

Maternal Serum Resistin Concentration in Gestational Diabetes Mellitus and Normal Pregnancies

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Abstract: Background; The physiological role of resistin in gestational diabetes remains controversial. Resistin is thought to be antagonist to insulin action in the peripheral tissues and act as a powerful regulator of glucose homeostasis. The goal of this work was to examine the fluctuations in resistin levels during gestation in healthy and diabetic mellitus women. Patients and methods: This study is a case-controlled study that was carried in Al-Zahraa University Hospital in the period from October 2011 to June 2013 in order to investigate the resistin level in the serum in healthy and diabetic mellitus women during gestational period. Results: There was highly significant increase in Resistin level (p-value = 0.005) from 26-28 weeks gestation to 36-38 weeks gestation in group A (diabetic patient). The conclusion of the current study was that there is elevation in serum resistin levels during pregnancy in patients with gestational diabetes.

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Key word: Resistin, diabetes mellitus, gestational diabetes

1. Introduction;

A different bioactive substances are secreted from adipose tissue secreted which usually accompanied with several conditions such as insulin resistance, chronic inflammation, and diabetes mellitus type 2. Resistin (adipokine) or firstly called adipocyte-secreted hormone which associated with obesity and resistance to insulin in rodents, where in human beings it is largely expressed and secreted by the macrophages. Several genetic and epidemiological investigations revealed that elevated in resistin concentration are coordinated with the advance of diabetes, cardiovascular disorder and insulin resistance (1).

Recently resistin is adipose-specific secreted hormone, which is considered as one of the family of cysteine-rich, c-terminal proteins (2). Resistin pharmacologically is possessing a powerful regulatory action of glucose homeostasis that is believed to antagonize the insulin action in the peripheral tissues (3).

The physiological role of resistin in diabetic pregnant women still controversial, whereas, some authors reported a drop in the level of resistin in GDM than in non-diabetic women which continued post labor (4). Although others found higher levels of serum resistin in diabetic pregnant women (5).

Recently, resistin has been found to express and secrete from the placenta of pregnant women (7),

proposing its crucial role in the appearance of insulin resistance during gestation (6), and levels of resistin elevate during the third trimester (8). On the other hand, it was found that the changes in the resistin serum level was parallel to resistin gene expression in the placental tissues during gestation, which may be involved in the pathogenesis of the insulin resistance cases presented in the 3rd trimester of diabetic pregnant women (9).

The level of resistin in normal humans are ranged from 7 to 22 ng/mL⁻¹ (10), this values was found to increased significantly in obese and diabetic patients (11). Resistin has been linked with several metabolic disorders but also with, inflammatory, immune-mediated and cancer diseases (12). In addition, it was found recently that human resistin is found too in macrophages and may be concerned in the association among inflammation and insulin resistance (13). Moreover, resistin play a role in the the pathogenesis of atherosclerosis through proliferation of vascular smooth muscle cells, stimulating endothelial dysfunction, formation of foam cells and inflammation in the arteries. Consequently, resistin is used for predilection of atherosclerosis and unfortunate clinical outcomes in individuals having cardiovascular disorder and heart failure. Also, recently they postulated that resistin is accompanying with atherogenic hypertension and dyslipidemia. The current article will concentrate on

the importance of resistin in the pathogenesis of inflammation and obesity-related disorders in human beings (1).

Some reports about the elevation of resistin concentration in diet-induced obesity and in genetic simulations of obesity and insulin resistance. Resistin is hence a candidate adipocyte-derived factor that contributes in vivo to insulin resistance. This proposition is braced by investigations in adipocytes, in those neutralization with resistin antiserum improved insulin-stimulated glucose utilization, and insulin action was diminished by recombinant resistin (14).

Aim of the Work

The purpose of this work was to investigate the alterations in maternal serum resistin along gestation in healthy and also in gestational diabetes mellitus women.

2. Patients and methods;

This study was a prospective case-controlled study that was conducted in Al-Zahraa University Hospital in the period from October 2011 to June 2013 in order to examine the changes in maternal serum resistin levels during pregnancy both in normal women as well as in women with gestational diabetes mellitus.

These 45 women were divided into two groups:

Group (A) study group:

Twenty five women with gestational diabetes mellitus.

Group (B) control group:

Twenty apparently healthy pregnant women have normal GTT.

Inclusion criteria; any pregnant women in singleton pregnancy between 26-28 weeks gestational age.

Criteria of exclusion:

- Twin pregnancy.
- Any associated congenital anomalies.
- Previous history of preeclampsia.
- Previous history of Pregnancy induced hypertension.
- Previous history of Diabetes or glucose intolerance.
- Any other significant endocrine disorder in the current pregnancy or in the past.

The nature and aims of the work were fully discussed with all women who agreed to participate in the study. The procedure was explained to every patient and a verbal consent was taken.

Methods of the study:

All women included in the study were subjected to the following:

History taking, complete physical and abdominal examination, abdominal ultrasound.

3-h oral glucose tolerance test (GTT):

The 3 hour OGTT is done after an overnight fast for at least 8 hours but not more than 14 hours after at least three days of unrestricted diet with more than 150gm of carbohydrates and client was at rest during the study (Carol., 2007).

Abnormal 3-hour 100 gram OGTT values according to the criteria established by **Carpenter and Coustan (1982)**.

- Fasting > 95 mg/dl One hour > 180 mg/dl
- Two hour > 155 mg/dl Three hour > 140 mg/dl

At least two out of four values must be equalled or exceeded to diagnose gestational diabetes.

1) Blood Sampling:

Blood samples were obtained by peripheral venipuncture with minimal stasis after aseptic conditions. 10 ml of blood were withdrawn from each case and control. The blood samples were taken in plain tubes, put in water bath at 37 °C for 30 minutes and centrifugation were done for 10 minutes at 4000 rpm, the resultant serum was collected, divided serum Glucose was measured at time then the rest of sample stored at -20°C for subsequent analysis of Resistin and Insulin.

2) Follow up:

Patients were followed up at Out Patient Clinic for antenatal care and immediately after diagnosis of GDM, these women were placed on an 1800 kcal/day low lipid (30%) and 20% protein diet, with special care to avoid simple carbohydrates.

3) Glucose measurement:

Fasting blood glucose was measured using a glucose peroxidase kits on Hitachi (Cobas C311) autoanalyzer using Rouché reagent kits (Neese, 1982).

4) Resistin measurement: Using of ELISA.

Statistical methodology:

Data were analyzed using Statistical Program for Social Science (SPSS) version 18.0.

3. Results

This study included 45 pregnant women, admitted to Al-Zahraa University Hospital, pregnant at 26-28wks gestational age are divided into two groups;

Group A: 25 pregnant women in singleton pregnancy suffering from gestational diabetes mellitus.

Group B: 20 pregnant women in singleton pregnancy with normal GTT.

Intable (1) shows: There was no statistically significant difference between the two groups as regard age, height, gravidity and Gestational age

(GA) at 26-28wks and 36-38wks gestation.

Table (1): Demographic data of all included women:

Parameters	Group A N=25	Group B N=20	t	p-value	sig
Age (years)	32.08±2.84	29.33±4.23	1.337	0.148	NS
Ht.	1.68±0.04	1.60±0.05	0.146	0.862	NS
Deliveries	1.88±1.12	1.51±1.09	1.031	0.309	NS
abortions	1.05±0.63	1.10±0.83	0.638	0.207	NS
GA (26-28wks)	27.18±0.80	27.16±0.71	0.096	0.924	NS
GA (36-38wks)	36.67±0.69	36.27±0.97	1.124	0.114	NS

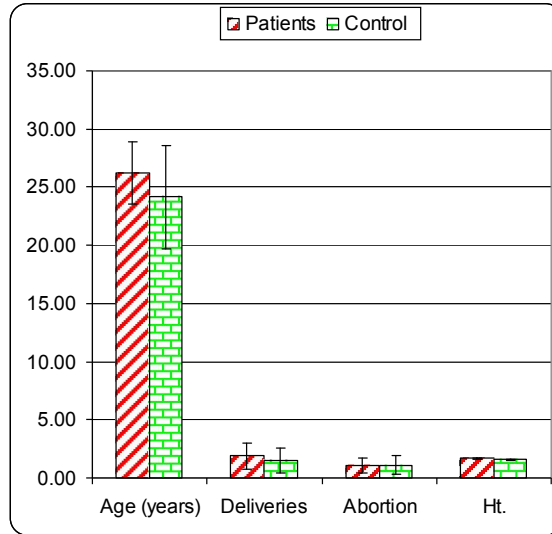


Figure 1: Comparison between patients and control as regard age, deliveries, abortion and Height.

Table (2): Statistics comparisons between Resistin, and BMI at 26 -28 wks and at 36 - 38 wks gestation in group-A (study group)

	26-28 wks gestation	36-38 wks gestation	t	P-value	Sig.
Resistin (ng/ml)	8.65±4.72	13.73±8.28	-3.097	0.005	HS 0.762
BMI	36.02±2.33	38.77±1.87	-10.954	<0.021	HS

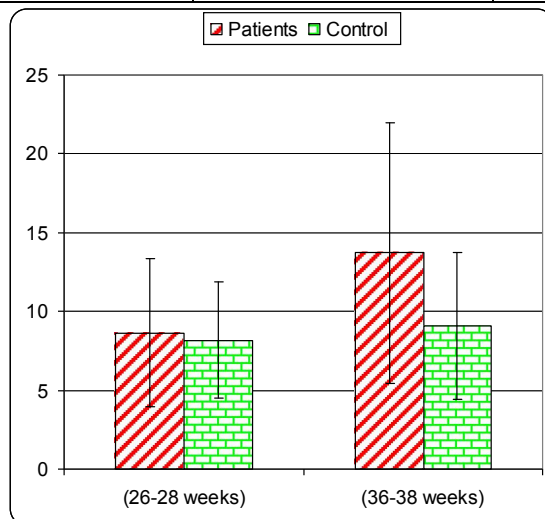


Figure 2: Comparison between patients and control as regard resistin (ng/ml).

Table (3): Correlation between resistin and EFW in groups A (study group) and B (control group) at 26-28wks gestation:

<i>Resistin</i>		<i>Group A</i>	<i>Group B</i>
<i>EFW</i>	Pearson Correlation (r)	0.016	0.040
	P-value	0.940	0.876
	N	25	20
	Sig.	NS	NS

This table shows: No statistically significant correlation between resistin (ng/ml) and EFW at 26-28wks gestation in both groups.

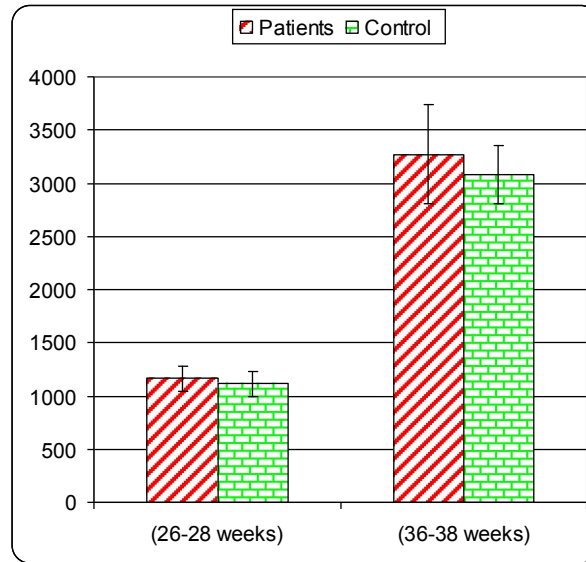


Figure 3: Comparison between patients and control as regard EFW.

Table (4): Correlation between resistin and EFW in groups A (study group) and B (control group) at 36-38wks gestation:

<i>Resistin</i>		<i>Group A</i>	<i>Group B</i>
<i>EFW</i>	Pearson Correlation (r)	0.288	0.259
	P-value	0.153	0.300
	N	25	20
	Sig.	NS	NS

This table shows: No statistically significant correlation between Resistin (ng/ml) and EFW at 36-38wks gestation in both groups

Table (5): Correlation between resistin and BMI in groups A (study group) and B (control group) at 26-28wks gestation:

<i>Resistin</i>		<i>Group A</i>	<i>Gup B</i>
<i>BMI</i>	Pearson Correlation (r)	0.227	0.151
	P-value	0.264	0.550
	N	25	20
	Sig.	NS	NS

This table shows: No statistically significant correlation between resistin (ng/ml) and BMI at 26-28wks gestation in both groups

Table (6): Correlation between resistin and BMI in groups A (study group) and B (control group) at 36-38wks gestation:

<i>Resistin</i>		<i>Group A</i>	<i>Group B</i>
BMI	Pearson Correlation (r)	0.163	0.118
	P-value	0.428	0.455
	N	25	20
	Sig.	NS	NS

This table shows: No statistically significant correlation between resistin (ng/ml) and BMI at 36-38wks gestation in both groups.

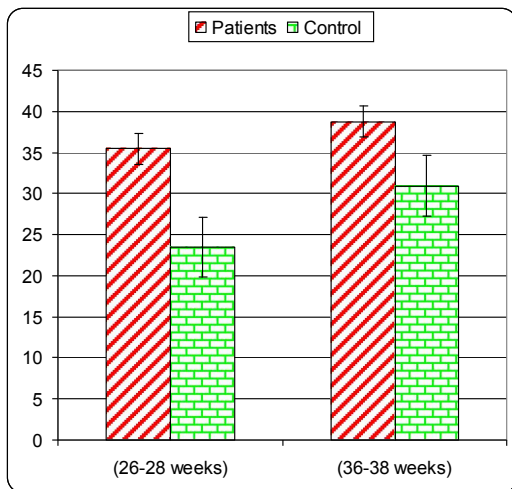


Figure 4: Comparison between patients and control as regard BMI.

4. Discussion

The current work was done to investigate the alterations in maternal serum resistin healthy and diabetic (GDM) pregnant women, and to assess the possible role of resistin as aintermediary of insulin resistance.

The current investigation revealed that there was no significant variationamongthe two groups with respect to height, age and gravidity. In agreement with our results **Nikolaos et al. (2011) (15)** found that no statistically significant difference between pregnant women with gestational diabetes mellitus and healthy pregnant women as regard age, heightand gravidity.

On the other hand **Jang et al. (1998) (16)** demonstrated that in the racially homogeneous population of Seoul, Korea, besides age and short stature is an independent risk factor for gestational diabetes mellitus. In addition, **Branchtein et al. (2000) (17)** found that that height < 150 cm was associated with a 60% increase in the odds of gestational diabetes mellitus, independently of age, obesity, skin color, parity, family history, and previous gestational diabetes mellitus. Also **Kousta**

et al. (18) found that South Asian and European women with a history of gestational diabetes mellitus were smaller than control women from anidentical ethnic sets with adjusting the age.

On contrary to our results **Bo et al. (2001) (19)** found that the Prevalence of diabetes mellitus pregnant women raised with age, from 1.5 / 1000 deliveries for women their ages ≤ 20 years to 4.2/1000 deliveries for women their ages ≥ 30 years.

The current work recorded that there was no significant variation (p - value =0.762) among the two studied groups with regard to Resistin hormone at 26-28 weeks GA and a statistically significant difference (p - value =0.038) at 36-38 weeks GA.

This results is in agreement with that of **Nikolaos et al. (2011) (15)** who had agreement with our results as they found in the gestational diabetes mellitus group, that serum resistin levels at weeks 26–28 of gestation did not varied significantly (P = 0.6) from those in the healthy group. In dissimilarity, the gestational diabetes mellitus group had significantly (P = 0.02) elevated resistin levels at 38 weeks of gestation in comparison with healthy control group.

Also **Youn et al. (2004) (9)** reported that plasma resistin concentrations are higher in patients with type II diabetes than in non-diabetic subjects. Also **Chen et al. (2007) (5)** have demonstrated that serum resistinlevelbefore delivery was significantly elevated in diabetic patients than in healthy one and significantly diminished post labor in both the gestational diabetes mellitus group and healthy group. In coordination with our data which revealed that serum resistin levels was elevated in gestational diabetes mellitus women versus healthy women group at the two measures. **Kuzmicki et al. (2009) (20)** also found that Resistin level in the serum was higher (21.9 ng·mL⁻¹) in diabetic patients (diabetes mellitus, type2) than in normal glucose tolerance (19.03 ng·mL⁻¹) pregnant women, where increase in serum resistin level was noticed in diabetic pregnant women, meanwhile, were associated with serum IL-6 concentrations, not insulin levels, postulating that fluctuation in insulin sensitivity of women having

gestational diabetes mellitus were augmented by inflammatory processes which may include resistin.

However; **Megia et al. (2008) (4)** reported lesser resistin concentrations in gestational diabetes mellitus than in healthy women and dropped post labor. Additionally, they have unsuccessfully found a definite connection among resistin status and insulin sensitivity within gestational period.

Shafir et al. (1994) (21) have issued a sequence of researches matching the body structure analysis of children of women with normal glucose tolerance (NGT) and gestational diabetes mellitus in 48 hours of labor. In spite of there was no significant variation in fat-free mass or birth weight among the studied groups, there was a significant elevation in fat mass and body fat percent in the infants of the gestational diabetes mellitus mothers, this is in agreement with our results.

On contrary **Silverman et al. (1995) (22)** found that in well controlled presentational diabetes mellitus or in gestational diabetes mellitus, macrosomia is the more common fetal growth disturbance. Also **Scholl et al. (2001) (23)** investigated the impact of maternal blood glucose in non-diabetic women on the weight of their offspring at labor. They noticed that the average weight of newly born infants elevated by 50 g and 200 g when the levels of maternal blood glucose was 99–130 mg% and above 130 mg%, respectively. Conversely, higher blood glucose concentrations were concomitant with a higher frequency of pregnancy difficulties. In contrast, hypoglycemic women was connected with decreased birth weight of infants at labor. All these investigations beside our results demonstrate that hyperglycemia in pregnant women resulting in increases in fetal weight.

Also **Langer et al. (2005) (24)** reported that in women with pregravid obesity and well controlled gestational diabetes mellitus on feed only, the probabilities of fetal macrosomia (infant weight greater than 4000 g), was significantly elevated in comparison with normal body mass index women. Similar results were found in lean and obese women with gestational diabetes mellitus, which was poorly organized on nutrition or insulin. In contrast, well organized gestational diabetes mellitus women, whether lean or obese managed with diet plus insulin had significant increased risk of macrosomia with increasing pregravid body mass index.

In contrast to our results **Catalano et al. (1994) (25)** found that children delivered from diabetic women showed an increase in body fat in contrast with weight-matched children of non-diabetic mothers. Moreover, **Pettitt et al. (26)** indicated that children born to Pima Indian women with uncontrolled glucose tolerance were extra obese than

infants of born from normal glucose tolerance even when they established diabetes in advanced life.

The present work demonstrated that there was a highly significant (p -value = 0.005) increase in Resistin level from 26–28 weeks gestation to 36–38 weeks gestation in group A (study group), this is in agreement with **Sagawa et al. (2002) (27)** who indicated to higher resistin gene expression in term placenta than in chorionic villi of early pregnancy and resistin concentration have been showed to be elevated at gestation than in non-pregnant women. However; its level was increased in our control group but not significantly.

Summary and conclusions

The goal from this research was to estimate the alterations in maternal serum resistin among gestation in healthy control women and in women with gestational diabetes mellitus, and to explore the probable role of resistin as a mediator of insulin resistance.

This work was a prospective case-controlled study that was conducted in Al-Zahraa University Hospital in the period from October 2011 to Jun 2013 in order to inspect the alterations in serum resistin levels during gestation in maternal blood of control and with gestational diabetes mellitus, and to explore the probable role of resistin as a mediator of insulin resistance.

Our work comprised 45 pregnant women between 26–28 weeks gestational age who underwent a 3-h oral glucose tolerance test (GTT) These 45 women were divided into two groups: **Group (A)** study group: Comprises 25 women with gestational diabetes mellitus and **Group (B)** control group: Comprises 20 healthy pregnant women with normal GTT.

Pregnant women with gestational diabetes mellitus defined as women with at least two out of four values of oral glucose tolerance curve must be equalled or exceeded to diagnose gestational diabetes.

All women included in the study were subjected to: detailed history was taken from each woman including present, past, obstetric history with special focus on history of gestational diabetes or glucose intolerance with previous pregnancy, medical history and family history especially for diabetes. Complete general examination including blood pressure, pulse, temperature, chest, heart with special focus on height and body weight for determination of Body Mass Index (BMI) and abdominal examination, Abdominal ultrasound: for detection of fetal viability, gestational age, number and detecting any abnormality and measurement of fetal weight, 3-h oral glucose tolerance test (GTT) and Blood sampling as the resultant serum was collected, divided serum Glucose

was measured at time then the rest of sample stored at -20°C for subsequent analysis of Resistin and Insulin.

Results of the current work demonstrated that there was no significant variation between the two groups with respect to age, height and gravidity. The finding of the present work indicated that there was highly significant variation between the two groups as regard body mass index at 26-28 weeks GA (p-value = <0.001) and at 36-38 weeks GA (p-value = <0.001) with highly statistically significant increase in BMI from 26-28 weeks gestation to 36-38 weeks gestation in both groups (p-value <0.001).

Results of the current study showed that there was no statistically significant difference between the two groups as regard estimated fetal weight (EFW) at 26-28 weeks gestation (p-value = 0.199) and at 36-38 weeks gestation (p-value = 0.118).

Results of the current study showed that there was highly statistically significant increase in Resistin level (p-value = 0.005) from 26-28 weeks gestation to 36-38 weeks gestation in group A (study group). The current study showed that there was no statistically significant correlation between the Resistin (ng/ml) and body mass index (BMI) in both groups (p-value = 0.264, 0.550) for group A (study group) and B (control group) sequentially at 26-28wks gestation and (p-value = 0.428, 0.455) for group A (study group) and B (control group) at 36-38wks gestation.

The current study showed that there was no statistically significant correlation between the Resistin (ng/ml) and estimated fetal weight (EFW) in both groups (p-value = 0.940, 0.876) for group A (study group) and B (control group) sequentially at 26-28wks gestation and (p-value = 0.153, 0.300) for group A (study group) and B (control group) at 36-38 wks gestation.

The conclusion of the current study was that there is elevated serum resistin levels during pregnancy in GDM.

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