Cord Leptin Level in Normal and Diabetic Pregnant Women

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ABSTRACT

Background: Diabetes in pregnancy is associated with many side effects that not only affect the mother but also the baby. Leptin acts as a cytokine that modulates critical processes. Cord blood provides a window view of two communicating circulations during pregnancy.

Objectives: To show the difference in cord leptin levels between normal, gestational diabetes, and insulin-dependent diabetes pregnancies and its correlation to other characteristics.

Methods: A prospective comparative cross-sectional study was conducted on 150 pregnant women (controls, gestational diabetes, and insulin-dependent diabetes groups) in Al-Emamain Al-Kadhemain medical city for a period of 8 months. Verbal consent was obtained from each participant. Samples were collected from the umbilical cord blood at birth. The Abcam's Leptin Human ELISA kit was used to quantify leptin levels. Comparisons of means were done using independent t-test, and correlation test.

Results: The mean maternal age of the control, gestational diabetes, and insulin-dependent diabetes groups were (27.26±5.95), (24.18±5.49), and (29.12±5.84) years respectively. The current study showed a significant difference in gestational age, and cord leptin levels among the three studied groups. Leptin levels were higher among gestational diabetes and insulin-dependent diabetes groups. Cord leptin levels had a significant positive correlation with gestational age and birth weight in the three study groups.

Conclusions: Measurement of cord leptin in diabetic mothers is advised as it has an important role in the growth of the fetus and has further effects during infancyand childhood.

Keywords: Leptin level, Cord blood sample, Gestational diabetes mellitus, Diabetes mellitus.

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Leptin; also known as the "satiety hormone", is a peptide hormone secreted chiefly from fat tissues and had received great attention [(1)]. It not only reduces food intake and increases energy expenditure through binding to its hypothalamic receptors and mending appetite-regulating neurons but also as its excess had been noted and tolerance identified in obesity, where both excess fats with increased blood levels of leptin impair the leptin passage across the blood-brain barrier and induce a leptin resistance [(2)]. Another theory suggests that the resistance is due to increased hypothalamic inflammation and endoplasmic reticulum stress related to lipid toxicity caused by chronic over nutrition[(3)].

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In addition to that, leptin controls the production of gonadotrophins, blastocyst formation, implantation, normal placentation, as well as fetoplacental communication[(1,2)].

It is well recognized that pregnancy tempts a state of leptin and insulin insensitivity in the brain, particularly the hypothalamus[(4)]. Hence, despite the high level of leptin and insulin in maternal circulation, food intake and glucose homeostasis is maintained to meet the needs of the growing embryo. The placenta represents the second leptin-producing tissue in humans and cord blood provides a window view of maternal and fetal communicating circulations during pregnancy. Leptin as a cytokine modulates critical processes such as proliferation,

protein synthesis, invasion, and apoptosis in placental cells [1].

Gestational diabetes mellitus (GDM) is defined as impaired carbohydrate tolerance resulting in hyperglycemia which first develops or becomes diagnosed during pregnancy [5]. The prevalence of GDM in the Middle East and North Africa region was 13% and in Iraq alone is 11.5% [6]. It is projected that 87.5% of diabetes is diagnosed as GDM, 7.5% have type 1 diabetes and the residual 5% have type 2 diabetes[7]. Studies suggest that the prevalence of DM among women of childbearing age is increasing which is believed to be attributable to more sedentary life, changes in diet, and the epidemic of childhood and adolescent obesity[8]. It has been reported that leptin is higher in the cord blood of DM and GDM babies[9].

Diabetes in pregnancy is associated with many side effects that not only affect the mother but also the baby like preterm labor and birth, urinary tract infections, pre-eclampsia, macrosomia, increased induction of labor, cesarean section rates, and increased neonatal intensive care stay. Placental vascular mal-perfusion, re-setting of expression of genes within the placental energy sensing and leading to insulin resistance[10-12]. GDM by itself increases the risk of long-term complications, including obesity, breast cancer, impaired glucose metabolism, and cardiovascular disease[13,14]. Insulin-dependent diabetes (IDDM) had been linked to leptinemia on previous occasions[15], yet the level of leptin was not demonstrated among pregnant.

The current study aims to explain the difference in cord leptin levels between healthy, GDM, and IDDM pregnancies and its correlation to other variables.

Methods

This study is a cross-sectional study conducted on 150 pregnant women in Al-Emamain Al-Kadhemain medical city, for a period of 8 months, from the first of January 2018 till the end of August 2018.

Women were included in this study and divided into three groups:

- Group A: a control group which included fifty women with uncomplicated healthy singleton pregnancies, gestational age range 33-41 weeks, with no previous predictor for DM and uneventful antenatal progress, with normal blood sugar and negative dipstick test

- Group B: gestational diabetes group includes fifty pregnant women complicated by gestational diabetes, gestational age rang 33-41 weeks; women in this group were using injectable insulin therapy.

- Group C: Insulin-dependent group includes of fifty pregnant women, gestational age range 33-41 weeks, women in this group were on injectable insulin therapy.

The women were selected while attending the labor ward at the department of Obstetrics and Gynecology. Group B and group C had blood sugar readings and HbA1c within good control range for the last two weeks before delivery.

Inclusion criteria

1. Pregnancy with singleton viable fetus.
2. Maternal age 16-38 years.
3. Parity 0-6.
4. Maternal body mass index 19-35 kg/m^2.
5. IDDM group and gestational diabetes group women are on injectable insulin therapy.

Exclusion criteria

1. Medical diseases that are associated with disordered glucose metabolisms, such as Cushing's disease and pancreatitis.
2. Patients of acute illness at the time of the study.
3. Fetal abnormality.

Women were approached and the study aim and procedure were explained, verbal consent was obtained from each participant. The demographic characteristics include maternal age, parity, gestational age, and BMI. Gestation was calculated from the first day of the last

menstrual cycle and/or the early ultrasound scan.

Full history was taken and a complete examination (general and obstetrics examination) was done for all participants.

Measurement of the blood sugar, sampling cord blood at delivery for leptin measurement, and the weight of the newborn (birth weight) were done for all groups. Blood samples were collected from the umbilical cord at birth (5 milliliters) using disposable plastic syringes. The blood was stored in plastic tubes and centrifuged at 5000 rpm for ten minutes at 4 ºC to obtain the serum, serum then was stored at 20 ºC. The Abcam's Leptin Human ELISA kit is designed for the quantitative measurement of leptin concentration in serum, samples applied at sandwich ELISA HRP labeled; the results were matched with the demographic characteristics of each participant

Analysis was done using Statistical Packagefor the Social Sciences version 22, Data were presented as mean ± standard deviation. Comparisons of means were done using an independent t-test, with a Pearson correlation test to detect the relationship between cord leptin and variables. The correlation coefficient value (r) either positive (direct correlation) or negative (inverse correlation) with value, < 0.3 represent no correlation, 0.3 - < 0.5 represent week correlation, 0.5 -< 0.7 moderate correlation, ≥ 0.7 strong correlation. In all statistical analyses, a P value of 5% or less is considered statistically significant.

Results

The mean maternal age of the control group was 27.26 ±5.95 years and the range was 16-33 years, while the mean maternal age of the GDM group was 24.18 ±5.49 years and the range was 19-30 years. The mean maternal age of the IDDM group was 29.12 ±5.84 years and the range was 23-38 years. A significant difference in maternal age between the control group, and the GDM group (p-value 0.008), while no significant difference in the maternal age between the control group and the IDDM group (p-value >0.05). The current study showed a significant difference in gestational age, and cord leptin levels between the three studied groups. Cord leptin levels were higher among GDM and IDDM groups, (Table 1).

The results show that the cord leptin level has a significant positive correlation with the gestational age in the three study groups, the control group (r 0.513), p value <0.001, in the GDM group and the IDDM group (r 0.559), p-value <0.001, r 0.530, p-value < 0.001, respectively, (Table 2).

The cord leptin level also has a significant positive correlation with the birth weight in the three groups, in the control group r 0.862, p-value <0.001; in the GDM group r 0.865, p-value < 0.001; in the IDDM group r 0.837, p-value < 0.001, (Figures 1, 2 and 3).

The cord leptin level has no significant correlation with maternal age, parity, BMI, and blood sugar levels in the three study groups.

Table 3 shows a comparison of cord leptin levels in gestational age < 37 weeks and gestational age ≥ 37 weeks, the result shows a statistically significant difference in the cord leptin level in the three study groups.

Table 1: The demographic characteristics of the control and the diabeticgroups included in the study.

Parameters	Control	GDM	IDDM
Age (yr.)	**27.26±5.9**	**24.18±5.4***	29.12±5.8
Parity	2.14±2.2	1.82±2.0	2.16±1.9
BMI (kg/m^2)	24.35±3.1	24.63±2.8	24.12±3.2
Gestational age (week)	**37.43±1.8**	**36.74±0.9***	**36.61±0.9***
Birth weight (kg)	3.24±0.5	3.13±0.4	3.39±0.4
Blood sugar (mmol/l)	4.6±0.5	4.53±0.5	4.94±1.1
Cord leptin(ng/ml)	**12.34±4.08**	**15.16±0.4***	**20.57±6.7****

*Compared with control group ($P < 0.05$), ** Compared with healthy group ($P < 0.001$).

Table 2: Correlation of cord leptin level with other parameters within the three study groups.

Parameters	Normal		GDM		IDDM	
	R	P	R	P	R	P
Age (yr.)	-0.137	0.350	0.266	0.064	0.036	0.807
Parity	0.091	0.535	0.066	0.651	-0.015	0.916
BMI (kg/m^2)	-0.174	0.232	0.119	0.416	0.084	0.566
Gestational age (week)	**0.513**	**<0.001**	**0.559**	**<0.001**	**0.530**	**<0.001**
Birth weight (kg)	**0.862**	**<0.001**	**0.865**	**<0.001**	**0.837**	**<0.001**
Bl. sugar (mmol/l)	-0.023	0.875	-0.038	0.798	-0.045	0.758

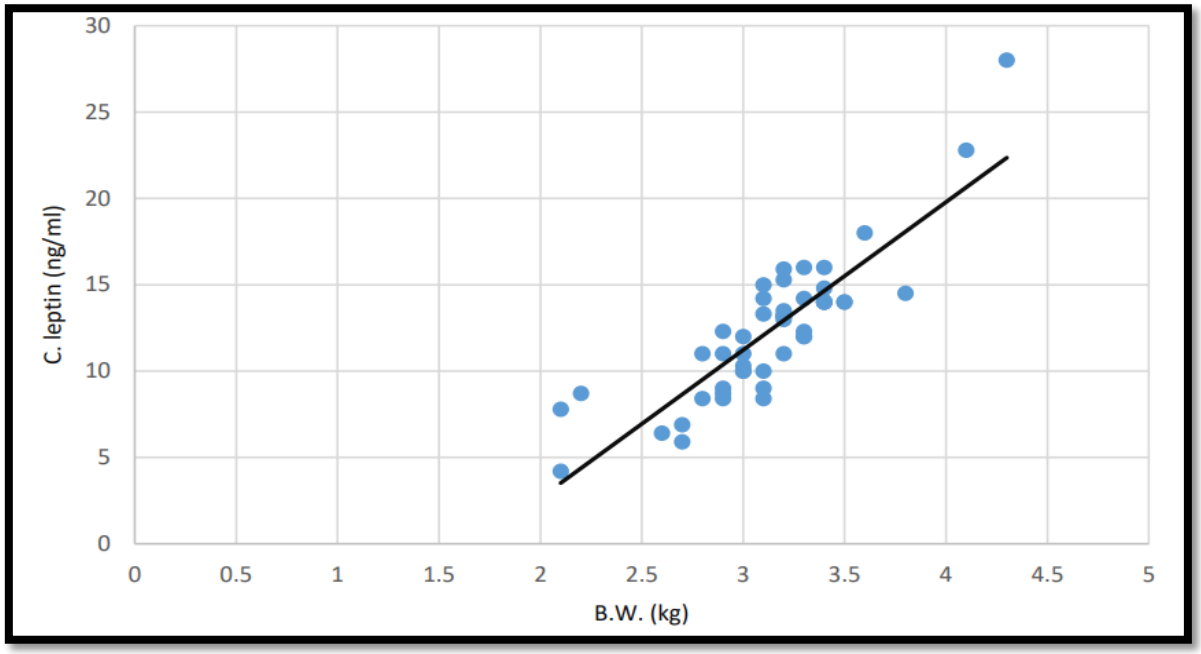

Figure 1: Correlation between cord leptin level and birth weight in control group (r =0.862; p value <0.001).

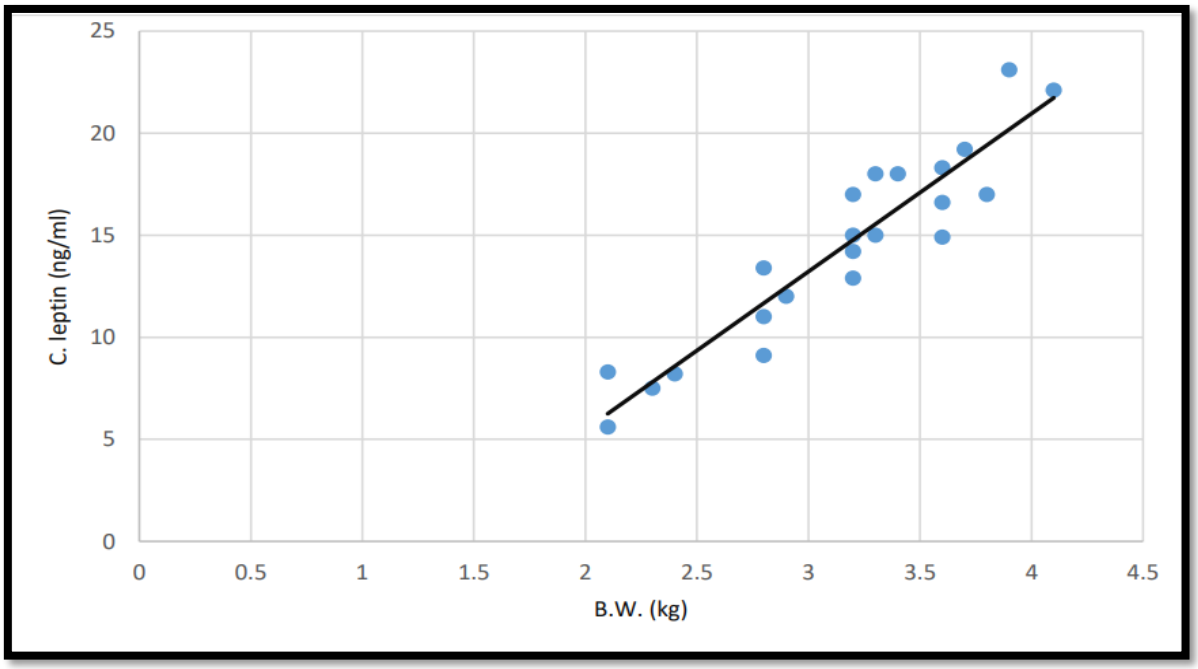

Figure 2: Correlation between cord leptin level and birth weight in the GDM group (r =0.865; p value <0.001).

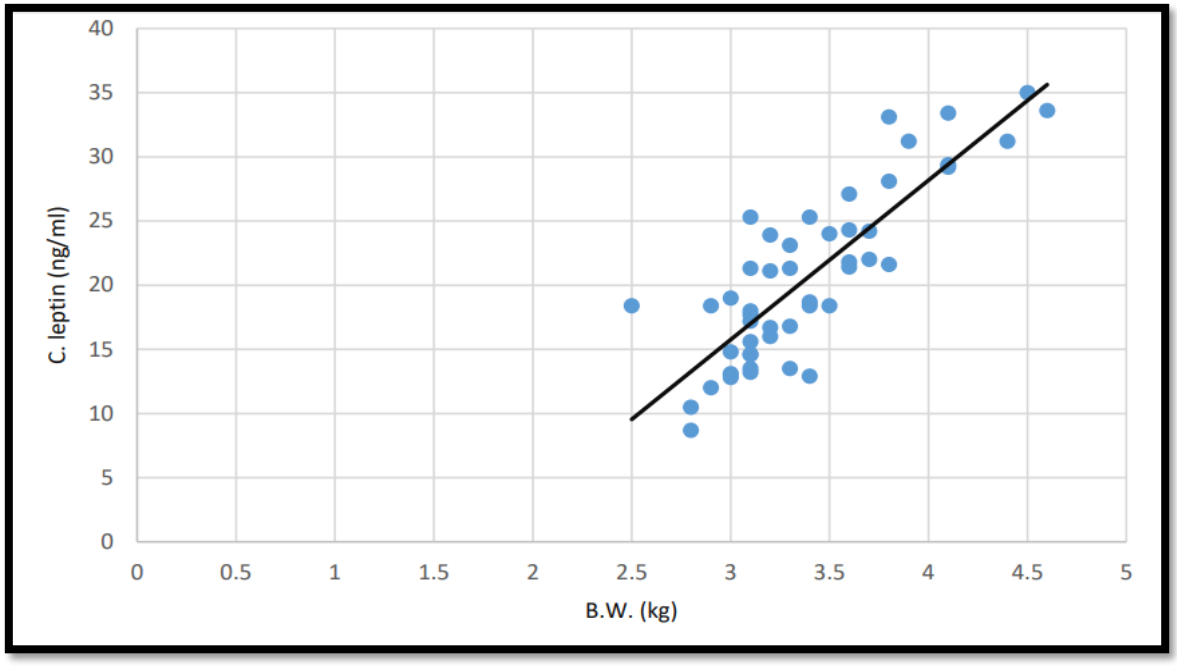

Figure 3: Correlation between cord leptin level and birth weight in insulin-dependent diabetes group (r =0.837; p value <0.001).

Table 3: Comparison of cord leptin levels according to gestational age in the three study groups.

Parameters	Gestational Age		P value
	< 37 wk. Mean ±SD	≥ 37 wk. Mean ±SD	
Control	10.9±3.45	13.53±4.23	**0.021**
GDM	11.38±4.42	16.83±4.83	**0.000**
IDDM	18.4±6.62	23.33±5.91	**0.007**

Discussion

In this study, it was found that leptin level in cord blood is significantly higher in both groups of diabetic pregnant women (GDM, IDDM) than in normal women. The current finding is consistent with results by Peltokorpi A et al [16], Xiao W et al [17], and Manoharan B et al [18].

The present study shows a statistically significant difference in leptin level in cord blood in relation to gestational age and this is consistent with findings reported by Tan K et al[19] and by Stefaniak M et al[20]. This might be due to a relationship between cord leptin levels and fetal weight. As the fetal weight increase with gestational age, leptin mRNA expression is increased by seven folds[21]. The study also showed that cord leptin was significantly lower in gestational age less than 37 weeks and higher in gestational age > 37 weeks which agrees with other published articles[17,22]. In the same context, the current study showed that cord leptin showed a significant correlation with birth weight, agreeing with Han L et al [23] and Stefaniak M et al [20] also in accordance with what had been stated in a study by Tan K et al where cord blood leptin had a positive association with neonatal abdominal adiposity [19] and others[24]. In this study, there was no statistically significant correlation between cord leptinlevel and maternal BMI, the same finding was reported by Stefaniak M et al[20] although maternal weight status usually affects the concentrations of leptin[25]. Yet BMI might not a reliable indicator during pregnancy, a study by Shroff et al showed only a moderate correlation between leptin levels and BMI [26]. This might suggest that the association between BMI and leptin levels is not apparent and other factors may disturb leptin levels.

In conclusion; cord leptin level is significantly higher in pregnancies complicated by GDM and IDDM in comparison to normal pregnancies. There was a statistically significant correlation between cord leptin level with gestational age and birth weight in the three study groups

We recommend assessing cord leptin in diabetic mothers because it has an important role in the growth of the fetus and has further effects during infancy and childhood. Further studies should track the relationship between glycemic control during pregnancy and cord leptin level in diabetic patients.

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Conflicts of interest: none.

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