Neonatal and Placental Birth Weight and Its Correlation with Leptin level in Maternal and Cord Blood

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ABSTRACT

Background: Leptin, the product of the obese gene, is a hormone that is synthesized by the adipocytes and secreted into the circulation. It regulates body weight, energy intake, and has a role in growth of fetus and placenta.
Objective: To investigate the correlation between maternal and cord blood leptin levels with neonatal body mass index and placental weight.
Methods: This is a prospective cohort study, carried out at Al-Yarmouk Teaching Hospital, Department of Obstetrics and Gynecology from March 2015 to January 2016. It included one hundred pregnant women from Baghdad who gave birth to equal number of full term infants. The leptin level was measured in mothers and cords blood serum and correlated its values with maternal BMI, neonatal weight and placental weight.
Results: Mean maternal leptin showed a statistically significant difference in comparison to cord serum leptin (18.01 and 8.89ng/ml, respectively) and was positively correlated to the maternal BMI, but not to the neonatal weight. A positive correlation between the mean cord serum leptin and the weight of the neonates ($r = 0.336$, $P = 0.001$) was found. There was no correlation between the maternal BMI and the neonatal weight. Similarly, no correlation established between the placental weight and the levels of leptin in the maternal or in the cord serum but a positive correlation between placental weight and neonatal weight, and mothers' BMI was observed. Finally, although a noteworthy difference between the mean leptin levels of neonates of two different sexes was observed (male 8.6ng/ml, female 9.16ng/ml), that difference couldn't reached a statistically significant level.
Conclusion: There is no correlation between maternal leptin level and fetal weight. A positive correlation between cord serum leptin and fetus weight was observed.
Keywords: Maternal leptin, Cord blood leptin, Neonatal and placental weight.

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Fetal growth is a complex process that is influenced by multiple factors and has far-reaching health implications. The control of fetal growth depends on multiple hormones, including both IGF-I and placental GH in the mother, and IGF-I rather than pituitary GH in the fetus. Leptin, which is produced by adipocytes and syncitiotrophoblast cells(1).

Leptin was originally identified in 1994 by Friedman. Leptin, the protein product of the *obese (ob*or *Lep)* gene, isa hormone synthesized by adipocytes that signals available energy reserves to the brain, and thereby influences development, growth, metabolism and reproduction(2).

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In pregnancy, important changes occur in the body weight of the mother, caused by sodium and water retention and by an increase in body fat tissue.

Leptin is mainly produced and secreted by fat cells in proportion to fat mass. It seems likely that placenta plays a role in increasing the maternal plasma leptin concentrations during pregnancy(3).

Elevated plasma leptin concentrations occur at the completion of organogenesis, leptin is involved in the development and maturation of a number of organs including the heart, brain, kidneys and pancreas. Elevated maternal plasma leptin is associated with maternal obesity, and reduced fetal plasma leptin is correlated with intrauterine growth restriction. Alterations in plasma leptin during development may be associated with an

increased risk of developing a number of adulthood diseases including cardiovascular, metabolic, and renal diseases via altered fetal development and organogenesis[4].

Leptin serum levels are increased in human obesity and in pregnancy. In pregnant women leptin serum levels increase continuously during pregnancy and reach higher levels than in comparable non pregnant women. Maternal serum leptin increases progressively, peaking in the second trimester, plateauing towards term and returns to pre-gestational levels after delivery[5].

Leptin can be detected in cord serum as early as 19 weeks, increasing with advancing gestation[6]. Postpartum leptin concentrations decrease around six weeks after delivery[7]. Therefore, leptin seems to be also involved in other regulating systems besides its role in regulating weight balance. It might further play an important role in sexual maturation, reproduction, during fetal growth and in early neonatal life[8].

In term infants leptin concentrations in cord blood showed a positive correlation to birth weight (BW) and body mass index(BMI)[9].

Term newborns with intrauterine growth restriction had significantly lower serum leptin levels than those with normal fetal growth[10]. Maternal leptin serum levels were not found to correlate with newborn leptin concentrations in cord blood[10]. Leptin levels may be independent of placental leptin production and may be taken as a marker of fat mass in human fetuses. Placental leptin production makes a substantial contribution to maternal circulating leptin levels during pregnancy[11].

Leptin synthesis occurs in utero. Low cord blood leptin concentration is implicated as a risk factor for small for gestational age (SGA) babies and high leptin concentration is implicated for large gestational age (LGA)[12]. Leptin levels were correlated with sex and body mass index (BMI). Mean leptin levels were more than twice as high in females than in males of corresponding weight status, especially among females of healthy weight who exhibited levels that were 5.7 times higher[13].

The aim of this study is to investigate the correlation between maternal and cord blood leptin levels and its relation to maternal BMI, neonatal and placental weight.

Methods

A prospective study carried out in the Department of Obstetrics and Gynecology at Al-Yarmouk Teaching Hospital in Baghdad, from the first of March 2015 to the end of January 2016. This study was approved by Iraqi Council of Medical Specialization (Iraqi Scientific Committee of Obstetrics and Gynecology). A verbal and written consent was obtained from each patient prior to the inclusion into the study.

This study included 100 pregnant women who were collected from labor - ward of obstetrical department; pregnant women were chosen by random collection.

Inclusion criteria: Pregnant woman with single viable fetus, at gestational age (37-40 weeks), patients presented with spontaneous onset of labor and were delivered by vaginal route. Exclusion criteria: Multiple pregnancies**,** patient with medical disease, smoker, patients with history of hyperemesis gravidarum in first trimester, patients who didn't know about her first trimester or pre pregnancy weight, patients taking any medication. General and obstetrical examination was done for them.

The body mass index was calculated (kg/m^2) depending on the patient weight in first trimester or pre-pregnancy weight. The routine investigations were done for them. In the labor ward 10 ml of blood was drown from the peripheral veins of the patients. Patient was observed till delivery.

After delivery the cord was cut and 5 ml of umbilical venous blood was drawn from the clamped cord using a syringe and needle under aseptic technique. The

neonates were taken, cleaning, and after resuscitation weighing them. After delivery of the placenta by controlled cord traction (CCT), the placenta was taken, cut the cord, wash by tap water and weigh it. Blood which collected from the mother before delivery and from fetal umbilical cord after delivery put in a tube containing EDTA. The blood was allowed to clot in plain tubes at room temperature. The serum was aspirated after centrifugation at 3000 rpm for 10 minutes. Then serum was divided into aliquots in eppendroff tubes and stored in at -20C° until used.

The DRG leptin ELISA kit (DRG instruments Gmbh, Germany) is a solid phase enzyme linked immunosorbent assay (ELISA) was based on the Sandwich principle.

Each patient assigned a serial identification number. The data were analyzed using Statistical Package for Social Sciences (SPSS) version 20. The categorical data presented as frequency and percentage tables. The continuous variables were presented as averages, standard deviations and range. The independent t - test was used to assess the significance of mean differences between the continuous variables. Pearson's correlation test was used to assess the correlation between the leptin level for both maternal serum and umbilical cord with other parameters, the correlation was considered weak when the coefficient of correlation (r) (0 - 0.3), moderate if (r= 0.3 – 0.7) and strong when (r>0.7). P-value less than 0.05 was used as the alpha level of significance.

Results

The present study included 100 pregnant ladies and 100 neonates. The obstetrical variables of the mothers including her maternal ages, gravity, parity, maternal body mass index and gestational age were describe in table 1.

The fetal variable of the study recorded 49 males and 51 females and calculate weights of newborn rates which about 25% below 2500g, 41% 2500-3500g, 26% 3500-4500 and 8% more than 4500g.

And we have also calculate the weight of placenta we got 20% below 550g and 38% more than 650g, (Table 2).

The statistical analysis of the result shown that the maternal leptin (18.01±7.54) ng/ml which was significantly higher than fetal cord blood leptin (8.89±3.7) ng/ml, $p<0.001$. When correlating neonatal gender with the maternal and cord blood leptin, no significant differences were present and the p value was 0.109 and 0.457, respectively, (Table 3).

No significant correlation between maternal leptin with their age, umbilical cord leptin, birth weight and placental weight (Table 4). While a significant positive correlation was found between the circulating leptin and the maternal body mass index (P value 0.001), (Figure 1).

No significant association was found between the umbilical cord leptin and maternal leptin, maternal age, maternal BMI and placental weight. The current study shown a positive correlation between the leptin values in the cord serum and birth weight of the neonate using Pearson's correlation test ($r=0.336$, $p=0.001$), (Table 5).

Table 1: Demographic characteristics of the mother, n=100.

Variables	Number	%
Maternal age (years)		
< 25	19	19%
25 - 35	46	46%
≥35	35	35%
Mean ±SD (Range)	31.4±7.1 (18-44) years	
Maternal body mass index (kg/m^2)		
<20	2	2%
20-25	27	27%
25-30	53	53%
≥30	18	18%
Mean ±SD (Range)	26.9±4 (18.6-38) (kg/m2)	
Gravida		
Primigravida	14	14%
Multigravida	96	96%
Mean ±SD (Range)	4.2±2.1 (1-7)	
Parity		
Nulliparous	14	14%
Primipara	17	17%
Multipara	69	69%
Mean ±SD (Range)	3±2.1 (0-6)	
Gestational age (weeks)		
37	23	23%
38	29	29%
39	27	27%
40	23	23%
Mean ±SD (Range)	38.6±0.4 (37 – 40) weeks	

Table 2: Number, percentage and average of main fetal characteristics, n=100.

Variables	Number	%
Gender of the baby		
Male	49	49%
Female	51	51%
Birth-weight (g)		
<2500	25	25%
2500-3500	41	41%
3500-4500	26	26%
>4500	8	8%
Mean ±SD (Range)	3460±616.6 (2607-5000) (g)	
Placental weight (g)		
<550	20	20%
550-650	42	42%
≥650	38	38%
Mean ±SD (Range)	625.5±72.4 (511-749) g	

Table 3: Mean differences in leptin levels, n=100.

Variables	Number	Leptin (ng/ml) Mean ±SD	p value
Maternal	100	18.01±7.54	<0.001*
Cord	100	8.89±3.7	
Neonatal gender		Cord Leptin (ng/ml) Mean ±SD	
Male	49	8.6±3.58	0.457
Female	51	9.16±3.82	
Neonatal gender		Maternal Leptin (ng/ml) Mean ±SD	
Male	49	16.8±6.9	0.109
Female	51	19.2±8	

Independent t-test, * significant at 0.05 level

Table 4: Correlation of maternal Leptin with their age, BMI, UC leptin, birth-weight and placental weight, n=100.

Parameters	Maternal leptin (ng/ml)	
	Correlation coefficient (r)	p-value
Umbilical cord leptin (ng/ml)	-0.138	0.172
Maternal age (years)	0.102	0.313
Maternal body mass index (kg/m2)	0.410	<0.001*
Birth-weight (g)	-0.008	0.941
Placental weight (g)	-0.091	0.369

* Correlation is significant at the 0.05 level (2-tailed).

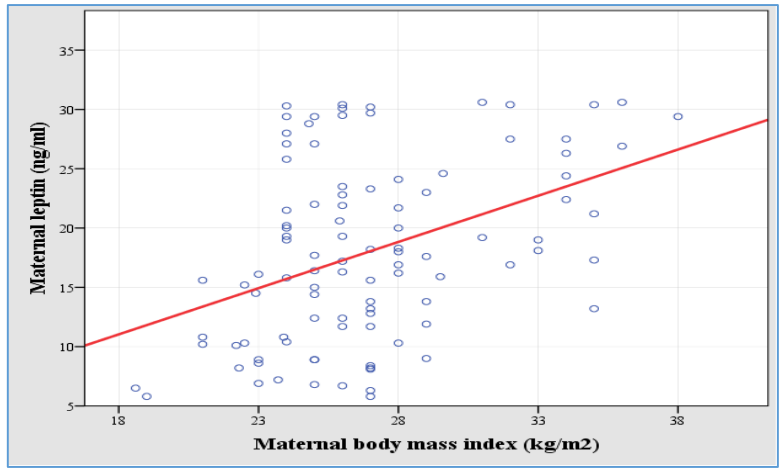

Figure 1: Correlation of maternal leptin with their BMI, n=100.

Table 5: Correlation of umbilical cord leptin with maternal age, BMI, leptin, birth-weight and placental weight, n=100

Parameters	Umbilical cord leptin (ng/ml)	
	Correlation coefficient (r)	P-value
Maternal leptin (ng/ml)	-0.138	0.172
Maternal age (years)	-0.03	0.766
Maternal body mass index (kg/m^2)	-0.094	0.35
Birth-weight (g)	0.336	0.001*
Placental weight (g)	-0.094	0.354

* Correlation is significant at the 0.05 level (2-tailed).

Discussion

It has been reported that the circulating amount of leptin in the maternal and cord serum might be used as an indicator of fetal growth[14]. Therefore, in this study we measured the concentration of leptin in the serum of pregnant women at the time of delivery and to investigate the correlation between the level of leptin in the serum of these women with the maternal BMI, birthweight, and the placental weight. In addition, we measured the concentration of leptin in the cord serum of the neonates right after birth and correlated these values with the fetal and placental weight.

In this study the maternal leptin was higher than cord leptin level which reached statistical significant differences as ($p < 0.001$). Such a conclusion was in part expected since a leptin hormone with a molecular weight of 16,000 Daltons cannot cross the placental barrier[15]. This result was in agreement with Rafeey M et al in 2007[16] who take 100 mother/neonate pairs, and all samples had detectable leptin levels. In the neonates, mean leptin cord blood level was 11.50 ± 8.33 0 ng/ml and in mothers was 25.45±17.59 this study founded a significant increased in maternal leptin in comparison to cord leptin concentration. Also, this result agreed by Ishrat S et al 2008[17], a study included 39 pairs of mothers and newborns and have the same conclusion.

The current study compered the leptin levels in the neonate of both sex. The result found that the female leptin level was higher than the male leptin level but the difference couldn't reach a statistical significance. This result agreed with Papadopoulou F et al in 2000[18], their study involved 85 infants and found that cord serum leptin values in the male neonates (n = 36) were 5.9± 4.4ng/ml, whereas in the female (n = 49) were 7.8±5.3ng/ml and also reported that the differences was not statistically significant. While Tome M et al 1997[19] and Jaquet D et al 1998[20] found a significant difference in cord serum leptin concentrations between neonates of the two genders.

This difference is well established in adults and is attributed to various factors. Some of these factors are the differences in fat distribution that exist between the two sexes, the stimulating effects of estrogens on the production of leptin, and the different sensitivity of the female and male adipose tissue towards different hormones[21].

As one of the main point of the present study was to search for possible biochemical markers of the newborns growth, so we evaluated the relationship between maternal serum leptin with placental and birth weight. Unfortunately, the results showed no correlations were established between these parameters. This result is in agreement with Ishrat S et al in 2008[17] who found no significant correlation maternal serum leptin and placental weight. While Tamura T et al in 1998[22] and Babay Z et al 2004[23] found that maternal leptin did not have any significant relation to birth weight and that did support our results.

Regarding the maternal BMI: in the current study there was a positive correlation between maternal serum leptin

and their BMI (r= 0.410, p < 0.001) at the time of delivery. This result agreed by Yang M 2005[24] who had demonstrate that maternal serum leptin related to BMI but this result disagree with Masuzaki H et al in 1997[25] and Sivan et al in 1998[26] who found no correlation between maternal serum leptin and maternal BMI. These different results might be attributed to the difference in the sample sizes or methodology.

Another finding in the present study was a positive correlation between cord serum leptin (8.89±3.7) ng/ml and birth weight (p=0.001) and this result agrees with Karakosta P et al in 2013[27], their study involved 638 mother-child births and found a higher cord leptin level associated with increased birth size. The leptin like hormone receptors found to be present in several fetal tissue (lung, liver and kidney) and assist in the regulation of brain and bone developments[28].

Leptin is derived from the placenta so it has important role in the control of placenta growth, function and consequently the growth of the fetus[29].

On other hand, there is no significant correlation between umbilical cord leptin with maternal BMI and placental weight (g) and this result agreed with Jahan S et al in 2007[30]. Also, the result found a positive correlation between placental weight and birth weight this result in agreement with Sanin LH et al in 2001[31], they studied 300 newborns right after delivery and found that for each gram increase in placental weight, birth weight is increased by 1.98 gram.

And Sawant D and Venkat S 2013[32] their study involved 53 healthy pregnant women with their 53 newborns and reported that fetal growth depended on placental growth.

In conclusion: Maternal leptin was positively correlated with maternal body mass index but not with the neonatal birth weight. There was negative correlation between maternal leptin and cord leptin and negative correlation between maternal leptin and placental weight, but there was positive correlation between cord blood leptin and neonatal birth weight and positive correlation between placental weight and neonatal birth weight.

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