# Study of Circulating Apelin in Type 1 Diabetic Patients and its Association with Glycemic Control in a Group of Egyptian Population

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**ABSTRACT**

**Background:** Type 1 diabetes mellitus (T1DM) is a common chronic and metabolic disease characterized by hyperglycemia as a cardinal metabolic feature. Chronic hyperglycemia proved to cause macro and microvascular complications. Studies proved that TIDM is associated with metabolic abnormalities and alteration of adipose tissue hormones (adipokines). Adipose tissue yields many adipocytokines that modulate insulin sensitivity and play essential role in the pathogenesis of diabetes. apelin is a multifunction neuropeptide, involved in the regulation of food intake, cell proliferation and angiogenesis.

**Objectives:** The aim of this study was to evaluate the level of serum apelin in type 1 diabetic patients and to its correlation with glycemic control.

**Patients and Methods:** This cross-sectional study was conducted on 100 Egyptian subjects including 60 type 1 diabetic patients admitted to Endocrinology and Diabetes inpatient and outpatient clinics, Ain Shams University Hospitals and 40 healthy control subjects, during the period from June 2019 to January 2020.

**Results:** plasma apelin levels were significantly higher in diabetic group when compared to controls. Significant negative correlation was found between the apelin level and HbA1c. The best cut off value of apelin between diabetic and control is > 180 with 99.7% accuracy. Serum apelin ≥180 (ng/L) had sensitivity of 96.6 %, moderate specificity of 97.5%, positive predictive value of 98.3% and Negative Predictive value of 95.1%.

**Conclusion:** Increased levels of serum apelin in T1DM patients could be considered as promising adipokine for the development of diabetic complications.

**Keywords:** Adipokines, Circulating apelin, Type 1 Diabetic Patients, Glycemic Control.

## INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a common, chronic and metabolic disease characterized by hyperglycemia as a cardinal metabolic feature. Long-term damage, dysfunction and failure of various organs especially eyes, kidneys, nerves, heart and blood vessels are caused by chronic hyperglycemia of diabetes. The incidence of T1DM is reported to be increasing by 3-5% per year, and the number of people with diabetes is estimated to reach 380 million by 2025 [1]. Several studies have shown that TIDM is associated with metabolic abnormalities and alteration of adipose tissue hormones (adipocytokines or adipokines) [2].

Apelin, a described adipocytokine, is abundantly expressed in adipose tissue and produced in many body parts by the endothelial cells. Apelin is a bioactive peptide, produced by white adipose tissue. It is synthesized as a prepropeptide then modified into smaller peptides with higher potency. It produces its effects through a cell surface G protein coupled receptor called APJ [3]. Preproapelin is cleaved from its C-terminus to produce a mature apelin peptides.

Its extensive tissue distribution suggests that the apelin /APJ system, also known as an apelinergic system, is involved in a wide range of functions including regulation of body fluid homeostasis, blood pressure, endocrine stress response, cardiac contractility, angiogenesis, and energy metabolism [4]. Additionally, apelin participates in pathological processes, including heart failure, obesity, diabetes, and cancer [5].

Apelin, as a member of the adipose tissue-derived peptides, might contribute to metabolic disorders. Some data have indicated that there is a correlation between plasma insulin level and apelin expression in adipocytes. Apelin plays a beneficial role in energy metabolism by increasing glucose uptake and insulin sensitivity [4]. One of the first apelin effects observed on glucose metabolism, apart from that on insulin secretion is apelin stimulated glucose transport and its glucose-lowering effect was additive to that of insulin [6]. Apelin inhibits lipolysis in adipocytes and is involved in angiogenesis in adipose tissue.

Literature data documented also that glucose arrival in the intestine causes its own absorption by inducing the paracrine secretion of apelin. A transient increase in blood glucose levels in the portal vein could induce rapid secretion of insulin, and an improved insulin sensitivity [7]. Thus, apelin could also regulate glucose metabolism, by promoting glucose absorption by the enterocytes and then by increasing portal blood glucose and insulin secretion. This could be in agreement with the fact that apelin was shown to increase GLP-1 secretion [8].

Levels of apelin and APJ mRNA increase in white adipose tissue and plasma with obesity. Hyperinsulinemia may be the main cause for the rise in the expression of apelin. Data showed a positive correlation between the level of apelin in plasma and the body mass index [9]. Patients with obesity have impaired insulin-stimulated vasodilation and increased ET-1 (endothelin 1) vasoconstriction, which may contribute

to insulin resistance and vascular damage. Apelin enhances insulin sensitivity and glucose disposal but also acts as a nitric oxide (NO)–dependent vasodilator and a counter-regulator of $AT_1$ (angiotensin II type 1) receptor–induced vasoconstriction so, apelin might beneficially impact obesity-related vascular dysfunction [10].

In diabetes-related diseases, such as retinopathy, nephropathy, or cardiomyopathy Apelin has a protective effect against oxidative stress and apoptosis [11].

Additionally, apelin play a role in retinal neovascularization under diabetic retinopathy. In diabetic cardiomyopathy Overexpression of apelin resulted in augmented myocardial angiogenesis, attenuated diabetic cardiac hypertrophy, and improved cardiac function. Literature data documented also that apelin has anti-inflammatory effects on the release of inflammatory mediators. It also inhibits release of reactive oxygen species (ROS) in adipocytes and promotes an expression of antioxidative enzymes [12].

**The aim of the current study was:** (i) Assessment of serum apelin levels in subjects with type 1 diabetes with comparison to non-diabetic controls, (ii) Investigate the relationship between serum Apelin levels and glycemic balance.

## PATIENTS AND METHODS

This cross-sectional study included a total of 60 type one diabetic patients and 40 healthy control subjects, attending at Endocrinology and Diabetes Inpatient and Outpatient Clinics, Ain Shams University Hospitals. This study was conducted between June 2019 to January 2020.

They were divided into 2 groups: **Group (1)**: **60** Type one Diabetic patients and Group **(2)**: **40** apparently healthy subjects as control group.

**Inclusion Criteria:**
1. Type one diabetic patients treated with basal –bolus insulin therapy or premix insulin therapy.
2. Egyptian nationality.
3. Age between 20 to 35 years, including males and females.
4. Accepting participation in the study.

**Exclusion Criteria:**
1. Patients with acute illness.
2. Patients with current or past history of heavy alcohol consumption.
3. Patients with chronic liver diseases, kidney diseases or chronic anemia.
4. Pregnant females
5. Patients who refused to be enrolled in the study

**All patients were subjected to the following:**
- Full **history taking**.
- Full **clinical examination**.

- **Anthropometric measurements** including height (cm), weight (kg) and Body Mass Index (kg/m$^2$).
- Measurement of **waist-to-hip ratio (WHR)**: Waist and hip circumferences were measured in centimeters at the lowest curvature between the ribs and the iliac crest and at the area of greatest gluteal protuberance, respectively.
- Measuring **blood pressure** (BP).
- Initial **laboratory assessment** including Complete blood count (CBC), kidney function tests, liver enzymes, fasting and 2hr postprandial plasma glucose. HA$_{1C}$, fasting serum HDL cholesterol, LDL cholesterol and triglycerides.
- Calculation of **Insulin resistance** using the eGDR according to the following equation: $24.31 − (12.22 × $ waist to hip ratio$) − (3.29 × $ hypertension$) − (0.57 × $ HbA1C$)$, where the units are milligrams per kilogram per minute and hypertension status was 140/90 mm Hg (or on medications). There is an inverse correlation between insulin resistance and eGDR. It should be emphasized that lower eGDR levels indicate greater insulin resistance.
- **Determination of serum apelin:** by using enzyme-linked immune sorbent assay (ELISA) based on the Biotin double antibody sandwich technology.

**Ethical consent:**
**An approval of the study was obtained from Ain Shams University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.**

*Statistical Methods*
The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc, Chicago, IL, USA). Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, student t- test, Paired t-test, Linear Correlation Coefficient and Analysis of variance [ANOVA] tests by SPSS V17. Qualitative (non-numerical) data were described in the form of number (frequency) and percentage. Quantitative (numerical) data were described in the form of range, median and standard deviation. Statistical presentation and analysis of the present study was conducted, using the mean, standard deviation, student t- test, Paired t-test, Linear Correlation Coefficient and Analysis of variance [ANOVA] tests by SPSS V17. Chi square test ($\chi2$) to calculate difference between two or more groups of

qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value < 0.05 was considered significant.

**RESULTS**

Table (1) shows that Group 1 is cases which included 60 subject with type I diabetes mellitus, of them 26 were males (43.33%) and 34 were females (56.67%).

**Table (1): Characteristics of group 1** (diabetic patients) **with regard to gender.**

| Gender | | |
|---|---|---|
| | N | % |
| **Male** | 26 | 43.33 |
| **Female** | 34 | 56.67 |
| **Total** | 60 | 100.00 |

Table (2) shows clinical characteristics of group 1. The range for age was 20-35 years, for duration of diabetes was 6-23 years, for BMI was 20.4-37.5 $Kg/m^2$, for systolic & diastolic blood pressure was 110-135 mmHg & 75-85 mmHg respectively.

**Table (2): Clinical and anthropometric Characteristics of group 1**(diabetic patients)

| Descriptive Statistics | | |
|---|---|---|
| | Range | Mean±SD |
| **Age (years)** | 20-35 | 26.100±4.825 |
| **Duration of DM (Years)** | 6-23 | 12.400±3.941 |
| **Body mass index ($Kg/m^2$)** | 20.4-37.5 | 25.568±3.257 |
| **W/H ratio** | 0.76-1.1 | 0.885±0.073 |
| **Systolic BP (mm Hg)** | 110-135 | 121.333±8.227 |
| **Diastolic BP (mm Hg)** | 75-85 | 81.167±4.051 |

Table (3) shows no significant differences between cases and controls regarding age (with a range of 20-35 years for cases, and 20-32 years for control group), BMI, and W/H ratio. There was significant difference between the two groups regarding SBP and DBP (p < 0.05).

**Table (3): Comparison between Clinical and anthropometric characteristics of the study groups**

| | | Groups | | | | Chi-Square Or T-Test | |
|---|---|---|---|---|---|---|---|
| | | Diabetic patients | | Controls | | $X^2$ or T | P-value |
| **Gender** | **Male** | 26 | 43.33 | 19 | 47.50 | 0.168 | 0.682 |
| | **Female** | 34 | 56.67 | 21 | 52.50 | | |
| **Age (years)** | **Mean±SD** | 26.100 ± 4.825 | | 26.450 ± 2.541 | | -0.421 | 0.675 |
| **Body mass index ($Kg/m^2$)** | **Mean±SD** | 25.568 ± 3.257 | | 24.858 ± 2.074 | | 1.224 | 0.224 |
| **Waist-to-hip ratio** | **Mean±SD** | 0.885 ± 0.073 | | 0.857 ± 0.071 | | 1.870 | 0.064 |
| **Systolic BP (mm Hg)** | **Mean±SD** | 121.333 ± 8.227 | | 117.750 ± 6.694 | | 2.294 | 0.024* |
| **Diastolic BP (mm Hg)** | **Mean±SD** | 81.167 ± 4.051 | | 74.250 ± 5.834 | | 7.001 | <0.001* |

Table (4) shows that as expected, fasting plasma glucose levels, 2 hr. postprandial plasma glucose and HbA1c were higher in subjects with T1DM in comparison with the controls with highly statistically significance (P- value <0.01). Cholesterol, TG and LDL were significantly increased while HDL was significantly decreased in subjects with T1DM compared to controls. eGDR was significantly lower in subjects with T1DM than in controls. Plasma **Apelin** concentrations were significantly higher in subjects with T1DM than in controls (p<0.001).

**Table (4): Comparison between laboratory markers of the study groups**

| | | Groups | | T-Test | |
|---|---|---|---|---|---|
| | | **Diabetic patients** | **Controls** | **T** | **P-value** |
| **FPS (mg/dL)** | **Mean±SD** | 157.683 ±6.974 | 88.700 ± 4.250 | 5.881 | <0.001* |
| **2hr PP (mg/dL)** | **Mean±SD** | 228.983 ±47.444 | 120.275 ± 8.665 | 6.092 | <0.001* |
| **HBA1$_C$ (%)** | **Mean±SD** | 9.510 ±1.838 | 5.265 ± 0.212 | 14.519 | <0.001* |
| **Total Cholesterol (mg/dL)** | **Mean±SD** | 189.217 ±17.797 | 161.875 ± 33.316 | 5.326 | <0.001* |
| **HDL Cholesterol (mg/dL)** | **Mean±SD** | 46.217 ±8.047 | 60.525 ± 7.786 | -8.824 | <0.001* |
| **LDL Cholesterol (mg/dL** | **Mean±SD** | 101.817 ±14.291 | 86.825 ± 12.409 | 5.411 | <0.001* |
| **TG (mg/dL)** | **Mean±SD** | 91.333 ±20.947 | 56.200 ± 12.529 | 4.917 | <0.001* |
| **eGDR (mg/kg/min)** | **Mean±SD** | 7.867 ±1.705 | 14.741 ± 3.149 | -9.601 | <0.001* |
| **Apelin (ng/L)** | **Mean±SD** | 481.167 ±13.519 | 116.500 ± 3.625 | 13.117 | <0.001* |

The table (5) showed that there were significant positive correlations between **serum apelin** and **weight, & BMI.** Also, there were significant positive correlations between **serum Apelin** and **LDL, But** significant negative correlation between **serum Apelin** and **HDL.** Apelin has significant positive correlation with **DBP** in diabetic group (p = 0.029). A significant negative correlation was found with HbA1c. While no significant correlation was found with age, waist to hip ratio, SBP, eGDR and duration of diabetes.

**Table (5): Correlation between serum apelin and all other parameters in diabetic group**

| | Apelin | |
|---|---|---|
| | **r** | **P-value** |
| **Age (Years)** | 0.206 | 0.115 |
| **Weight (KG)** | 0.321 | 0.012* |
| **Height (cm)** | -0.142 | 0.280 |
| **BMI (Kg/m$^2$)** | 0.553 | <0.001* |
| **FPS (mg/dL)** | -0.005 | 0.968 |
| **2hrPP (mg/dL)** | -0.117 | 0.372 |
| **HBA1$_C$ (%)** | -0.263 | 0.042* |
| **T. Cholesterol (mg/dL)** | 0.005 | 0.972 |
| **HDL (mg/dL)** | -0.280 | 0.030* |
| **LDL (mg/dL)** | 0.560 | <0.001* |
| **TG (mg/dL)** | 0.193 | 0.140 |
| **eGDR (mg/kg/min)** | 0.071 | 0.588 |
| **W/H ratio** | 0.029 | 0.828 |
| **SBP (mm Hg)** | 0.226 | 0.082 |
| **DBP (mm Hg)** | 0.281 | 0.029* |
| **Duration of DM (Years)** | 0.070 | 0.593 |

Table (6) shows the best cut off value of Apelin between diabetic and control is > 180 with 99.7% accuracy. **Serum Apelin ≥180** had sensitivity of 96.6 %, moderate specificity of 97.5%, positive Predictive value of 98.3% and Negative Predictive value of 95.1%

**Table (6): ROC curve of best Cut off value to differentiate between diabetic and control group**

| ROC curve between Diabetic patients and Controls | | | | | |
|---|---|---|---|---|---|
| **Cutoff** | **Sens.** | **Spec.** | **PPV** | **NPV** | **Accuracy** |
| >180 | 96.67 | 97.50 | 98.3 | 95.1 | 99.7% |

## DISCUSSION

All included patients in this study were type one diabetic patients and treated with basal – bolus insulin therapy or premix insulin therapy. With mean age 26.1± 4.8 years and mean duration of diabetes 12.4± 3.9 years, including 45males (45%) and 55 females (55%). All female patients included in this study were not pregnant throughout the course of the study.

In our study we found that fasting plasma apelin concentrations were significantly higher in patients with T1DM in comparison with healthy subjects, ranging from 160 to 800 ng/l with mean ±SD of 481.167 ±173.519 and with statistical significance (p-value <0.001). This was in agreement with **Alexiadou et al.** [13] who carried his study on 100 type 1 diabetic adult, non-obese patients with BMI 24.1±. 033 to avoid any interference of BMI with the levels of apelin. We also agreed with **Meral et al.** [14] who carried their study on 30 children with T1DM with mean age was 8.6±4.3 year and mean duration of the disease was 4+2.6 years. This was comparable with the study of **Dayem et al.** [15] who studied apelin and vascular affection in a sample of adolescents Type 1 Diabetic Egyptian patients with their mean age were 16.3 ± 1.5 years and mean duration of diabetes were 9.4 ± 2.9 years. The same results have been shown by **Al-Suhaimi et al.** [16] in their study on Saudi children with age ranging from 3 to 14 years.

Most of the studies on humans have shown that apelin action on glucose metabolism is additive to insulin as it increases glucose uptake and transport in tissues. All reported previous actions of Apelin make it an anti-diabetic agent [17].

Thus, our study hypothesized that increased levels of apelin in T1DM is a result of compensatory mechanism devoted to decreased insulin levels and to overcome insulin resistance in these patients.

However, another published study found no difference in apelin between type 1 diabetic patients and controls [18]. The population in this study was very different from our population in terms of diabetes duration (6·4 ± 7·1 years vs 12.4 ± 3.9 years in our study), age (25 ± 14 years vs 26.1 ± 4.8 years in our study) glycated hemoglobin A1c (7.1±1.6 vs 9.510±1.838 in our study), BMI (22·2 ± 7 vs 25.5 ± 3.2). These differences between the populations could be one explanation for the contradictory results in these two studies.

In the contrast to our result **Polkowska et al.** [19] who carried their study on type one diabetic children aged 4–18 years had found that apelin concentrations were lower in diabetic children as compared to their healthy peers.

As regard the correlation of apelin with glycemic control, we found negative correlation between apelin and HbA1c (P-value 0.042). This is in agreement with **Habchi et al.** [20], who found that serum apelin levels were negatively correlated to HbA1c in type 2 diabetic patients.

This is in contrary with a previous study **Sabry et al.** [21] who stated that there is a highly significant positive correlation between serum apelin and HbA1c in diabetic subjects. This difference may be explained by difference in demographic criteria of the included diabetic group as their study was carried on 40 patients with T1DM, their mean age was 9.15 ± 3.64 years, and the mean duration of disease was 4.5 years compared to 12.4 ± 3.9 years in our study. Adding the fact that patients with T1DM in our study were treated with insulin for a longer duration which plays an important role in apelin secretion and expression. The same positive correlation was observed in **Dayem et al.** [15] whom study was carried on a sample of Adolescent Type 1 Diabetic Egyptian patients with their mean age were 16.3 ± 1.5 years and mean duration of diabetes were 9.4 ± 2.9 years.

On another side **Alexiadou et al.** [13] reported no significant correlation between apelin and HbA1c.

So, our results suggested that circulating Apelin is associated with the better glycemic control. This is maybe explained by that the influence of Apelin on insulin sensitivity. So increased apelin level observed in insulin-resistance in diabetic patients, could suggest a compensatory role to reduce insulin resistance and to improve impaired insulin secretion [15].

From our results, we can consider patients with T1DM at higher risk of developing premature atherosclerosis because of hyperlipidemia and thus, should be screened well for this serious complication. According to the guidelines of the American Heart Association, type 1 diabetes in children and adolescents can be regarded as the equivalent of ischemic heart disease.

However, other studies found no correlation between serum apelin levels and plasma lipids levels **Meral et al.** [14] in a study of apelin in type 1 diabetic children between the age of 5 and 9 years with mean duration of the disease was 4+2.6 years. Also, **Habchi et al.** [20] reported No correlation between apelin and serum lipids in their study which included type 1 diabetic patient with mean age 41 ± 15 years, mean diabetes duration 21 ± 13 years.

We could explain our results with the fact that apelin was shown to inhibit lipolysis according to **Than et al.** [22] and increases the stability of lipid vacuoles making them more resistant to lipases. All these findings support our results that Apelin is associated with increased serum lipids and thus can be used as a predictor of premature atherosclerosis in T1DM patients.

As regard correlation with blood pressure, we found a significant influence of serum Apelin on diastolic blood pressure, it increases with increased serum apelin levels, but it does not affect systolic blood pressure which was consisting with previous study [21]. Also, **El Wakeel et al.** [23] reported a significant positive correlation between apelin and SBP, DBP in his study of Serum Apelin and Obesity-Related Complications in

Egyptian Children. Our observation wasn't in line with **Rittig** *et al.* [24], who evaluated the relation between apelin serum levels, body fat distribution and insulin sensitivity/resistance as dependent cardiovascular risk factors; blood pressure was reported to be unaffected by serum Apelin levels.

Hence, from our result we can consider increased levels of serum apelin in T1DM as predicting factor for the further development of vascular complications of DM in these patients.

In our study there was a significant positive correlation between apelin and BMI with a P-value <0.001, r= 0.553, the same correlation with weight demonstrated with P-value 0.012, r= 0.321 suggesting that obesity is probably a main determinant of increased apelin levels. This agreed with **Boucher** *et al.* [25] who found similar results and supposed that adipose tissue is a major source of apelin release.

This increase might be a compensatory mechanism against myocardial dysfunction with obesity. This also came in agreement with a study done by **Sheibani** *et al.* [26] who carried their study on obese women and have shown that plasma Apelin levels were increased in obesity and positively correlated with BMI also they have shown that aerobic exercise was associated with weight and plasma apelin reduction levels.

However, **Reinehr** *et al.* [27] reported no significant relationship between Apelin and weight status and demonstrated that weight loss in obese children was not associated with changes in apelin concentrations, but we should consider that this study was carried on a younger, non-diabetic age group.

Also, not in line with our results **Castan-Laurell** *et al.* [28] underlined that obesity, per se, is probably not the main determinant of increased plasma Apelin concentrations since circulating Apelin levels are not necessary significantly correlated to the body mass index (BMI). **Habchi** *et al.* [20] found no correlation between serum Apelin levels and BMI in diabetic patients.

In contrast to our result regarding Apelin and obesity **Polkowska** *et al.* [19] have shown a negative correlation of Apelin with body mass and BMI in diabetic children.

Explanation regarding our results for increased levels of apelin observed in obesity as we supposed that adipose tissue is a major source of Apelin release, and that expression of Apelin and Apelin receptors (APJ) both increase in fat cells of obese subjects and this increase could be a mechanism to counterpace insulin resistance.

Our results have shown that eGDR is lower in type 1diabetic patients compared to healthy subjects which means higher insulin resistance in diabetic group. Apart from insulin deficiency, insulin resistance is found in type 1 diabetes mellitus, both at onset and course of the disease. **Fourlanos** *et al.* [29] concluded that insulin resistance was identified as an independent risk factor for progression to diabetes in at-risk children with subclinical islet autoimmunity (i.e., positive for islet antibodies).So we could consider insulin resistance as a primary disorder in T1DM

We found no significant correlation between Apelin and insulin resistance marked by eGDR which was in agreement with **Meral** *et al.* [14] who found no significant correlation between the Apelin and insulin sensitivity as assessed by daily insulin dose (U/kg/d) in children with T1DM.So we could assume that regulation of Apelin seems not to be related to the insulin sensitivity in patients with T1DM.

We found no correlation between apelin concentrations and duration of DM which is in agreement with **Dayem** *et al.* [15] in the study on Egyptian diabetic patients.

Finally, we could assume that "hyperapelinemia" is a sort of negative feedback mechanism which combats hyperinsulinemia in obesity or type 2 diabetes. The higher levels of apelin found in our patients with T1DM could be an attempt to compensate for the lack of insulin in the same way that raised apelin levels in obesity or type 2 diabetes could possibly try to overcome insulin resistance and substitute the relative "lack" of insulin.

The accuracy Apelin assay is 99.7% with cut off >180 between non-diabetic and diabetic, with sensitivity 96.69% and specificity 97.50%. NPV (negative predictive value) is 95.1% and PPV (positive predictive value) is 98.3 %.

## CONCLUSION

It could be concluded that that apelin concentrations is increased in type 1 diabetic patients compared to healthy controls. The potential association of apelin with insulin secretion and action may reveal new pathways in the pathogenesis of type 1 diabetes. Understanding the physiological role of this adipokine in glucose homeostasis and the mechanisms underlying its action is a challenge that could lead to new therapeutic targets. Also, increased levels of serum apelin in T1DM patients may be considered as predicting factor for the ongoing development of vascular sequels, so measuring serum apelin in these patients is of benefit for early detection of disease complications. Positive correlation was found between Apelin with HbA1c as a marker for glycemic control so Apelin may have a promising role as biomarkers in T1DM.We also suggested that obesity is a determinant factor in plasma levels of Apelin.

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