Impact of Adropin, Adiponectin, and Insulin Variations in Type 2 Diabetes

Hala Abdullah Ali [1*], Iktifaa Abdel Hamid [1]

Abstract

Background: Diabetes Mellitus is a chronic condition impacting biological fitness and overall health, with projections indicating a significant rise in cases globally. This study investigates the levels of adropin and adiponectin hormones in patients with Type 2 Diabetes Mellitus (T2DM) in Iraq, aiming to elucidate their potential roles in the disease's pathophysiology. Methods: Ninety blood samples were collected from 50 T2DM patients (25 females, 25 males) and 40 healthy individuals (20 females, 20 males) in Kirkuk between October 2023 and January 2024. Hormone levels were analyzed using the Enzyme-Linked Immunosorbent Assay (ELISA) technique. Samples were categorized based on gender, age, and body mass index (BMI). Results: Adropin levels were significantly lower in T2DM patients (1369 ± 76.8 ng/ml) compared to healthy controls (1606 ± 42.5 ng/ml), with male patients showing a more pronounced decrease than females. In contrast, no significant difference was observed in adiponectin levels between diabetic patients (179.4 ± 28.9 mg/L) and controls (182.0 ± 38.6 mg/L). Additionally, age did not significantly affect adropin levels, while adiponectin levels were consistent across genders and age groups in both diabetic and control participants.

Conclusion: The study indicates a significant reduction in adropin levels among T2DM patients, suggesting its potential role in diabetes pathophysiology, irrespective of age. Adiponectin levels remained unaffected by diabetes status, gender, or age, indicating a complex relationship that warrants further investigation. These findings emphasize the importance of managing blood glucose levels and highlight the need for further research into the mechanisms linking adropin with metabolic processes in T2DM.

Keywords: Type 2 Diabetes Mellitus, Adropin, Adiponectin, Insulin, Hormonal Biomarkers

Significance | This study revealed significant hormonal differences in adropin, adiponectin, and insulin between T2DM patients and healthy individuals in Kirkuk.

*Correspondence. Hala Abdullah Ali, College of Education for women, Biology Department, Tikrit University
E-mail: Hala.Ali23@st.tu.edu.iq

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Introduction

Diabetes Mellitus is a chronic condition affecting an individual's biological fitness. According to the World Health Organization (WHO), more than 171 million individuals were diagnosed with diabetes in 2000, with projections of up to 366 million by 2030. In Iraq, statistics from 2019 indicated that over 13.9% of adults suffer from diabetes (Saeedi et al., 2019). This chronic and serious condition significantly impacts the lives, well-being, and families of individuals worldwide, ranking among the top ten causes of death among adults (International Diabetes Federation, 2017). Chronic hyperglycemia encompasses metabolic disorders primarily resulting from insulin secretion disorders, varying degrees of insulin resistance, or both (Naz & Ahuja, 2022). By 2030, the number of diabetic patients is expected to rise to 113 million, reaching 151 million by 2045 (Naz & Ahuja, 2022). Studies have shown a global increase in diabetes prevalence, influenced by factors such as genetics, age, obesity, psychological stress, geographic location, climate, social factors, and nutrition (Alaa,

Author Affiliation.
[1] College of Education for Women, Biology Department, Tikrit University, Iraq.

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2018). Generally, diabetes is characterized by postprandial hyperglycemia due to insulin resistance or absolute insulin deficiency, either as an autoimmune condition leading to beta-cell destruction (Type 1) or as a condition caused by insulin deficiency despite intact beta cells, due to receptor dysfunction (Care, 2018). The American Diabetes Association (ADA) classifies diabetes into four main categories: Insulin-Dependent Diabetes Mellitus (Type 1, T1DM), Non-Insulin-Dependent Diabetes Mellitus (Type 2, T2DM), Gestational Diabetes Mellitus (GDM), and other specific types (ADA, 2018). T1DM, T2DM, and GDM are the most common types, with T2DM characterized by abnormally low insulin production or insulin resistance (Rabbani et al., 2022).

Individuals with obesity are six times more likely to develop T2DM compared to those in good health, although not all obese individuals are at risk of diabetes (Aguayo-Mazzucato et al., 2019). Adropin and adiponectin proteins play a crucial role in metabolic balance and energy, acting as anti-obesity and anti-diabetic hormones (Wu et al., 2022). This study aims to assess the levels of adropin and adiponectin hormones in patients with type 2 diabetes.

Materials and Methods

Ninety blood samples were collected from volunteers, including 50 samples from patients with type 2 diabetes (25 females and 25 males) and 40 samples from healthy individuals (20 females and 20 males). The samples were collected from private laboratories in Al-Shaabi and Al-Hajjaj areas in Kirkuk between October 1, 2023, and January 15, 2024, and analyzed in the central laboratories of the College of Pharmacy, University of Tikrit. The age range of the samples was 25-50 years. Patient samples were categorized based on gender, age, and body mass index (BMI), with 20 control samples from healthy females and 20 from healthy males. The levels of adropin and adiponectin hormones were estimated using the Enzyme-Linked Immunosorbent Assay (ELISA) technique.

Results

The results in Table 1 indicate a significant decrease ($P \leq 0.05$) in the concentration of adropin hormone when comparing diabetic patients (1369 ± 76.8 ng/ml) with the control group (1606 ± 42.5 ng/ml). There was no significant difference ($P \geq 0.05$) in the concentration of adiponectin hormone between diabetic patients (179.4 ± 28.9 mg/L) and the control group (182.0 ± 38.6 mg/L). The results in Table 2 indicate variations in adropin levels based on gender among the studied groups. A significant difference ($P \leq 0.05$) was found, showing a decrease in adropin levels among male patients (1272 ± 81.4) compared to female patients (1462 ± 83.3). Conversely, in the control group, adropin levels were higher in males (1880 ± 79.7) compared to females (1331 ± 88.5). There was no significant difference ($P \geq 0.05$) in adiponectin levels between male patients (179.5 ± 25.4) and female patients (188.8 ± 23.0). Similarly, no significant difference was found in adiponectin levels in the control group between males (187.8 ± 34.3) and females (176.3 ± 31.0). The results in Table 3 show variations in adropin levels based on age among the studied groups. No significant difference ($P \geq 0.05$) was found between the age groups.

Discussion

Hormonal variables are essential indicators of balance in the natural and environmental conditions surrounding the body, as well as the body's internal homeostasis in terms of energy balance and weight maintenance. The current study shows that adropin levels in the blood of patients with type 2 diabetes decreased compared to the control group. This finding aligns with the study by Kutlu et al. (2019), who found a decrease in adropin levels in patients with insulin resistance (IR) compared to the control group without IR. Additionally, adropin enhances glucose tolerance, reduces insulin resistance, and promotes carbohydrate consumption over fat for energy production by enhancing insulin-induced GLUT4 expression on the cell surface (Bozic et al., 2021). Zang et al. (2018) reported that adropin levels decreased in T2DM patients, especially those who are overweight or obese. The first evidence linking adropin to obesity and the risk of metabolic syndrome in humans was presented by Butler et al. (2012), who found low adropin levels in obese patients, which increased with weight loss. Changes in adropin levels may be a potential indicator for predicting obesity and related diseases such as type 2 diabetes. Adropin regulates glucose oxidation by activating pyruvate dehydrogenase in muscles (Zhang & Chen, 2022). This study found a negative relationship between serum adropin and blood sugar levels, consistent with previous research (Alzoughhool et al., 2021; Hosseini et al., 2016), which indicated a negative relationship between adropin and blood sugar levels and increased insulin sensitivity. One potential reason for adropin's role in maintaining metabolic balance is its promotion of glucose utilization over fatty acids, improved glucose tolerance, and reduced insulin resistance. A study by Li et al. (2009) found that higher adiponectin levels consistently associated with a lower risk of T2DM in diverse population groups. Adiponectin is one of the strongest and most stable biochemical predictors of type 2 diabetes, despite epidemiological studies not determining causal relationships. Consistent correlations among diverse populations and dose-response relationships in studies suggest adiponectin as a promising target for reducing T2DM risk.

Adropin levels are not significantly affected by the gender of diabetic patients. Research shows that adropin levels can be influenced by factors such as obesity, cardiovascular diseases, and energy metabolism (Muhammed et al., 2022). While there is a relationship between adropin and diabetes, the direct mechanism of adropin's action in diabetic patients is not fully understood. Additionally, a study on the effect of the SGLT2 inhibitor

Table 1. Adropin, Adiponectin, and Insulin Hormones Concentration

Hormone	Patients (n=50)	Control (n=40)	P-Value
Adropin (mg/dL)	1369 ± 76.8	1606 ± 42.5	0.035 *
Adiponectin (mg/dL)	179.4 ± 28.9	182.0 ± 38.6	0.852 ns
Insulin (mg/dL)	28.7 ± 5.3	48.3 ± 7.3	0.011

Table 2. Adropin, Adiponectin, and Insulin Hormones Concentration by Gender

Hormone	Patients (Males, n=25)	Patients (Females, n=25)	Control (Males, n=20)	Control (Females, n=20)	P-Value
Adropin (mg/dL)	1272.9 ± 81.4c	1462.0 ± 83.3b	1880.0 ± 79.7a	1331.0 ± 88.5bc	0.028 *
Adiponectin (mg/dL)	179.5 ± 25.4a	188.8 ± 23.0a	187.8 ± 34.3a	176.3 ± 31.0a	0.691 ns
Insulin (mg/dL)	23.24 ± 4.74c	33.98 ± 7.77b	43.90 ± 8.10a	42.65 ± 9.96a	0.011

Table 3. Adropin, Adiponectin, and Insulin Hormones Concentration by Age

Age Group (Years)	**Patients**	**Control**	**P-Value**
25-35	1520.0 ± 54.3a	1520.0 ± 55.9a	0.729 ns
36-45	1518.1 ± 54.8a	1506.0 ± 55.5a	
46-50	1495.0 ± 40.7a	1504.0 ± 57.2a	
Adiponectin (mg/dL)	198.0 ± 23.7a	179.2 ± 28.7a	0.915 ns
	176.7 ± 18.82a	188.0 ± 19.8a	
	170.2 ± 30.55a	179.2 ± 13.86a	
Insulin (mg/dL)	41.03 ± 6.33ab	50.90 ± 5.71a	0.056 *
	25.09 ± 3.87c	49.30 ± 8.10a	
	25.25 ± 3.40c	36.86 ± 4.86bc	

dapagliflozin on adropin levels found no significant gender-based differences (Berezin et al., 2023). Overall, adropin appears to play a role in various metabolic processes and may serve as an indicator for T2DM and its complications (Hu & Ning, 2022). Further research is needed to fully understand the relationship between adropin and diabetes in different patient groups. The gender of diabetic patients significantly affects adiponectin levels. Research by Dullaart et al. (2007) shows that plasma adiponectin levels are significantly lower in men compared to women, regardless of diabetes status. Among diabetic patients, women have significantly higher adiponectin levels than men. Additionally, diabetic patients with abdominal obesity have lower adiponectin levels than those without (Nayak et al., 2007). Gender differences play a crucial role in physiological changes related to adiponectin levels, with women having higher leptin/adiponectin ratios than men (Selthofer et al., 2018).

Lower adropin levels are commonly associated with metabolic disorders such as obesity, diabetes, chronic kidney disease, heart failure, and diabetes. Berezin et al. (2023) showed that SGLT2 inhibitors could modify adropin levels, increasing them in diabetic patients with heart failure. The relationship between adropin and age-related conditions suggests that age may play a role in regulating adropin in diabetic patients. While specific effects of adropin on diabetes were not directly addressed in this study, understanding adropin's role in metabolic regulation and potential protection against neurodegenerative diseases could benefit diabetic patients, particularly in managing cardiomyopathy and diabetic foot complications (Sanjeevirraj et al., 2023). The results highlight the importance of managing blood glucose levels, especially in older patients, to reduce long-term complications associated with diabetes. Sharif et al. (2024) investigated diabetic retinopathy in elderly individuals with T2DM and found that the risk varies with age and gender, with a higher risk in older women.

Conclusion

There is a decrease in adropin levels in patients with type 2 diabetes compared to healthy individuals, regardless of the patient's gender. However, when considering age, no significant differences were found between the age groups. There is no significant difference in adiponectin levels in patients with type 2 diabetes compared to healthy individuals, nor are there significant differences based on age and gender.

Author contributions

H.A.A. conceptualized the study, developed the methodology, prepared the original draft, and collected the data. I.A.H. wrote, reviewed, and edited the manuscript, analyzed the data, and contributed to the review and editing process.

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Competing financial interests

The authors have no conflict of interest.

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