA, Mahariski PA, Yuwono J, Bhargah V, Prabawa IP, Manuaba IB, Rina IK. High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. Vascular health and risk management. 2019 Jun 5:149-57.
[31] Behrooz M, Vaghef-Mehrabany E, Maleki V, Pourmoradian S, Fathifar Z, Ostadrahimi A. Spexin status in relation to obesity and its related comorbidities: a systematic review. Journal of Diabetes & Metabolic Disorders. 2020 Dec;19(2):1943-57.
[32] Kota SK, Meher LK, Kota SK, Jammula S, Krishna SV, Modi KD. Implications of serum paraoxonase activity in obesity, diabetes mellitus, and dyslipidemia. Indian journal of endocrinology and metabolism. 2013 May 1;17(3):402-12.
[33] Tiwari BK, Pandey KB, Abidi AB, Rizvi SI. Markers of oxidative stress during diabetes mellitus. Journal of biomarkers. 2013;2013(1):378790.

[34] Sabahelkhier MK, Awadllah MA, Idrees AS, Rahheem AA. A study of lipid profile Levels of Type II Diabetes Mellitus. Nova J Med Biol Sci. 2016;5(2):1-9.
[35] Elsherbini H, Elsayed B, Seada SG, El-sayed SF. Spexin Protects Against Oxidative Stress-Induced Apoptosis of Sciatic Nerve Among Rats with Diabetic Peripheral Neuropathy. Zagazig University Medical Journal. 2025 Oct 26;31(12).
[36] Walewski JL, Ge F, Lobdell IV H, Levin N, Schwartz GJ, Vasselli JR, Pomp A, Dakin G, Berk PD. Spexin is a novel human peptide that reduces adipocyte uptake of long chain fatty acids and causes weight loss in rodents with diet-induced obesity. Obesity. 2014 Jul;22(7):1643-52.