Role of Visfatin and Chemerin in Occurrence and Development of Gestational Diabetes in Pregnant Women

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Abstract

A case-control study was carried out in Kirkuk city from March to July 2019. The number of pregnant women (with gestational diabetes) understudy were 50 whose ages were between 17-42 years old to estimate the level of visfatin and chemerin in pregnant women with gestational diabetes. These patients attended to Kirkuk General Hospital to gynecology unit for pregnancy follow up. The control group who were matched to the pregnant women studied, included 30 healthy non-pregnant women. Blood was collected from each patient and control enrolled in this study for assessment of HbA_{1c}, blood glucose level, visfatin and chemerin levels. The study showed no significant difference between studied cases and the control group regarding patient age and gestational age at sampling and parity (P>0.05) while there was a significant difference between studied cases and the control group regarding systolic and diastolic blood pressure. The study showed that the highest mean level of visfatin was found in pregnant women with gestational diabetes comparing with healthy control (14.6±3.11 *v.s.* 7.81±3.01ng/ml) (P: <0.01). The study showed that the highest mean level of chemerin was found in pregnant women with gestational diabetes comparing with healthy control (78.92±18.44 v.s. 78.92±18.44 ng/ml) (P: ≤0.05). The study showed that the highest mean level of visfatin was found in pregnant women who have elevated level of glucose and HbA1c (5.75±3.81 and 5.91±3.67 ng/ml) respectively, as compared with patients with normal level of glucose and HbA1c (4.61±2.99 and 3.95±2.12 ng/ml) respectively (P: ≤0.01). The study showed that the highest mean level of visfatin was found in pregnant women who have elevated level of glucose and HbA1c (148.9±25.7 and 158.6±23.5 ng/ml) respectively, as compared with patients with normal level of glucose and HbA1c (111.5±14.6 and 105.1±15.7 ng/ml) respectively (P: ≤0.05). The study concluded that, there was a highly significant relation of visfatin and chemerin with gestational diabetes mellitus in pregnant women

Keyword: *Gestational diabetes; Visfatin; Chemerin; HbA1c*

Introduction

Important alterations in maternal metabolism and increased insulin resistance coincide with the progressive accumulation of adiposity during the course of normal pregnancy. Insulin resistance shows an increase in the late second trimester to levels that are observed in type 2 diabetes mellitus (T2DM) [(1)]. Most pregnant women remain normoglycemic due to adequate beta-cell compensation for this higher insulin secretion. When the beta-cell compensation for insulin resistance and hepatic glucose production is inadequate, gestational diabetes mellitus (GDM) ultimately develops [(2)]. Moreover, 10% to 50% of GDM cases are reported to develop T2DM in the postpartum period [(3)]. It is a major cause of morbidity and premature mortality from long-term complications such as cardiovascular disease, blindness, renal failure, amputations and stroke. The types of diabetes have been classified by the WHO[(2)]. Type 1 diabetes (previously referred to as insulin-dependent diabetes mellitus or IDDM) is due to absolute insulin deficiency and is usually an autoimmune disease leading to the destruction of the insulin-secreting beta cells in the pancreas. In some cases the cause of destruction of the beta cells is not known[(3)]. Type 2 (previously known as non-insulin dependent diabetes mellitus or NIDDM) results from relative insulin deficiency that may be associated with varying degrees of insulin action defects known collectively as insulin resistance[(4,5)]. In the Arab world, it had been estimated that 11-20% of population had D.M especially in oil producing

gulf countries[6]. It has mentioned that 10 % of Iraqi population had D.M. The first stage in type II diabetes is the condition called insulin resistance; although insulin can attach normally to receptors on liver and muscle cells, certain mechanisms prevent insulin from moving glucose into these cells where it can be used[7,8]. Most type II diabetics produce variable, even normal or high, amounts of insulin, and in the beginning this amount is usually sufficient to overcome such resistance[1]. Chemerin and visfatin are bioactive molecules that regulate numerous physiological functions such as energy equilibrium, insulin action, inflammatory response and vascular homeostasis[9]. In addition to its immunomodulatory effects, chemerin was reported to be associated with components of the metabolic syndrome and the parameters of type II diabetes including body massindex (BMI), plasma triglyceride (TG) levels, and blood pressure. Chemerin was shown to modulate the expression of adipocyte genes involved in glucose and lipid homeostasis[10]. So the aim of the study was to estimate the level of visfatin and chemerin in pregnant women with gestational diabetes .

Material and Method

A case-control study was carried out in Kirkuk city from March to July 2019. The number of pregnant women (with gestational diabetes) understudy were 50 whose ages were between 17-42 years old. These patients attended to Kirkuk General Hospital to gynecology unit for pregnancy follow up. The control group who were matched to the pregnant women studied, included 30 healthy non-pregnant women.

Five ml of blood was collected by vein puncture using Vacutainer tubes from each patient enrolled in this study. Blood samples were placed into two sterile test tubes, in one of them 2.5 ml of blood was put in test tube containing anticoagulant EDTA and used for assessment of HbA_{1c} test using (immunefluorescent, ichroma, Korea). The second part of sample was 2.5 ml was placed in plane tubes and centrifuged, the obtained sera were then aspirated and transferred into clean test tubes for estimation of blood glucose level (Biomerieux, France), visfatin and chemerin levels (Koma biotech, ELISA, USA).

Statistical Analysis

Computerized statistically analysis was performed using Mintab ver 18.0 statistic program. Comparison was carried out using Chi-square (X^2) for determination of the *P.* value.

Findings

As shown in Table 1. There was no significant difference between studied cases and the control group regarding patient age and gestational age at sampling and parity (P>0.05) while there was a significant difference between studied cases and the control group regarding systolic and diastolic blood pressure (P <0.05).

Table 1: Clinical characteristics of studied women

Parameters (Mean±SD)	Pregnant women	Control group
No.	50	30
Maternal age (yeas)	32.5±4.2	32.2±6.2
Gestational age	33.4±7.5	35.4±6.6
Parity, median (Range)	2 (1–7)	2 (1–6)
Mean 24 h SBP, mm Hg	128.7±11.5 *	110.8±7.4
Mean 24 h DBP, mm Hg	83.5±6.9*	69.4±8.3
Maximal SBP, mm Hg	167±24.1*	119.0±10.2
Maximal DBP, mm Hg	109.1±22.7*	74.7±13.3

The study showed that the highest mean level of visfatin was found in pregnant women with gestational diabetes comparing with healthy control (14.6±3.11 *v.s.* 7.81±3.01ng/ml) (P: <0.01).

Table 2: Levels of visfatin in pregnant women and the control group

Visfatin level (ng/ml)	Pregnant women	Control group	P. value
Mean±SD	14.6±3.11	7.81±3.01	0.001

The study showed that the highest mean level of chemerin was found in pregnant women with gestational diabetes comparing with healthy control (78.92±18.44 v.s. 78.92±18.44 ng/ml) (P: ≤0.05), Table 3.

Table 3: Levels of chemerin in pregnant women and the control group

Chemerin level (ng/ml)	Pregnant women	Control group	P. value
Mean±SD	78.92±18.44	49.67±12.87	0.001

The study showed that the highest mean level of visfatin was found in pregnant women who have elevated level of glucose and HbA1c (5.75±3.81 and 5.91±3.67 ng/ml) respectively, as compared with patients with normal level of glucose and HbA1c (4.61±2.99 and 3.95±2.12 ng/ml) respectively (P: ≤0.01), Table 4 and 5.

Table 4: Relation of visfatin with glucose level in pregnant women.

visfatin level (ng/ml)	Blood glucose level		P. value
	Normal	Elevated	
No.	10	40	≤ 0.01
Mean	4.61	5.75	
SD	2.99	3.81	

Table 5: Relation of chemerin with HbA1c level in pregnant women.

visfatin level (ng/ml)	HbA1c level		P. value
	Normal	Elevated	
No.	15	25	≤ 0.01
Mean	3.95	5.91	
SD	2.12	3.67	

The study showed that the highest mean level of visfatin was found in pregnant women who have elevated level of glucose and HbA1c (148.9±25.7 and 158.6±23.5 ng/ml) respectively, as compared with patients with normal level of glucose and HbA1c (111.5±14.6 and 105.1±15.7 ng/ml) respectively (P: ≤0.05), Table 6 and 7.

Table 6: Relation of chemerin with glucose level in pregnant women.

chemerin level (ng/ml)	Blood glucose level		P. value
	Normal	Elevated	
No.	40	140	≤ 0.05
Mean	111.5	148.9	
SD	14.6	25.7	

Table 7: Relation of chemerin with HbA1c level in pregnant women.

chemerin level (ng/ml)	HbA1c level		P. value
	Normal	Elevated	
No.	55	125	≤ 0.05
Mean	105.1	158.6	
SD	15.7	23.5	

Discussion

Various adipokines contribute to diabetogenic resistance to insulin, especially during the last half of pregnancy. This study mainly focused on potential alterations of specific adipokine concentrations (chemerin, RBP-4, and visfatin) in pregnant women with GDM. Here, we demonstrate that there were no significant differences in these adipokines between pregnant women with GDM and healthy pregnant women in the second trimester. However, the women with GDM were more likely to be overweight compared to matched healthy controls. Chemerin has been proposed to be an insulin-sensitizing adipokine; its secretion has been demonstrated to increase, presumably as a compensatory mechanism, in insulin-resistant subjects

Berndt *et al* [11] found that there was a significant relation of visfatin and type 2 diabetic regardless of their obesity. Consistent with our findings, Haider *et al* [12] showed that the release of visfatin by adipocytes in response to hyperglycaemia is dependent on the duration and extent of glucose elevation and is inhibited by insulin administration. It has been demonstrated that insulin does not influence visfatin synthesis in adipocytes and there is no difference in serum visfatin between type 2 diabetic subjects treated with insulin infusion or oral hypoglycaemic agents [12,13]. Additionally, the influence of insulin sensitizing agents on serum visfatin level has not been confirmed yet [10]. These findings suggest that fasting glucose levels, but not insulin resistance, may play a key role in the elevation of visfatin levels in newlydiagnosed type 2 pregnant women. Additionally, we showed that along with fasting glucose, triglycerides is also directly and independently associated with visfatin, which is consistent with previous findings [13]. Esteghamati *et al* [14] found that Serum visfatin is highly associated with type 2 diabetes mellitus independent of insulin resistance and obesity. Result of Haddad *et al* [15] revealed that the T2DM group has the highest serum levels of chemerin compared to the control

groups. Current evidence regarding the association of visfatin concentration with GDM is contradictory. Some studies demonstrated increased serum levels of visfatin in women with GDM [16,17], while others reported that visfatin concentrations were significantly lower in women with GDM [18,19]. In a meta-analysis, Berezin *et al* [20] suggested that the use of visfatin may predict increasing of HbA1c level in DM patients. In this study, we found increased visfatin levels in T2DM patients, as reported in previous studies [21]. Despite the high number of studies evaluating the role of adipokines in GDM in the existing literature, interpretation of the results is somewhat laborious for several reasons. First, the diagnostic criteria for GDM vary greatly. Second, the gestational age at the study times ranges from early first trimester to late third trimester. Third, diverse assay methods may also cause heterogenous results. Obesity is accompanied by altered secretion of adipokines from adipose tissue [22,23]. Adipokine levels are usually higher in obese women. Although we demonstrated that pregnant women with GDM had higher BMI values than healthy pregnant women, there were no differences in the levels of the studied adipokines between the two groups. This may be due to the regulation of various adipokines by pregnancy or to insufficient matching of control and GDM patients for BMI.. Thirdly, visfatin-mediated NAD biosynthesis that regulates glucose-stimulated insulin secretion may explain increased levels of visfatin in T2DM patients as a compensatory mechanism for β-cell functioning. Finally, because of the pro-inflammatory properties, these elevated levels could be attributed to the chronic low-grade inflammation present in T2DM. Several researches examined the association between serum chemerin concentrations in patients with T2DM [23-25]. However, it is controversial whether chemerin is related to T2DM in humans. It has been shown that chemerin in 3T3-L1 adipocytes improves insulin stimulated glucose uptake through the insulin signaling. This suggested that chemerin may regulate insulin sensitivity of adipose tissue [26], In that case with increase in chemerin concentration, the concentration of insulin should decline, but the experiment showed, FSI were positively correlated with serum chemerin.

Conclusions

There was a highly significant relation of visfatin and chemerin with gestational diabetes mellitus in pregnant women

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Kirkuk health directorate and all experiments were carried out in accordance with approved guidelines.

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