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# The Concentration of Adrenomedullin in Obese Subjects with and without Diabetes Compared with Healthy Control

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**Abstract:** ***Adrenomedullin is a potent vasodilator and antioxidative peptide. Adrenomedullin was found currently to be released by adipose tissue and associated with many diseases. This study done to investigate the association between adrenomedullin and obesity in subjects with or without diabetes. The study included 25 obese type II diabetes women, 25 obese women and 30 healthy women who attended to outpatient clinic at the department of endocrine, Al-Kindy hospital during the period between 2014-2016. Evaluation the concentration of serum adrenomedullin, Insulin, Glucagon by immunoassay kits. All participants were subjects to anthropometric measurements included body mass index. the result of this study has shown highly significant differences in the mean of BMI, serum adrenomedullin, insulin, glucagon and glucose in diabetic obese women group than control group (p<0.001). Marked increase in serum adrenomedullin, insulin and glucose in diabetic obese women than obese women group (p<0.001). from this study we can conclude that adrenomedullin may play a role in diabetic obese and obese subjects since all patients have highly significant elevation in serum adrenomedullin level.***

**Keywords**: Adrenomedullin, Diabetes mellitus, obesity

## 1. Introduction

Adrenomedullin is a 52 amino acid peptide hormone recently learned with more than one services, originally isolated from the human pheochromocytoma and adrenal medulla (1). Adrenomedullin has been proven to have a awesome variety of features, from regulating cellular progress and differentiation, through modulating hormone secretion and antimicrobial outcome (2). ADM might act as autocrine, endocrine or paracrine mediator in various biological systems (3). ADM prospects as a possible disease modulator comes from the observation of increased concentration in blood in many disease states. For instance, elevated ADM concentration was observed in diabetes, the explanation and cardiovascular diseases (3). In healthy subjects the extent of plasma adrenomedullin in circulating is as little as in picomolar range, just like the atrial natriuretic peptide and the ADM concentration changes with a purpose to catch up on the vasoconstrictive effects. Many stories reported that the increased in ADM stage related with severity of sickness state (4). Several studies have been made in the association between ADM and diabetes such Martinez et al (1996) show that ADM plays a role in glucose metabolism and insulin balance (5). ADM could act as cytokine and hormone to regulate the glucose uptake, balance of electrolyte and hormone released (6,7). It is involved in pancreatic endocrinology, mainly in insulin secretion (8). Obesity is a chronic disease characterized by excess body fat which occur when energy input is greater than energy output (positive shift of the energy) (9). It is associated with an increased rate of morbidity and mortality (10). The incidence of obesity problems has elevated in contemporary years, making weight problems a international epidemic (11). Obesity is a multifactorial disorder (12), and It's the result of a joint result of genetic and environmental explanations (13). Moreover, obesity is a hazard element for a couple of continual diseases, most peculiarly hypertension, type 2diabetes, dyslipidemia and coronary heart disorder (14). Obesity incidence is speedily raised in industrialized nations and a tremendous hazard component for many critical sicknesses like diabetes and any disease has insulin resistance as a long-established pathogenic denominator (15). Obesity is related to dysregulation of energy stability results in raised fats mass because of hyperplasia and hypertrophy of white adipose tissues. This study and others have shown that adrenomedullin belongs to the adipokines family (16-18).

## 2. Subjects and Methods

**Subjects:** this study was carried out during April 2014 till February 2016. It included 25 diabetic obese women with age range of 30-48 years and 25 obese women with age range of 30-47 years and 30 healthy women with age range 30-47 years. All women were attending AL-Kindy teaching hospital. All women of the current study were subjected to anthropometric measurements including Body Mass Index (BMI) and the study groups divided into normal BMI (25-29.9 kg/m$^2$) and obese BMI (>30 kg/m$^2$) (19).

**Methods:** Ten milliliters of blood were collected into plain tube in the morning after 12 hour fast. Serum was obtained after centrifugation of blood at 3200 rpm for 10 minute was separated and segregate into small parts for measurements of serum adrenomedullin, insulin, and glucagon by ELISA technique (mybiosource, USA). Serum glucose was determined by enzymatic methods of spectrophotometry (kit from BioMereux, France) (20).

## 3. Results and Discussion

Twenty-five diabetic obese and twenty-five obese women with mean age ± SEM (39.0 ±1.1; 38.2±1.5, respectively), and thirty healthy women with mean age ± SEM (38.5±1.3) were included in this study. Statistical analysis shows highly significant differences in BMI, serum ADM, insulin, glucagon, and glucose in diabetic obese group when

compared to control group (p<0.001). Also found significant high elevation in the mean of serum ADM, insulin, and glucose in diabetic obese than in obese group p<0.001 (Table 1).

**Table 1:** Clinical characteristics data of different study groups

| *Clinical characteristics* | *Control group (N=30)* | *Diabetic obese group (N=25)* | *Obese group (N=25)* |
|---|---|---|---|
| Age | 38.5±1.3 | 39.0± 1.1 | 38.2±1.5 |
| BMI | 23.7 ±0.4 | 33.8± 0.8 a*** | 34.4 ± 0.8 a*** |
| FBG (mg/dl) | 100 ± 3.2 | 131±3.7 a***, b*** | 106±2.8 |
| Insulin | 57.1± 4.8 | 143.8± 7.5 a***, b*** | 58.1±4.8 NS |
| Glucagon(pg/ml) | 153.3± 9.5 | 145.8± 10.6 a*** | 142.9±6.5 a*** |
| ADM(pg/ml) | 80.1± 4.4 | 494.6± 35.8 a***, b*** | 196.3± 15.6 a*** |

• Results expressed as Mean±SEM.
a ANOVA test: Diabetic Obese and Obese vs control group:p<0.001
b ANOVA test: Diabetic Obese vs Obese group: p<0.001; NS: Not Significant.

Statistical analysis revealed significant elevation in the mean of insulin in diabetic obese group (p<0.01) as compared with obese group and control group, while the mean serum insulin in obese group showed no significant differences from that of the control group (p>0.05).

ANOVA test illustrate significant elevation in the mean of glucagon concentration in obese group compared to control group (p<0.01). Group comparisons revealed high significant elevation in the mean of BMI in diabetic obese and obese group as compared with control group (p<0.05). Person correlation shows positively high significant correlation between ADM and insulin (p<0.01), between ADM and glucagon (p<0.01), and between insulin and glucagon (p<0.01) in diabetic obese group table 2.

**Table 2:** The correlation between parameters of diabetic obese group

| Parameter 1 | Parameter2 | p-value | r |
|---|---|---|---|
| Adrenomedullin | Insulin | <0.01 | 0.49 |
| Adrenomedullin | Glucagon | <0.01 | 0.45 |
| insulin | glucagon | <0.01 | 0.55 |

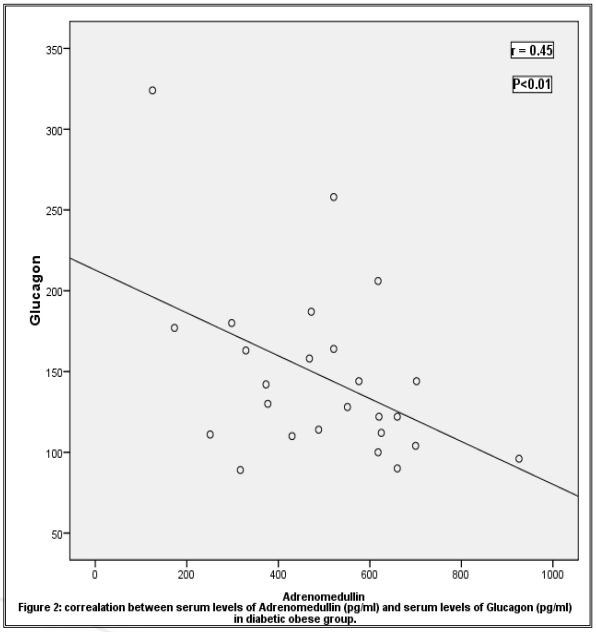


**Figure 1:** The correlation between serum level Adernomedullin and glucagon in diabetic obese group.

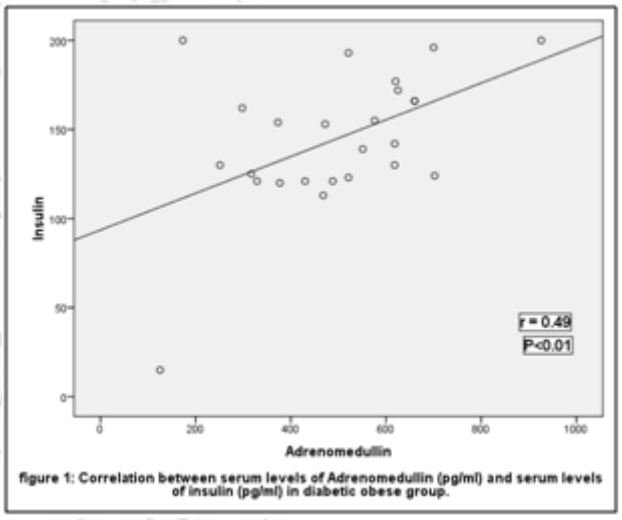


**Figure 2:** The correlation between serum level Adernomedullin and insulin in diabetic obese group.

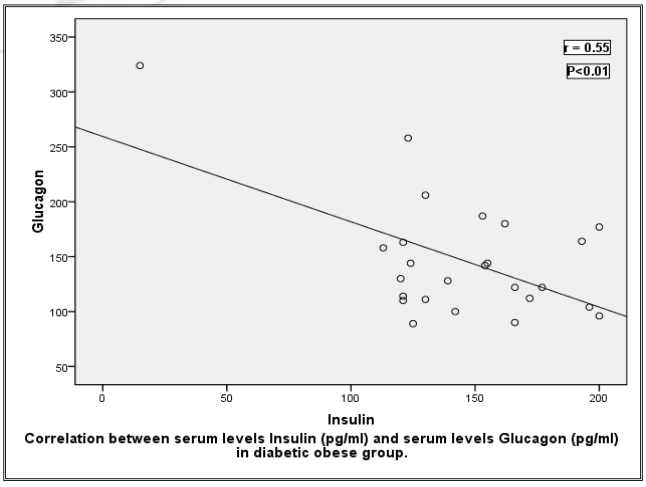


**Figure 3:** The correlation between serum level insulin and glucagon in diabetic obese group.

The action of adrenomedullin as hormone and a cytokine help to regulate uptake of glucose and hormone secretion (21). Therefore, it can be anticipated that ADM contributes to diabetes and even results in the progress of diabetic problems (22). The expression of ADM increases during immune disease and inflammation (23).

Previous studied suggest that the adrenomedullin can act on the control of insulin resistance. It has been shown that the deficiency of AM induces insulin resistance in mice (24) and that acute hyperinsulinemia elevated circulating AM concentration in patients with diabetic (25) or in uncomplicated obese subjects (26). In obese and/or diabetic patients, AM may, in turn, interact with the regulation of insulinemia (26–28).

The mechanism of increased serum level of adrenomedullin in the inflammatory process varies after the onset of inflammation. ADM could inhibition the overproduction of pro-inflammatory cytokines and modulate production of cytokines (26). Present results reveals that the concentration of ADM increased with increase the concentration of insulin level in diabetic obese group this finding is agreement with other study found there was a concomitant elevated in serum ADM concentration with elevating serum insulin production and a significant positive correlation between serum insulin concentration and serum ADM in type 2 diabetic patients (29).

Results of present study were in line with the study who found that Adrenomedullin level was higher in diabetic patients than in controls ($P<0.001$) (30). Other researchers examined of patients with hyperglycemia that reported similar rise in adrenomedullin level in patients with diabetes even though the source of this elevated adrenomedullin is unknown, they suggested that the patients with hyperglycemia are characterized by elevated circulating adrenomedullin levels (31). In the same studies, the effect of adrenomedullin in blood glucose modulation was examined used obese diabetic rat and they found that adrenomedullin rise blood glucose concentration.

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