

# Estimating Apelin\_36 Level in Obese and Non-obese Patients with Type2 Diabetes Mellitus

Maryam Moayd mohammed \*  $\square \boxtimes$ , Fayhaa M. Khaleel  $\square \boxtimes$ 

Department of Chemistry, College of Science for women, University of Baghdad, Baghdad, Iraq. \*Corresponding Author.

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# Abstract

Risk factors for cardiovascular disease include obesity and Type 2 diabetes mellitus. The aim of this study is to evaluate Apelin-36 levels in Type2 diabetic(obese and non-obese) Iraqi patients, finding out whether Apelin-36 is a future indicator of cardiovascular disease, and is an indicator of obesity or diabetes, or an indicator of both diseases , when compared to obese control subjects without diabetes This study included 120 subjects: 30 obese Diabetic type2 patients, 30 non-obese Diabetic Type2,60 as obese control group, adults between the ages from 30 to 65 years .The participants' FBS, lipid profile (Cho ,Tri, HDL, LDL, and VLDL), HbA1C, Apelin-36 level, BMI , and waist-to-hip ratio were evaluated. Apelin-36 levels were significantly higher in obese Type 2 patients (27.68±0.67) than in non-obese patients  $(18.08\pm0.96)$  and obese control without diabetes individuals  $(10.23\pm0.29)$ (P<0.05). In comparison to obese type2 diabetic patients, obese control group ,non-obese type2 patients the BMI increased (p<0.05) (35.191±0.88, 32.05±0.35, 26.53±0.47). The mean values of Cho, tri, HDL, and VIDI do not differ significantly from those of the control groups. There is a significant difference in LDL levels between the obese patients and controls in the study's participants (p<0.05).(Area Under the Curve) in the study = 0.980, indicating a perfect ROC test for correctly identifying individuals .Higher levels of Apelin-36 play an important role, which increases directly with obesity, resulting in an increase in the secretion of adipokines (Apelin-36) in the blood. Increasing BMI, lipid levels, and duration of the disease also contribute to the development of diabetes complications.

Keywords: Adipose tissue, Apelin-36, Body mass Index (BMI), Lipid profile, Type2 Diabetes (T2D).

# Introduction

Apelin-36 (human) is derived from the apelin peptide which acts as a ligand for the apelin receptor (APJ). G protein-coupled receptors have been linked to cardiovascular disorders, obesity, diabetes, and cancer. Apelin-36 is a long peptide fragment that is found in many parts of the brain, spinal cord, and other organs <sup>1</sup>. The apelin peptide with 36 amino acid residues is designated apelin-36.

Numerous studies have found that Apelin-36 is linked to a number of diseases, such as : Type2 Diabetic <sup>2,3</sup>. apelin-36 was isolated from bovine stomach tissue to induce APJ <sup>4</sup>. Apelin-36 has been associated with two main categories of biological activity: cardiovascular (increasing cardiac contractility and decreasing blood pressure) and metabolic (improving glucose homeostasis and

decreasing body weight). It has been hypothesized that APJ modulates these two activities. Apelin-36 is considered the most active isoform with the greatest activity on cardiovascular homeostasis<sup>5</sup> .Apelin is a newly discovered peptide that has been identified as an internal receptor ligand and is present in several organs such as the brain, heart, lungs, and kidneys, as stated in the article. This peptide has a preproapelin precursor with seventyseven amino acids, and there are many different sub-molecular structures with different biological functions <sup>6</sup>. It is produced and secreted from white adipose tissue. It starts as preproapelin, a 77-aminoacid protein that is then broken into shorter active pieces. The physiopathology of disorders like hypertension, heart failure, cardiovascular disease, Type 2 diabetes, and obesity may be also influenced by apelin signaling <sup>7</sup>.

Obesity is defined as having a BMI of more than 30 kg/m2 as a result of long-term energy imbalance caused by excessive calorie consumption and inadequate calorie expenditure .This condition is distinguished by an excessive buildup in the form of triglycerides of fat in adipose tissue, which will be used as nutrients by other tissues through lipolysis in the event of a nutrient deficit <sup>8</sup>. The accumulation of extra body fat that has the possibility of affecting health is referred to as obesity, which is the outcome of an imbalance between energy intake and expenditure, whereby more calories are consumed than are expended through exercise<sup>9</sup>. Diabetes and obesity are currently pandemic diseases with a rising incidence, with hundreds of millions of individuals diagnosed with obesity or diabetes around the world. Obesity is currently classified as a heterogeneous syndrome (defined by the combination of hereditary and environmental variables)<sup>10</sup>. Adipokines are a genus of bioactive compounds that play an important role in insulin

# Materials and Methods

## Subjects and Methodologies

The research was done at Baghdad's National Diabetes Centre and Mustansiriyah University. In this study, 120 people with T2DM who were taking metformin and sulfonylurea drugs took part in the study. Based on the results of their medical exams, there were 60 obese control and 60 patients, 30 obese T2DM patients and 30 non-obese T2DM patients. The range of ages was 30–65 years. Questionnaires were made which show the



sensitivity and secretion, inflammation, metabolism, energy expenditure, and cardiovascular function.<sup>11</sup> Adipose tissue is mostly made up of cells called adipocytes. It helps store energy in the form of fats and is a key hormonal organ because it makes hormones like leptin, estrogen, resisting, and the protein tumor necrosis factor alpha<sup>12</sup>. Long recognized, the association between obesity and Type 2 diabetes mellitus shows why there are so many people with Type 2 diabetes in many places. Genome wide association studies have shown that there are more links between obesity, its metabolic problems, and genetic factors<sup>13</sup>.Cardiovascular disease is a major risk for people with Type 2 diabetes. Since obesity is often linked to high blood pressure and high cholesterol, many high-risk fat people have these conditions and exhibit a confluence of metabolic and cardiovascular risk factors<sup>14</sup>.

Diabetes mellitus (DM) is a big public health problem that affects more than 400 million people around the world <sup>15</sup>. This metabolic disorder causes ongoing capillary, macrovascular, and nerve problems that get worse over time and can be fatal <sup>16</sup>. For a long time, Type 2 diabetes (T2DM) used to be called non-insulin-dependent diabetes or diabetes that started in adults with insulin resistance, which could get worse over time and could lead to absolute resistance. However, in the last ten years, decreased  $\beta$ -cell function has been found to be a major problem in T2DM<sup>17</sup>. This study aims to evaluate Apelin-36 Levels in obese and non-obese type2 Iraqi patients without any complicated stages, and compare them with controlled obese people without diabetes. The study also aims at finding out whether Apelin-36 is a future indicator of cardiovascular disease, and whether Apelin-36 is a good indicator of obesity or diabetes, or a stronger indicator of both diseases.

anthropometric and biological traits of each group. Each person in this study who took part (both patient and control) had 10 mL of venous blood taken with a throwaway needle. The blood was divided into two halves. The serum from one was collected in a gel tube after being drawn into it . After the blood had coagulated, the tube was spun at 3000 rpm for 10 minutes at room temperature, and the other was drawn into an EDTA tube and tested for HbA1c. Using a kit from My (BioSource-



U.S.A.), enzyme-linked immunoassay (ELISA) was used to measure the total amount of Apelin-36 in human blood. Cobas c111 (Germany) was used to measure the fasting glucose (FBS) and lipid profile, and HbA1c. Body Mass Index was calculated using the formula [weight in kg / height in  $m^2$ ] <sup>18</sup> waist - hip ratio (waist cm  $\div$  hip cm)<sup>19</sup>.

#### **Statistical Analysis;**

The data was analyzed using Statistical Packages for the Social Sciences (SPSS Version 26). ANOVA test for difference between three independent variables, Tukey-test, ROC curve and estimation by looking at the linear regression and the correlation coefficient (r) between the values were used in the statistics test. The data was presented as (mean  $\pm$  standard error). Numbers were

#### **Results and Discussion**

Table 1, Fig. 1 shows how the mean ages and BMIs of all the groups studied in this study are spread out. Both patient groups exhibited a considerable rise when compared to the control groups. There is a significant difference between the age ratios of the obese control group and patients groups according to statistics and the P-Value ( $p \le 0.05$ ), ages taken from 30 to 65 randomly. According to the international ranking of BMI values, they were divided into: (normal weight, overweight, obese people and extreme weight). According to statistics, it was found that there is a significant difference between BMI values P-Value ( $p \le 0.05$ ) and the studied groups. In the present investigation, all analyzed groups were matched in age. Table 1, Fig. 1 shows the age mean value ±SD between two groups (patients and control). The patients' group showed age mean value  $\pm$ SD (53.16  $\pm$  1.43) for obese and  $(56.53 \pm 1.16)$  for non-obese, while the control group  $(46.2 \pm 1.31)$  and the age range (30-65) years in control and patients. There was a significant value ( $p \le 0.05$ ) of age when comparing the two groups. Above this age range, a person may

statistically significant when (p<0.05) and not statistically significant when  $(p \ge 0.05)$ 

#### **Inclusion Criteria**

- 1. Subjects aged 30 to 65 years old and free of disease.
- 2. Obese and non-obese with type2 diabetes and (control obese without type2 diabetes) of male and female, the age range of all subjects from was 30 to 65.

#### **Exclusion Criteria**

- 1. Patients with type1 diabetes.
- 2. Patients with any complication Type 2 disease.
- 3. Thyroid diseases.
- 4. Pregnancy or breastfeeding

have a higher risk of developing a complication of the disease.

The body mass index (BMI) was different between the studied groups ( $p \le 0.05$ ). The highest value of BMI in the obese type2 group was (35.19±0.881) as shown in the (mean  $\pm$  SE) of BMI in Table.1 as shown in the (mean  $\pm$  SE) of BMI .There was a statistically significant difference ( $p \le 0.05$ ) between waist circumference (WC) and the Hip Circumference (HIP) in the studied groups. The maximum proportion of fat accumulation at the abdomen and hip was observed in obese persons with Type 2 diabetes. Compared to the non-obese and obese controls. Table 1 and Fig. 1 display the mean values of the Waist-to-Hip ratio for each of the categories examined in the current study. The body mass index (BMI) and waist circumference (WC) are used to evaluate obesity and abdominal obesity, and obesity is a risk factor for numerous diseases. As shown in the table of median values for the BMI and the W/H ratio, the highest values of BMI and WC appeared in obese individuals more frequently than in non-obese individuals.



Table 1. The Age and BMI and value of Waist to Hip	o of the cases and the people in the comparison
group	

Groups	Obese Control	Obese T2DM	Non-obese T2DM	P-value
Parameters	Group (1)	Group (2)	Group (3)	
	No. (60)	No. (30)	No. (30)	
Age (year)	46.2±1.31 <sup>a</sup>	53.16±1.43 <sup>b</sup>	56.53±1.16 <sup>b</sup>	**0.0001
	(45)	(53)	(55)	
BMI $(kg/m^2)$	32.05±0.35 <sup>a</sup>	35.19±0.88 <sup>b</sup>	26.53±0.40°	**0.0001
	(31)	(34)	(27)	
Waist (cm)	112.08±1.37 <sup>a</sup>	117.63±2.24 <sup>b</sup>	101.76±1.61°	**0.0001
	(112)	(115.5)	(100)	
Hip (cm)	$111.51 \pm 1.44^{ab}$	118.26±2.75 <sup>b</sup>	105.33±1.99 <sup>a</sup>	**0.0001
-	(112)	(115.5)	(101.5)	
W/H ratio	0.99±0.01ª	0.99±0.011ª	0.95±0.01ª	0.098
	(1)	(0.99)	(0.95)	

- Data were presented as Mean  $\pm$  SE (Median)

- Non-significant variations are denoted by identical small letters

-the small letters(a, b and c) refers to there a significant difference or not, different letters mean a significant difference.

\*\*Significant difference between means using ANOVA -test at 0.01 level.

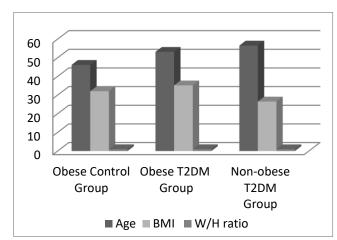


Figure 1. the relation of Age and BMI and W/H ratio with groups

Duration of diabetes mellitus and hyperglycemia showed that there is a significant difference

between patients and the duration of disease P-value  $(p \le 0.05)$ , according to statistics, it was found that (76.7 %) of obese people are more likely to develop diabetes at an early stage. When comparing the percentages of people with Type 2 diabetes for (obese and non-obese people), one can notice that the percentage of obese people with diabetes for more than 5 years (76.7%) is greater compared to the non-obese (50%) as it appeared for each category less than 5 years and above 5 years .Therefore, the obese are more likely to develop diabetes than the non-obese, according to the percentage of patients, as shown in Table 2.

Table2	. Durati	on dia	abet	tic betwe	en pati	ents an	id obese	control	group.	
Groups Parameters				Obese c Group (		Obese group		Non-ol Group	bese t2dm	P-value
				No. (60)		No. (3		No. (30	. ,	
				No.	%	No.	%	No.	%	-
Duration of disease (years)	Less years	than	5			7	23.3	15	50	**0.0001
	More years	than	5			23	76.7	15	50	
- data were presented as	s mean ±	se (me	dian	l)						
**significant difference	between	means	s usi	ng anova	-test at (	).01 leve	el.			

a? Duration diabatic between nationts and abo

In general, biochemical parameters in Table 3 and Fig. 3 reveal a statistically significant difference (p≤0.05)between the control and patient groups in FBS for the control group, obese, non-obese( 95.77±1.45, 200.93±9.67, 229.83±19.26) respectively. In addition, HbA1c demonstrated a statistically significant difference ( $p \le 0.05$ ) between the obese control group and those with diabetes patient groups, (obese, non-obese) 5.22±0.05,  $8.11\pm0.21$ ,  $8.45\pm0.41$  respectively. As a result of the body's cells' disability to benefit from glucose due to insulin deficiency that is secreted from the pancreas gland, blood plasma levels of glucose rise, resulting in different metabolic changes. This current study agrees with ( Abdulahi, Aguade and Yohannis<sup>20</sup> and Fasil <sup>21</sup> who considered diabetes complications and poor glycemic control as being prevalent. The elevated risk of developing diabetic foot and cardiovascular illnesses has been linked to hyperglycemia, and other studies showed a connection between hyperglycemia and the development of diabetes complications (micro- and macrovascular issues). Therefore, the use of HbA1c



as a blood glucose monitoring tool offers the additional advantage of identifying diabetics at risk for such issues<sup>22,23</sup>. This study is also in agreement with <sup>24</sup> that proved that non-obese diabetic patients have a higher HbA1c level than obese diabetic patients, as well as higher fasting blood sugar levels. There is a difference between the values of the obese control group and those of the obese and non-obese with diabetes HbA1c is an essential predictor of long-term glycemic management since it might represent the prior three months' cumulative glycemic history as sugar levels increase in both obese and non-obese diabetics. Not only does HbA1c provide a highly accurate but It also correlates well with the risk of long-term complications from diabetes. In individuals with diabetes, an elevated HbA1c is also considered an independent risk factor for coronary heart disease and stroke <sup>25</sup>. Also, Table 3 and Fig. 2 show that the values of Cholesterol, Triglyceride, HDL, and very low-density lipoprotein (VLDL) non-significant difference between the patient and control group but LDL showed a significant difference ( $P \le 0.05$ ).

Table 5. Shows table FBS, HDATC, and hpid profile between patients and obese control groups							
Groups Parameters	Obese Control	Obese T2DM	Non-obese T2DM	P-value			
	Group (1)	Group (2)	Group (3)				
	No. (60)	No. (30)	No. (30)				
FBS (mg/dL)	95.77±1.45 <sup>a</sup>	200.93±9.67 <sup>b</sup>	229.83±19.26 <sup>b</sup>	**0.0001			
	(98)	(199)	(197)				
HbA1C (mg/dl)	$5.22 \pm 0.05^{a}$	8.11±0.21 <sup>b</sup>	8.45±0.41 <sup>b</sup>	**0.0001			
	(5.2)	(8.05)	(7.75)				
Cholesterol (mg/dL)	185.07±5.39 <sup>a</sup>	180.63±14.9 <sup>a</sup>	$180.88 \pm 8.35^{a}$	0.913			
	(197)	(161.5)	(173)				
TG (mg/dL)	184.42±11.15 <sup>a</sup>	$178.03 \pm 17.8^{a}$	158.83±12.11 <sup>a</sup>	0.404			
	(189.42)	(146)	(141)				
HDL-C (mg/dL)	37.99±1.32ª	42.142±2.54 <sup>a</sup>	$41.1 \pm 1.75^{a}$	0.194			
	(36)	(40.5)	(40)				
LDL-C (mg/dL)	112.76±4.26 <sup>b</sup>	$85.76 \pm 5.85^{a}$	106.76±7.39 <sup>b</sup>	**0.003			
	(122.5)	(87)	(103)				
VLDL-C (mg/dL)	37.68±2.48 <sup>a</sup>	35.43±3.58 <sup>a</sup>	36.13±4.48 <sup>a</sup>	0.875			
-	(38.2)	(29)	(32.5)				
- Data were presented a	as Mean + SF (Median)	)					

Table 3. Shows table FBS, HbA1c, and lipid profile between patients and obese control grou	Table 3. Shows table FBS	HbA1c, and lipid	profile between patie	nts and obese control group
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- Data were presented as Mean  $\pm$  SE (Median)

- Non-significant variations are denoted by identical small letters

-the small letters (a, b and c) refers to there a significant difference or not, different letters mean a significant difference.

\*\*Significant difference between means using ANOVA-test at 0.01 level.

The result is an increase in small dense LDL, which is one of the hallmarks of diabetic dyslipidemia, it is also associated with a greater risk of cardiovascular disease .This also agrees with <sup>26</sup> study. The results are in agreement with <sup>27</sup> who found in their study that people with Type 2 diabetes who took sulfonylurea-based treatment had better blood sugar control and lower LDL cholesterol levels. Microvascular problems are more likely to happen to people with Type 2 diabetes who have



hyperglycemia .In fact; LDL cholesterol levels may underestimate cardiovascular risk in diabetes. Even

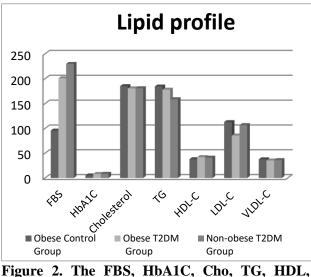


Figure 2. The FBS, HbA1C, Cho, TG, HDL, LDL. VLDL

Table 4 and Fig. 3 show the average levels of Apelin-36 (nmol/mL) for all of the groups that were studied in this study. Table 4 shows that the level of Apelin-36 is higher in the obese with Type 2 group than in the non-obese with Type 2 group and the obese control group without diabetes  $(p \le 0.001)$ , and that Apelin-36 levels are higher in the obese with Type 2 group compared to the obese control group. This suggests that the Apelin-36/ APJ. The receptor system may be an effective therapeutic target for Type 2 diabetes. The explanation for that may be the result of an increase

when the LDL goal is met, people with T2DM still have a high chance of CVD events.<sup>28</sup>

in hyperlipidemia in the body, and since it is the Apelin-36 that increases directly with obesity (high body mass index), this leads to an increase in the secretion of adipokines (Apelin-36) in the blood, as Apelin-36 works to break down fats by strengthening pathways that include protein kinase activated with adenosine monophosphate.

Obesity is a common cause of many diseases, as it results from excessive secretion of fat from the fatty tissue that occurs as a result of an imbalance between the release of energy and its consumption, resulting from excessive consumption of food and lack of exercise or genetic factors. Obesity increased cardiovascular disease and coronary heart disease, chronic disease and metabolic syndrome by increasing resistance to insulin. On the other hand, the visceral tissue in the abdominal area causes metabolic syndrome if it is not eliminated, thus increasing the risk of various other complications<sup>29</sup>

, The incidence of cardiovascular is greater in diabetes patients compared to non-diabetic people, which indicates that metabolic and cardiovascular illnesses are serious health concerns that may occur independently or in conjunction with one another Among other well-known adipokines, apelin (acute and chronic therapy) has been demonstrated to exhibit therapeutic effects in the pathophysiology of the cardiovascular system and in Type 2 diabetes in a variety of animal models and in people. These findings were made possible by the fact that apelin was able to inhibit the progression of the disease  $^{30}$ .

Table 4. Levels of Apelin-36 in the patient group and the comparison group								
Groups	Obese Control	Obese T2DM	Non-obese T2DM	P-value				
Parameters	Group (1)	Group (2)	Group (3)					
	No. (60)	No. (30)	No. (30)					
Apelin-36	10.23±0.29 <sup>a</sup>	27.68±0.67 <sup>b</sup>	18.08±0.96°	**0.0001				
(nmol/mL)	(9.57)	(27.64)	(18.01)					
_		1						

- Data were presented as Mean  $\pm$  SE (Median)

- Non-significant variations are denoted by identical small letters

-the small letters (a, b and c) refers to there a significant difference or not, different letters mean a significant difference.

\*\*Significant difference between means using ANOVA-test at 0.01 level.

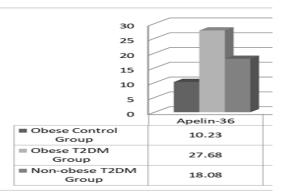


Figure 3. Apelin-36 with diabetic group and obese control group.

Correlations between Apelin-36 and chemical parameters in patients with Type2 (obese and nonobese), and the obese control group. In Table 5, the relationships between the study factors individuals with Type 2 diabetes and the control groups with Apelin-36 are shown. Here, there is no link between Apelin-36 and the other groups, so the study showed that Type 2 diabetes patients had a higher Apelin-36 amount than obese people.

 Table 5. The correlation of Apelin-36 with all parameters

L							
	Apelin-36 (pg/ml)						
	Obese		Obese	Non-obese			
	Control		T2DM	T2DM			
	Group (1)		Group (2)	Group (3)			
	No. (60)		No. (30)	No. (30)			
Age (years)	R	044	.232	.261			
	Р	.738	.218	.164			
Weight (kg)	R .073		014	.089			
	Р	.580	.940	.638			

Length (cm)	R	.114	095	.135			
	Р	.384	.619	.476			
BMI	R	064	009	009			
(Kg/m2)	Р	.629	.963	.963			
W/H ratio	R	141	081	.217			
	Р	.284	.672	.250			
FBS (mg/dL)	R	092	123	123			
	Р	.487	.517	.518			
HbA1C %	R	162	.152	187			
	Р	.216	.422	.322			
Cholesterol	R	.100	073	123			
(mg/dL)	Р	.448	.701	.519			
TG (mg/dL)	R	.065	.001	277			
	Р	.621	.995	.139			
HDL-C	R	.066	162	.079			
(mg/dL)	Р	.619	.393	.678			
LDL-C	R	.039	.060	203			
(mg/dL)	Р	.768	.753	.281			
VLDL-C	R	.037	007	171			
(mg/dL)	Р	.778	.971	.366			
*Correlation is s	signifi	cant at th	e 0.05 level.				
**Correlation is	signi	ficant at t	he 0.01 level.				

#### **ROC Analysis for Apelin-36**

In this study, the ROC curve is utilized to discriminate between the patients with type 2 diabetes and people who didn't have it. The result of the ROC (area under the curve) analysis of Apelin-36 = (0.980) and that excellent result, a perfect ROC test which is correctly identified by these study .This is a positive accurate result confirming that Apelin -36 has a good relationship with obesity and with type 2 diabetes patients. Table 6, Fig. 4 shows the area under the curve for Apelin-36 with type2 diabetes patients.

Area Ui	nder the Curve	;					
Test Re	sult Variable(s	s): Apelin-36					
Area	Std. Error <sup>a</sup>	Asymptotic	Cut-Off	Sensitivity	1 -	Asymptotic	95% Confidence
		Sig. <sup>b</sup>	Point		Specificity	Interval	
		-				Lower	Upper Bound
						Bound	
.980	.011	.000	13.614	.950	.067	.958	1.000
a. Unde	r the nonparar	netric assumption					
	hypothesis: tru	-					





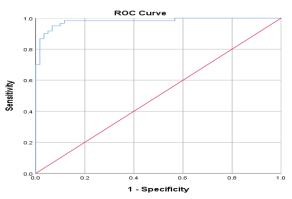


Figure 4. ROC analysis for Apelin-36

In Table 7, Fig. 5 the result of the ROC analysis of patients groups for (FBS and HbA1C )

In this study, the ROC analysis shows a positive result of FBS is an excellent result (0.989), and for HbA1C is the excellent result (0.997). HbA1c is positively associated with cardiovascular diseases such as atherosclerosis of the carotid and coronary arteries, ischemic heart disease, ischemic stroke, and hypertension  $^{31,32}$ . According to the results of his study, there was a strong link between HbA1c and the type of cardiac angioplasty, high blood pressure, and heart block. This means that diabetic

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people should have a better handle on their HbA1c levelTable 7 and Fig. 5 show the area under the curve. The HbA1c is much higher in obese diabetic patients and controls than in those who are not fat and who are not diabetic <sup>33</sup>. And another researcher showed that hyperglycemia is mostly to blame for the higher risk of deadly cardiovascular disease. Regarding HbA1c, another study came to the same conclusion which indicated that complications were substantially related to diabetes duration and Hba1c level.

Risks of microvascular complications determine chronic hyperglycemia and a number of metabolic syndrome components in patients with T2DM. HbA1c predicts the risk of diabetic complications in patients with diabetes due to its function as an indicator of the mean blood glucose level .While enhancing, glycemic control could decrease the incidence of cardiovascular events in diabetic patients <sup>34</sup> that study agrees with <sup>35</sup> .High HbA1c fluctuation is linked to a higher chance of death from any cause and from heart disease, as well as problems from diabetes. The link between how often hypoglycemia happens, how variable HbA1c is, and death shows that intermittent hypoglycemia makes things worse for diabetes people.

Table 7. ROC curve analysis of FBS and HbA1C.							
Area Under the Curve Test Result Variable(s)	Area	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95%	Confidence Interval		
				Lower Bound	Upper Bound		
FBS	.989	.011	.000	.968	1.000		
HbA1C	.997	.003	.000	.991	1.000		

The test result variable(s): fbs, hba1c has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

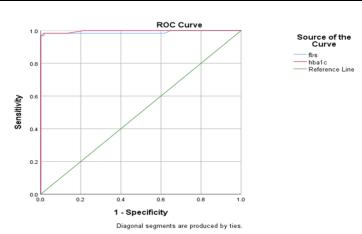


Figure 5. ROC curve analysis of FBS and HbA1C

# Conclusion

The current study demonstrated that Apelin-36 is directly correlated with obesity (high body mass index) and it observed that the way Apelin-36 affects blood lipids is similar to how it affects fatty tissue. Therefore, Apelin-36 may be used as a (cardiovascular) biomarker. This is due to the relationship of cardiovascular disease with obesity and Type 2 diabetes, Obesity ,BMI and excessive lipid and duration of disease increased

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#### **Authors' Declaration**

- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are ours. Furthermore, any Figures and images, that are not ours, have been included with the necessary permission for re-publication, which is attached to the manuscript.

#### **Authors' Contribution Statement**

M.M.M. collected the data, and analyzed samples, figured out what it meant, and wrote the report. F.M.K. performed the necessary tasks for the paper,

#### References

- Wysocka MB, Pietraszek-Gremplewicz K, Nowak D. The role of apelin in cardiovascular diseases, obesity and cancer. Front Physiol. 2018; 9: 557. <u>https://doi.org/10.3389/fphys.2018.00557</u>.
- Cheng J, Luo X, Huang Z, Chen L. Apelin/APJ system: A potential therapeutic target for endothelial dysfunction-related diseases .J Physiol Rev. 2019 Aug; 234(8): 12149-60. https://doi.org/10.1002/jcp.27942.
- He Q, Wang Y, Yang H, Wang J, Zhang J, Liu D. Apelin 36 protects against lipopolysaccharide induced acute lung injury by inhibiting the ASK1/MAPK signaling pathway. Mol Med Rep. 2021; 23(1): 1-. https://doi.org/10.3892/mmr.2020.11644.
- 4. Schinner S, Scherbaum WA, Bornstein SR, Barthel A. Molecular mechanisms of insulin resistance. Diabet Med. 2005; 22(6): 674-82. https://doi.org/10.1111/j.1464-5491.2005.01566.x.

cardiovascular disease and coronary heart disease, and damage to the vessels, are risk factors for type 2 diabetes and its complications. Patients with type 2 diabetes mellitus are significantly more susceptible to cardiovascular morbidity and mortality. The risk of cardiovascular in patients with T2DM diabetic compared to non-diabetic with obesity subject, therefore, T2DM people need to lose weight to lower their risk of heart disease.

Baghdad and the National Diabetic Centre at AL-Mustansiriyah University.

- Authors sign on ethical consideration's approval.
- Ethical Clearance: The project was approved by the local ethical committee at University of Baghdad.
- No animal studies are present in the manuscript.
- No potentially identified images or data are present in the manuscript.

including the analysis, design of interpretations, revision, and proofreading.

- Galon-Tilleman H, Yang H, Bednarek MA, Spurlock SM, Paavola KJ, Ko B, et al . Apelin-36 modulates blood glucose and body weight independently of canonical APJ receptor signaling. J Biol Chem.. 2017; 292(5): 1925-33. https://doi.org/10.1074/jbc.M116.748103.
- Ali SE, Khaleel FM, Ali FE. A study of apelin-36 and GST levels with their relationship to lipid and other biochemical parameters in the prediction of heart diseases in PCOS women patients. Baghdad Sci J.. 2020; 17(3): 0924-.http://dx.doi.org/10.21123/bsj.2020.17.3(Suppl.).09 24.
- Jaid HK, Khaleel FM, Salman IN, Abd BA. Estimation of Apelin Levels in Iraqi Patients with Type II Diabetic Peripheral Neuropathy. Baghdad Sci J. 2023. <u>https://doi.org/10.21123/bsj.2023.7566</u>.
- 8. Cheong LY, Xu A. Intercellular and inter-organ crosstalk in browning of white adipose tissue:



molecular mechanism and therapeutic complications. Mol Biol Cell. 2021; 13(7): 466-79. https://doi.org/10.1093/jmcb/mjab038.

- Blüher M. Obesity: global epidemiology and pathogenesis. Nat Rev Endocrinol. 2019; 15(5): 288-98. https://doi.org/10.1038/s41574-019-0176-8.
- Sitar-Taut AV, Coste SC, Tarmure S, Orasan OH, Fodor A, Negrean V, et al. Diabetes and obesity— Cumulative or complementary effects on adipokines, inflammation, and insulin resistance. J Clin Med. 2020; 9(9): 2767. <u>https://doi.org/</u> 10.1161/01.ATV.0000198392.05307.aa.
- Mittal B. Subcutaneous adipose tissue & visceral adipose tissue. Indian Med. Gaz . 2019 May; 149(5): 571. <u>https://doi.org/10.4103%2Fijmr.IJMR\_1910\_18</u>
- Abed BA, Hamid GS. Evaluation of Lipocalin-2 and Vaspin Levels in In Iraqi Women with Type 2 Diabetes Mellitus. Iraqi J Sci. 2022; 63 (11): 4650-4658.<u>https://doi.org/10.24996/ijs.2022.63.11.3</u>.
- Cypess AM. Reassessing human adipose tissue. N Engl J Med. 2022 Feb 24; 386(8): 768-79. <u>https://doi.org/10.1056/NEJMra2032804.</u>
- Piché ME, Tchernof A, Després JP. Obesity phenotypes, diabetes, and cardiovascular diseases. Circ Res.. 2020; 126(11): 1477-500. https://doi.org/10.1161/CIRCRESAHA.120.316101.
- 15. Khursheed R, Singh SK, Wadhwa S, Kapoor B, Gulati M, Kumar R, et al. Treatment strategies against diabetes: Success so far and challenges ahead. European J Psychopharmacol. 2019; 862: 172625.

https://doi.org/10.1016/j.ejphar.2019.172625.

- Padhi S, Nayak AK, Behera A. Type II diabetes mellitus: a review on recent drug based therapeutics. Biomed Pharmacother. 2020; 131: 110708. <u>https://doi.org/10.1016/j.biopha.2020.110708</u>.
- Artasensi A, Pedretti A, Vistoli G, Fumagalli L. Type 2 diabetes mellitus: a review of multi-target drugs. Molecules. 2020; 25(8): 1987. <u>https://doi.org/10.3390/molecules25081987</u>.
- Escrivá-Martínez T, Galiana L, Rodríguez-Arias M, Baños RM. The binge eating scale: Structural equation competitive models, invariance measurement between sexes, and relationships with food addiction, impulsivity, binge drinking, and body mass index. Front Psychol. 2019; 10: 530. https://doi.org/10.3389/fpsyg.2019.00530.
- Motamed N, Perumal D, Zamani F, Ashrafi H, Haghjoo M, Saeedian FS, et al. Conicity index and waist-to-hip ratio are superior obesity indices in predicting 10-year cardiovascular risk among men and women. Clin Cardiol. 2015; 38(9): 527-34 .<u>https://doi.org/10.1002/clc.22437</u>.
- 20. Abdulahi AM, Aguade AE, Yohannis HK. .Longitudinal modeling of fasting blood sugar variation over time among adult diabetic patients in case of Adama hospital medical college, Health Sci

Baghdad Science Journal

 Rep
 2022;
 5(6):
 e951.

 https://doi.org/10.21203/rs.3.rs-253888/v1
 .
 .

- Fasil A, Biadgo B, Abebe M. Glycemic control and diabetes complications among diabetes mellitus patients attending at University of Gondar Hospital, Northwest Ethiopia. Diabetes Metab Syndr Obes: Targets Ther. 2022: 75-83. <u>https://doi.org/10.2147/DMSO.S185614</u>.
- 22. Weykamp C. HbA1c: a review of analytical and clinical aspects. Ann Lab Med.. 2013; 33(6): 393. https://doi.org/10.3343/alm.2013.33.6.393.
- Butler AE, English E, Kilpatrick ES, Östlundh L, Chemaitelly HS, Abu-Raddad LJ, et al. Diagnosing type 2 diabetes using Hemoglobin A1c: a systematic review and meta-analysis of the diagnostic cutpoint based on microvascular complications. Acta Diabetol. 2021; 58: 279-300. <u>https://doi.org/10.1007/s00592-020-01606-5</u>.
- Zayr FH, Mohammed HA, Jasim AH, Salih MZ. Study of glycated hemoglobin (Hba1c) in obese diabetics patients and non obese diabetics patients. world. 2016; 13: 15 <u>http://dx.doi.org/10.1056/NEJM1990/10/11.3231503</u>
- 25. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomark Insights. 2016 Jan; 11: 95–104. https://doi.org/10.4137/BMI.S38440.
- 26. Zhang Y, Yang J, Ye J, Guo Q, Wang W, Sun Y. Separate and combined associations of physical activity and obesity with lipid-related indices in nondiabetic and diabetic patients. Lipids Health Dis. 2019; 18: 1-9. <u>https://doi.org/10.1186/s12944-019-0987-6.</u>
- Fonseca VA, Rosenstock J, Wang AC, Truitt KE, Jones MR. Colesevelam HCl improves glycemic control and reduces LDL cholesterol in patients with inadequately controlled type 2 diabetes on sulfonylurea-based therapy. Diabetes Care. 2008; 31(8): 1479-84. <u>https://doi.org/10.2337/dc08-0283</u>.
- Chapman MJ, Ginsberg HN, Amarenco P, Andreotti F, Borén J, Catapano AL,. Triglyceride-rich lipoproteins and high-density lipoprotein cholesterol in patients at high risk of cardiovascular disease: evidence and guidance for management. Eur Heart J Case Rep. 2011; 32(11): 1345-61. https://doi.org/10.1093/eurheartj/ehr112.
- 29. Jang SH, Paik IY, Ryu JH, Lee TH, Kim DE. Effects of aerobic and resistance exercises on circulating apelin-12 and apelin-36 concentrations in obese middle-aged women: a randomized controlled trial. BMC women's health. 2019; 19(1): 1-8. https://doi.org/10.1186/s12905-019-0722-5.
- Castan-Laurell I, Dray C, Valet P. The therapeutic potentials of apelin in obesity-associated diseases. Mol Cell Endocrinol. 2021; 529: 111278. https://doi.org/10.1016/j.mce.2021.111278.



- 31. Prasad K. Does HbA1cc play a role in the development of cardiovascular diseases?. Curr Pharm Des. 2018; 24(24): 2876-82. https://doi.org/10.2174/13816128246661809031219 57.
- 32. Adel SM, Seyedian M, Nourizadeh M. The relationship between HbA1c and cardiovascular events in diabetic patients with coronary angioplasty: A cross-sectional study. J Family Med Prim Care. 2022; 11(2): 772–774.<u>https://doi.org/10.4103%2Fjfmpc.jfmpc\_1206\_2</u>1.
- 33. Salman EM, Hasan BF. The effect of obesity and Insulin Resistance on Liver Enzymes in Type2

Diabetes Mellitus. Baghdad Sci J. 2015; 12(3): 536-45.<u>https://doi.org/10.21123/bsj.2015.12.3.536-545</u>.

- 34. Al-Attaby AK, Al-Lami MQ. Effects of duration and complications of type 2 diabetes mellitus on diabetic related parameters, adipocytokines and calcium regulating hormones. Iraqi J Sci.. 2019; 11: 2335-2316 <u>https://doi.org/10.24996/ijs.2019.60.11.5</u>.
- 35. Lee S, Liu T, Zhou J, Zhang Q, Wong WT, Tse G. Predictions of diabetes complications and mortality using hba1c variability: a 10-year observational cohort study. Acta Diabetol . 2021; 58: 171-80. https://doi.org/10.1007/s00592-020-01605-6.

# تقدير مستوى الابلين-36 عند البدناء وغير البدناء من مرضى السكري النوع الثانى

## مريم مؤيد محمد ، فيحاء مقداد خليل

قسم الكيمياء ، كلية العلوم للبنات، جامعة بغداد ، بغداد ، العراق.

#### الخلاصة

تشتمل عوامل الخطر لأمراض القلب و الأوعية الدموية في السمنة و مرض السكري من النوع2. الهدف من هذه الدراسة هو تقييم مستويات الابلين-36 في مرضى السكري النوع2 (البدناء و غير لبدناء ) العراقيين .مع معرفة ما اذا كان الابلين-36 مؤشر مستقبلي لأمراض القلب و الاوعية الدموية ,وهل هو مؤشر للسمنة ام لمرض السكري ام مؤشر قوي لكلا المرضين ,بمقارنة مع الاشخاص الذين يعانون من البدانة و لا يعانون من مرض السكري . شملت هذه الدراسة 20 شخصا": 30 مريضا" يعانون من السمنة و السكري . شملت هذه الدراسة 120 شخصا": 30 مريضا" من غير البدناء و يعانون من السكري . شملت هذه الدراسة 120 شخصا": 30 مريضا" من غير البدناء و يعانون من السكري ي من عرع , و 60 عينه بدناء استخدمت كمرجع كونترول . و الاعمار تتراوح يوع2 , و 30 عينه بدناء استخدمت كمرجع كونترول . و الاعمار تتراوح من 30 الى 56 عاما". من غير البدناء و يعانون من السكري نوع2 , و 60 عينه بدناء استخدمت كمرجع كونترول . و الاعمار تتراوح الابلين-36 على 100 الى 56 عاما". من غير البدناء و يعانون من السكري نوع2 , و 60 عينه بدناء استخدمت كمرجع كونترول . و الاعمار تتراوح الابلين-36 عاما". من غير البدناء و يعانون من السكري نوع2 , و 60 عينه بدناء استخدمت كمرجع كونترول . و الاعمار تتراوح الابلين-36 عاما". من غير البدناء و يعانون من السكري نوع2 , و 60 عينه بدناء استخدمت كمرجع كونترول . و الاعمار تتراوح الابلين-36 عاما". و كامن الماكري الذي يشمل 200 الى 20.5 الماكري العام و ملف الدهون الذي يشمل 200 المال المال المال الابلين-36 من السكري الابلين-36 عاما". من خال معري النوع 2 الذين يعانون من السمنة المفرطة ((27.6) 20.5 مال المال المال المال الحرض البدناء من السكري الغير بدناء ((20.5) 30.5 مال 20.5 مال 20.5 مال 20.5 مال 20.5 مال 20.5 مال 20.5 ماليناء من المون ماليمني عانون من مالسنة و التي عانون المؤري الولا و الموط الي الي الدين يعانون ما مالم و التي عانون ما الممن الماليم و الدي يادور . (27.5) 20.5 مال 20.5 مال 20.5 مال 20.5 ماليما قراد مالي ماليم و المال و الول ياديناء من الكونترول الموط الى و لابليناء و الدي يادور . و 20.5 مال 20.5 مالم 20.5 مال 20.5 مال 20.5 مالم 20.5 مالم مال و الدي يادوا ما المول قو و المام و و الدي يا الممنة و الدو ما و الول يا و

الكلمات المفتاحية: الانسجة الدهنية, الابلين-36, مؤشر كتله الجسم, ملف الدهون, داء السكري من النوع الثاني.