The Effect of Leptin Level in Pregnancy Complicated by Intrauterine Growth Restriction on Neonatal Outcome, in an Iraqi Center

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Abstract

Background: Fifteen percent of small for gestational age are small as a result of fetal growth restriction, which could be due to maternal, placental or fetal factors. It is an important clinical problem associated with increase perinatal mortality and morbidity. Leptin is a protein that produced by many tissues including the placenta (syncytiotropholoast). Dysregulation of leptin metabolism may be implicated in preeclampsia and IUGR pathogenesis.

Aim of the study: To study the trend of leptin level alteration in maternal serum and cord blood in pregnancies complicated by fetal growth restriction and its relation with fetal outcome.

Methods: An Analytic, cross- sectional study conducted in Al-Elwyia Maternity Teaching Hospital and Alkindy College of Medicine, from October 2009 to June 2010. Sixty seven pregnant women were included and they were divided into two groups: The first group (A) included 34 pregnant women with Intrauterine growth restricted fetuses with and without maternal diseases and the second group (B), included 33 pregnant women with normal pregnancies. Samples from maternal blood and umbilical cord blood were obtained at the time of delivery and leptin level was measured by Enzyme linked immunesorbant assey (ELISA) test.

Results: Umbilical cord leptin level was significantly lower in group A (medain1ng/ml) compared with group B (median10.2ng/ml); P<0.001, and maternal serum leptin was also significantly lower in group A (median19.8ng/ml) compared to control group B (median31.8ng/ml), P 0.042.

Newborn weight for age (Z score) and maternal body mass index were the most important and the only statistically significant determinants of cord blood leptin, while only maternal body mass index had a strong and statistically significant positive association with maternal serum leptin.

In group A, there was a linear correlation between cord blood leptin and placental weight, P<0.001, and a linear correlation between Apgar score at 5minutes and cord blood leptin level, P<0.001.

Conclusion: Women who had growth restricted fetuses had significantly lowered umbilical cord leptin level and maternal serum leptin level than women who had normal fetuses and the outcome of such fetuses could be related to leptin level.

Key words: Intrauterine growth restriction, cord blood leptin, maternal serum leptin

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Introduction

Intrauterine Growth Restriction (IUGR) is failure of a fetus to grow according to its genetic potential, and its birth weight < 10^{th} percentile adjusted for gestational age. Fetal growth restriction has been synonymous with small for gestational age (SGA), but in fact the majority of SGA are healthy but small (constitutionally small) and indeed, 15 % of SGA are small as a result of fetal growth restriction, this is due to pathophysiological changes with maternal, placental or fetal factors involved. It is an important clinical problem associated with increase perinatal mortality and morbidity. The Incidence of IUGR is about 4-7%. [1, 2, 3, 4]

Intrauterine Growth Restriction, could be symmetrical IUGR in 20% where the fetal entire body is proportionally small and arise from factors cause early onset IUGR, as congenital or chromosomal abnormalities and intrauterine infections, or could be asymmetrical in 80% of the cases; where the fetus is undernourished and is directing most of its energy to maintaining growth of the vital organs such as the brain and heart, at the expense of the liver, muscle and fat. This type usually results from placental insufficiency, they are usually late onset, and these infants have small abdominal circumference (due to decrease liver size), scrawny limbs (because of decrease muscle

size) and thin skin (because of decrease fat). [2]

The problem could be diagnosed by precise dating; that is accurate LMP and early U/S (8-13) weeks with clinical assessment of the fetal size. Ultrasound examination by estimating the fetal weight by biometric measurements including abdominal circumference (which is single best indicator of IUGR and has 95% sensitivity if <2.5th percentile, this value is for reference ranges based on normal pregnancy only, while if its below the 10th percentile for reference ranges based on a mixed group of high and low risk pregnancies).[5] Other measures including, head circumference, femur length and biparietal diameter. Decrease Liquor volume is a common finding in IUGR, as 85% of IUGR cases have oligohydramnios. [2] Umbilical artery Doppler study shows increase resistance which lead to reduce flow in diastolic component of the fetal cardiac cycle in the umbilical artery, this reduce flow with absent flow or at most extreme reversed end diastolic flow, reflect progressive degree of placental pathology and as a result there is increase Systolic /Diastolic (Sys/Dias) ratio with IUGR. [2, 4, 5]

Once fetal growth restriction is diagnosed, management options are limited to timely delivery, balancing the risks of continuing with the pregnancy against the risks of prematurity. [4]

Leptin

The human leptin has 167 amino acid sequences containing one disulphide bond. Its molecular weight is a round 16 KDa. The main source of leptin is white adipose tissue. But it can also be produced by brown adipose tissue, placenta (syncytiotropholoast), ovaries, skeletal muscles, stomach (lower part of fundic glands), mammary epithelial cells, bone marrow, pituitary gland and liver. [6]

Many physiological roles have been suggested for leptin in pregnancy; of them, having an autocrine and paracrine mechanism that is necessary for the maintenance of pregnancy. [7, 8] Also it plays a role in the early conceptus development and suggests its place among the array of active regulators during the opposition and adhesion phases of implantation. [9] It can regulate fetal growth, facilitate angiogenesis, [10, 11] enhance pulmonary development in utero and play a role in the maturation of intestinal mucosa. [12, 13]

Dysregulation of leptin metabolism may be implicated in preeclampsia and IUGR pathogenesis.

We conducted this study to evaluate the trend of leptin level alteration in maternal serum and cord blood in pregnancies complicated with intrauterine fetal growth restriction in comparison with normal pregnancy and to evaluate the possible relation with maternal body mass index (BMI), placental weight, other obstetrical parameters and neonatal outcome.

Methods

It is an analytic cross-sectional study. That had been conducted at Al-Elwiya Maternity Teaching Hospital in collaboration with Alkindy College of Medicine; physiology department during the period from the first of October 2009 – First of June 2010. The study protocol was approved by the hospital administration and the ethical and scientific committee at Alkindy College of Medicine.

All the pregnant women with singleton term pregnancies who were admitted to the hospital with the suspicion of IUGR over the study period of time were enrolled and after taking a detailed history and performing physical examination, the diagnosis was confirmed depending on:

The confirmation of gestational age according to Last menstrual period and early ultrasounds, abdominal circumference and estimated fetal weight $<10^{th}$ centile for gestational age estimated by ultrasound which had been confirmed by abnormal biophysical profile and Umbilical artery Doppler study. All women at term pregnancies with confirmed diagnoses of IUGR were included, while those with unreliable dating or had no confirmatory

early U/S or whose fetuses show major congenital malformations were excluded from the study.

The control group was including those women with normal term singleton pregnancies admitted for elective Cesarean Section, without maternal or fetal disease. All pregnant women informed verbally about their participation in the study and their acceptance was insured. The study samples consist of 67 pregnant women;

First group (group A): Thirty four pregnant women with IUGR, who were not in labour and without major fetal congenital malformation (**cases**), who they were further divided according to the presence or absence of certain maternal disease as pre-eclampsia (PE) or anemia.

Second group (group B): Thirty three pregnant women with normal singleton term pregnancy, who were not complicated by IUGR, or by maternal medical disease, nor they were in labour (**control**).

Maternal blood samples were obtained from the antecubital vein in the obstetric ward. Cord blood samples (umbilical arterial blood) were obtained from the babies post partum immediately after clamping of the cord, all samples were centrifuged and all sera were freeze and stored at -20◦ c until determination of leptin level. Leptin levels were measured at the laboratory by ELISA test.

Neonatal outcomes were assessed regarding birth weight, Apgar score at 5minutes and looking for newborn complications including; respiratory distress syndrome, meconium aspiration and neonatal death. The placenta was weighted immediately after clamping of the cord.

Data were analyzed using SPSS13 computer software. An expert statistical advice was sought for. The difference in median serum leptin (quantitative non-normally distributed variable) between 2 groups was assessed by non-parametric test (Mann-Whitney), while between more than two tests Kruskall-Wallis test was used. The statistical significance, strength and direction of linear correlation between 2 quantitative variables (one of which being non-normally distributed variable) was assessed by Spearman rank linear correlation coefficient. P value less than 0.05 was considered statistically significant. Multiple linear regression model was used to study the independent and net effect of selected explanatory (independent) variables on serum leptin as a response (outcome) variable.

Weight for age Z score (WAZ) score: was used to assess the newborns birth weight compared to a standard (reference) population of the same age and sex. The standard population depending on USA National Center for Health Statistics 2000.A normal range correspond to the 3rd and 97th percentile (i.e +2SD or - + 2 Z scores). WAZ score of the newborns can be classified into the following categories: severe IUGR (WAZ<-3), moderately severe IUGR (WAZ<-2.5to<-3), mild IUGR(WAZ<-2to<-2.5), accepTable - birth weight(WAZ<0 to -2) and well nourished (WAZ>0).[14]

Results

After analysis of data of 67 pregnant women: group A including 34 cases with IUGR and group B including 33 pregnant women with normal pregnancy as a control, the unit of measurement of leptin level used was (ng/ml). The following results were got:

As shown in Table - 1; the median maternal serum leptin and median cord blood leptin level in group A were significantly lower, compared to group B. Where the study groups were further classified according to the birth weight measured as Z score (compared to US standard newborn population). The median maternal serum leptin failed to comply with a statistically significant positive trend with WAZ categories of the newborn with (P=0.07). While, the median cord blood leptin shows an obvious positive trend with newborn WAZ ordered categories with (P<0.001), as shown in Table - 2.

Cases with IUGR whether uncomplicated by maternal disease or with maternal disease (Anemia, PE), have no association with maternal serum leptin level, with (P=0.31), nor associated with cord blood leptin (P= 0.98), as shown in Table - 3.

There was a strong linear correlation between Apgar score at 5 minutes and cord blood leptin (P<0.001) in both groups, as shown in figure 1. No diagram is shown for the linear correlation between Apgar score at 5 minutes and Maternal serum leptin since there is no correlation (r=0.07 P=0.56[NS]) and regarding the control group; the Apgar score was above 7 for all newborns.

There was no statistically significant differences between cases and controls in parity, gravidity, nor with history of abortion, (P= 0.94), as shown in Table - 4.

There was no statistically significant difference between cases and controls regarding maternal age in years, nor with gestational age in weeks, but there was statistically significant difference between cases and control regarding maternal BMI, (P=0.012) and placental weight, (P<0.001), in both group as shown in Table - 5.

Also there was a strong linear correlation between cord blood leptin and placental weight, (P<0.001) in both groups, as shown in figure 2. But no diagram is shown for the linear correlation between placental weight and maternal serum leptin level since there is no correlation (r=0.14, p=0.26).

As shown in Table - 6 & 7; for group A, there was no correlation between maternal serum leptin neither cord blood leptin of the newborn whith (respiratory distress syndrome, meconium aspiration or early neonatal death), while there was a positive correlation between maternal BMI and maternal serum leptin and cord blood leptin level but it was not statistically significant(P=0.11) for the former while it was for the latter as (P=0.037), and there was a strong association between maternal serum leptin and gender of newborn, as male gender associated with higher maternal serum leptin level and was statistically significant (P=0.03), while cord blood leptin, was higher in female babies compared to males, but it was not statistically significant (P=0.29).

While in group B; the control group, there were no complications for the newborn but there was a positive correlation between maternal serum leptin level and maternal BMI but not statistically significant (P=0.19), but there was no correlation between cord blood and maternal BMI. While there was higher maternal serum and cord blood leptin in male gender compared to female gender, but not statistically significant, (P=0.32) and (P=0.65) respectively as shown in Table - 8 & 9.

The net association between birth weight (measured in its standardized units as WAZ score) and cord blood leptin was tested by multiple linear regression model to adjust for possible confounding effect of maternal BMI, fetal gender in addition to parity, gravidity and maternal age as shown in Table - 10.

The net association between birth weight (measured in its standardized units as WAZ score) and maternal serum leptin was also tested by multiple linear regression model to adjust for possible confounding effect of maternal BMI, fetal gender in addition to parity, gravidity and maternal age as shown in Table - 11

Discussion

In this study we explored the relation of the vital hormone; leptin with regard to its level in cord blood and maternal serum in IUGR pregnancies, compared to normal pregnancies. We found that leptin concentration in the umbilical cord blood of IUGR newborns was significantly lower compared to control, (P<0.001), suggesting that fetus adipose tissue is a major source of leptin, this result is in agreement with previous studies.[15,16] Also maternal serum leptin was significantly lower in IUGR group compared to normal control group, (P=0.042), but other studies had shown different result in this aspect; were some

showed elevated level in such pregnancies, while others showed similar level or reduced when compared to control group. [17, 18, 19] That difference could be explained by the difference in sample size and race between different studies.

We also found that IUGR newborn weight is strongly positively correlated with cord blood leptin even when the severity of IUGR is taken into account (P<0.001), this was also reported by others. [20, 21] At the same time we found that maternal serum leptin was associated with IUGR as a crude definition but failed to show an association with the severity of IUGR (P=0.05) and that was also reported by Laivouri et al, 2006. [22]

When we took the causes of IUGR into consideration, we found that pregnancies with IUGR with maternal disease (anemia) showed the lowest cord and maternal leptin level. While IUGR pregnancies complicated by (PE) showed the highest values for both and IUGR uncomplicated by maternal disease is in between. This may be explained by the fact that in cases of IUGR with hypertension, the newborns are more prone to prolong chronic hypoxia which is leptin promoter. Also maternal serum leptin was higher in IUGR with hypertension which is in line with previous results, as describing an elevated leptin expression in placenta and elevated maternal leptin concentration in pregnancy complicated by IUGR and/or pre eclampsia. [23] Although this didn't show statistically significant association (P=0.31) for maternal serum leptin and (P=0.98) for cord blood leptin, and this may be explained by the small sample size of our study.

The study show strong positive liner correlation between Apgar score at 5 minutes with cord blood leptin (P=0.001), but no correlation to maternal serum leptin (P=0.56) in both groups, beside that the mean Apgar score at 5 minutes was significantly lower among cases compared to control, this was in contrast to other study which show no relation between leptin level in cord blood or maternal serum with Apgar score at 5 minutes after delivery. [24] While the placental weight, were significantly lower in IUGR group compared to control (p<0.001) and there was a positive correlation between cord blood leptin concentration and placental weight (p<0.001) in both groups, this is in agreement with previous study as reported by Schupring et al 1997. [25]

The net association between birth weight (measured in its standardized units as WAZ score) and cord blood leptin was tested by multiple linear regression model to adjust for possible confounding effect of maternal BMI, fetal gender in addition to parity, gravidity and maternal age. The model showed that the newborn WAZ score followed by maternal BMI were the most important and the only statistically significant determinants of cord blood leptin. For each one unit increase in WAZ score the cord blood leptin is significantly increased by an average of 3.7 ng /ml after adjusting for other explanatory variables included in the model and for each one unit increase in maternal BMI the cord blood leptin is significantly increased by an average of 0.86 ng/ml after adjusting for other explanatory variables included in the model. Our study showed a positive correlation between cord blood leptin level and maternal BMI in IUGR group but not in the control group, and there was a positive relation in both groups by multiple linear regression analysis, which may be explained by that: the better maternal nutrition and highest body weight and BMI, the better nutrition and energy support to the fetus and subsequently highest newborn weight and cord blood leptin because cord blood leptin level is related to the newborn anthropometry. This was in contrast to other study, [20] who showed no relation between cord blood leptin and maternal BMI. The remaining independent variables like maternal age, gestational age at birth and parity had no obvious or statistically significant association with cord blood leptin. The newborn male gender is associated with lower cord blood leptin of

2.1 ng/ml compared to females after adjusting for other explanatory variables, but this effect was not significant statistically. The model was statistically significant and able to explain 50.1% of observed variation in the dependent variable (cord blood leptin), as shown in Table - 10. While in regard to this aspect, other studies showed that there was no sex difference of leptin level in cord blood at term [25, 26], this in contrast to the situation in adults where consistently higher level of leptin are found in serum from females than from males, [27] one possible explanation for the absence of gender difference of leptin level at birth might be that the body fat mass of neonate is not gender specific, while other study shows a gender difference with higher serum leptin for females fetuses was observed during last weeks of gestation and was confirmed at birth regardless of the growth status, suggesting that sexual dimorphism already exists in utero. [16]

The net association between birth weight (measured in its standardized units as WAZ score) and maternal serum leptin was also tested by multiple linear regression model to adjust for possible confounding effect of maternal BMI, fetal gender in addition to parity, gravidity and maternal age. The model showed that the newborn WAZ score had no important or statistically significant association with maternal serum leptin after adjusting for other explanatory variables included in the model. Only maternal BMI had a strong and statistically significant positive association with maternal serum leptin. For each one unit increase in maternal BMI the maternal serum leptin is significantly increased by an average of 7.8ng/ml. Which was also agreed with previous studies. [24, 28] But this was in contrast with others, [25] who showed that BMI at delivery do not correlate with leptin levels in maternal serum, and that was explained by the poor correlation of maternal BMI and weight measurements with fat tissue expansion during pregnancy, while Hiroko et al,[28] showed that serum leptin level is well known to be correlated with body adiposity in non pregnant women, as for pregnant women and that Maternal BMI remains a significant determinant for placenta leptin concentration as this is the case in this study.

After adjusting for other explanatory variables included in the model. The remaining independent variables like maternal age, fetal gender, gestational age at birth and parity had no obvious or statistically significant association with maternal serum leptin. The model was statistically significant and able to explain 25.5% of observed variation in the dependent variable (maternal serum leptin), as shown in Table - 11. But there were no previous studies correlating maternal serum leptin and gender of newborn. These conflicting results may be explained by the wide and variable distribution of leptin values observed in each study.

Conclusions

Growth restricted fetuses had umbilical cord blood leptin concentration significantly lower than those in normal fetus, and it was positively correlated to newborn birth weight and maternal serum leptin level was significantly lower in mothers with IUGR compared to normal pregnant mother. Only Apgar score at 5 minutes was significantly lowered and correlated to cord blood leptin in IUGR. Further studies for longer duration with larger sample size are needed to determine a clear relation between leptin level and specific causes of IUGR (maternal, fetal or placental causes). Meanwhile using different gestational age for leptin level measurements to determine its predictive value for early detection of IUGR and its relation to fetal outcome.

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Tables and Figures:

Table - 1: The study groups' difference in median maternal serum and cord blood leptin level:

	Controls (Normal birth weight) (n=33)	**Cases (IUGR) (n=34)**	**P (Mann-Whitney)**
Maternal serum Leptin			**0.042**
Range	(13.5 - 165)	(6.8 – 147.6)	
Median	31.8	19.8	
Interquartile range	(23.8 - 48)	(13.03 - 51.4)	
N	33	34	
Cord blood Leptin			**<0.001**
Range	(1.1 - 32)	(0.05 – 16.46)	
Median	10.2	1	
Interquartile range	(6.72 - 18.35)	(0.28 - 1.93)	
N	33	34	

Table - 2: The median maternal serum and cord blood leptin by neonatal WAZ score categories:

	Severe IUGR (WAZ<-3) (n=8)	Moderately severe IUGR (WAZ<-2.5 to -3) (n=12)	Mild IUGR (WAZ<-2 to -2.5) (n=14)	AccepTable - birth weight (WAZ<0 to -2) (n=28)	Well nourished (WAZ>0) (n=5)	P (Kruskal-Wallis)
Maternal serum Leptin						**0.07[NS]**
Range	(15.8 - 104.1)	(6.8 - 147)	(7.82 - 147.6)	(13.5 - 165)	(22.8 - 113)	
Median	21.5	12.95	35.23	31.75	37.09	
Interquartile range	(18.58 - 31.28)	(9 - 37.03)	(16.25 - 65.33)	(21.13 - 48.3)	(24.6 - 78.45)	
N	8	12	14	28	5	
r=0.24 P=0.05[NS]						
Cord blood Leptin						**<0.001**
Range	(0.2 - 4.13)	(0.07 - 16.46)	(0.05 - 8.23)	(1.1 - 32)	(6.63 - 28.98)	
Median	0.7	1	1.15	9.49	17.1	
Interquartile range	(0.35 - 1.65)	(0.12 - 2.75)	(0.4 - 1.93)	(6.5 - 18.06)	(10.17 - 23.09)	
N	8	12	14	28	5	
r=0.67 P<0.001						

Table - 3: The difference in maternal serum and cord blood leptin according to the presence or absence of maternal causes of IUGR:

	IUGR (Uncomplicated by maternal disease) (n=14)	IUGR (Anemic mother) (n=6)	IUGR (mothers with PE) (n=14)	P (Kruskal-Wallis)
Maternal serum Leptin				**0.31[NS]**
Range	(7.82 - 147.6)	(6.8 - 24.26)	(8.9 - 147)	
Median	20.7	16.55	23.8	
Interquartile range	(12.53 - 84.53)	(7.51 - 22.42)	(15.05 - 49.93)	
N	14	6	14	
Cord blood Leptin				**0.98[NS]**
Range	(0.05 - 8.23)	(0.07 - 4.93)	(0.07 - 16.46)	
Median	1	0.85	1.15	
Interquartile range	(0.4 - 2.2)	(0.17 - 3.18)	(0.28 - 1.43)	
N	14	6	14	

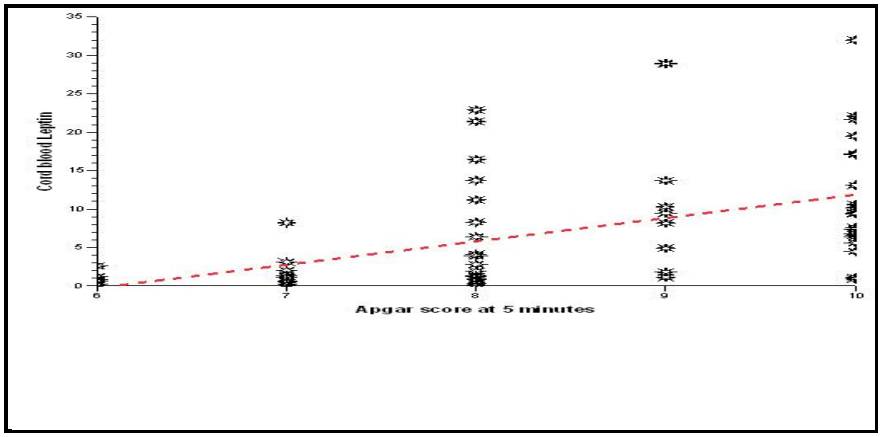

Figure 1: scatter diagram with fitted regression line showing the linear correlation between apgar score at 5 minutes and cord blood leptin .(r=0.48,p<0.001)

Table - 4: the study groups difference in relation to parity, gravidity and history of abortion:

	Controls (Normal birth weight) (n=33)	Cases (IUGR) (n=34)	P (Mann-Whitney)
Parity			**0.63[NS]**
Range	(0 - 6)	(0 - 6)	
Median	1	1	
Interquartile range	(0 - 3)	(0 - 2)	
Gravidity			**0.47[NS]**
Range	(1 - 8)	(1 - 9)	
Median	3	2	
Interquartile range	(2 - 4)	(2 - 4)	
History of abortion			**0.94[NS]**
Range	(0 - 2)	(0 - 2)	
Median	0	0	
Interquartile range	(0 - 1)	(0 - 1)	

Table - 5: The study groups difference in relation to maternal age, gestational age, maternal BMI and placental weight:

	Controls (Normal birth weight) (n=33)	Cases (IUGR) (n=34)	P (t-test)
Maternal age (years)			**0.83[NS]**
Range	(17 - 35)	(17 - 42)	
Mean	26.5	26.2	
SE	0.79	1	
Gestational age at birth (weeks)			**0.11[NS]**
Range	(37 - 41)	(37 - 42)	
Mean	38.6	38.1	
SE	0.2	0.19	
Body mass index (Kg/m2)			**0.012**
Range	(23 - 36.3)	(20.2 - 32.7)	
Mean	26.8	25.3	
SE	0.47	0.33	
Placental weight (gm)			**<0.001**
Range	(400 - 600)	(200 - 500)	
Mean	503.6	323.8	
SE	10.47	11.39	

Figure 2: scatter diagram (with fitted regression line) showing a strong linear correlation between cord blood leptin and placental weight.

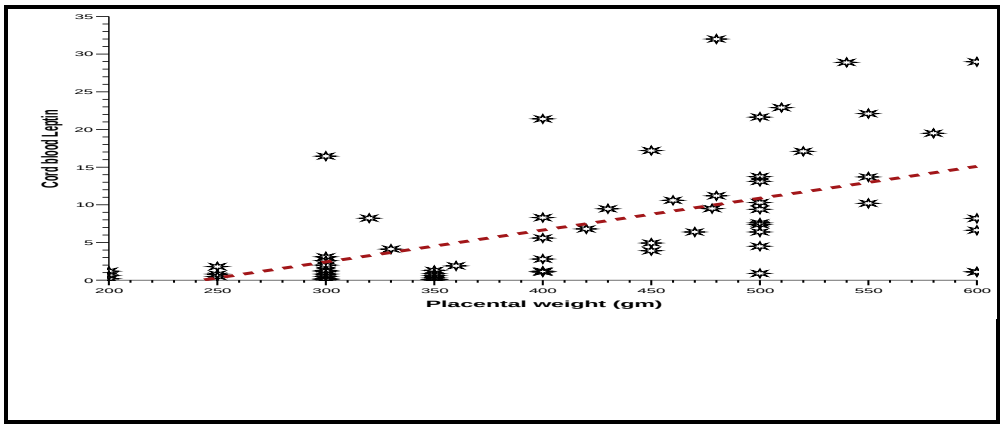

Table - 6: The median maternal serum leptin by selected independent variables among IUGR cases:

	Maternal serum Leptin				
	Range	**Median**	**Interquartile range**	**N**	**P**
Respiratory distress syndrome					**0.97[NS]**
Negative	(6.8 - 147.6)	21.5	(13.03 - 57.43)	22	
Positive	(9.3 - 147)	19	(12.85 - 42.75)	12	
Meconium aspiration					**0.94[NS]**
Negative	(6.8 - 147.6)	19.8	(12.88 - 54.6)	32	
Positive	(16.1 - 27.9)	22	(16.1 - **)	2	
Death of the newborn					**0.65[NS]**
Negative	(6.8 - 147.6)	19.7	(12.8 - 49.8)	31	
Positive	(15.8 - 104.1)	19.9	(15.8 - **)	3	
BMI categories					**0.11[NS]**
Normal (<25)	(6.8 - 112.3)	16.1	(9.3 - 42.1)	15	
Overweight (25-29.9)	(8.9 - 147)	20.85	(16.65 - 51.4)	18	
Obese (30+)	(147.6 - 147.6)	147.6	(147.6 - 147.6)	1	
r=0.165 P=0.57[NS]					
Newborn gender					**0.03**
Female	(6.8 - 147)	15.8	(9.3 - 27.9)	19	
Male	(10.8 - 147.6)	32.4	(17.8 - 78)	15	

Table - 7: The median cord blood leptin by selected independent variables among IUGR cases:

	Cord serum Leptin				
	Range	Median	Interquartile range	N	P
Respiratory distress syndrome					0.09[NS]
Negative	(0.05 - 8.23)	0.7	(0.09 - 1.83)	22	
Positive	(0.3 - 16.46)	1.2	(0.95 - 2.45)	12	
Meconium aspiration					0.66[NS]
Negative	(0.05 - 16.46)	1	(0.35 - 1.98)	32	
Positive	(0.08 - 1.8)	0.94	(0.08 - .)	2	
Death of the newborn					0.27[NS]
Negative	(0.05 - 16.46)	1.1	(0.3 - 2)	31	
Positive	(0.2 - 0.8)	0.6	(0.2 - .)	3	
BMI categories					0.037
Normal (<25)	(0.05 - 4.13)	0.6	(0.08 - 1.3)	15	
Overweight (25-29.9)	(0.2 - 16.46)	1.2	(0.73 - 2.15)	18	
Obese (30+)	(8.23 - 8.23)	8.23	(8.23 - 8.23)	1	
r=0.375 P=0.19[NS]					
Newborn gender					0.29[NS]
Female	(0.07 - 16.46)	1.1	(0.3 - 2.8)	19	
Male	(0.05 - 8.23)	0.9	(0.2 - 1.2)	15	

Table - 8: the median maternal serum leptin by selected independent variables among control group:

	Maternal serum Leptin				
	Range	**Median**	**Interquartile range**	**N**	**P**
BMI categories					**0.19[NS]**
Normal (<25)	(13.5 - 44.3)	32.4	(15 - 44.1)	5	
Overweight (25-29.9)	(14.51 - 154.3)	31.7	(23.8 - 48)	25	
Obese (30+)	(28.5 - 165)	113	(28.5 - .)	3	
r=0.243 P=0.17[NS]					
Newborn gender					**0.32[NS]**
Female	(13.5 - 165)	28.45	(19.28 - 44.2)	20	
Male	(15.28 - 67.61)	37.09	(26.75 - 49.93)	13	

Table - 9: The median cord blood leptin by selected independent variables among control group:

	Cord serum Leptin				
	Range	**Median**	**Interquartile range**	**N**	**P**
BMI categories					**0.06[NS]**
Normal (<25)	(9.4 - 28.98)	11.2	(9.8 - 25.54)	5	
Overweight (25-29.9)	(1.1 - 28.9)	8.3	(6.4 - 15.43)	25	
Obese (30+)	(13.1 - 32)	17.2	(13.1 - .)	3	
r=-0.071 P=0.69[NS]					
Newborn gender					**0.65[NS]**
Female	(1.1 - 32)	9.44	(6.5 - 17.18)	20	
Male	(1.1 - 22.9)	10.6	(7.42 - 20.45)	13	

Table - 10: multiple linear regression model with cord blood leptin as the dependent (response) variable and newborn waz score, gender, maternal bmi and selected maternal variables as independent (explanatory) variables:

	Unstandardized partial regression coefficient	P	Standardized partial regression coefficient
Newborn weight for age z score	3.73	<0.001	0.559
Newborn male gender compared to females	-2.12	0.17[NS]	-0.13
Parity	-0.46	0.52[NS]	-0.096
Body mass index (Kg/m2)	0.86	0.011	0.257
Maternal age (years)	0.05	0.83[NS]	0.032
Gestational age at birth (weeks)	0.57	0.42[NS]	0.081

P (Model) <0.001

Table - 11: multiple linear regression model with maternal serum leptin as the dependent (response) variable and newborn waz score, gender, maternal bmi and selected maternal variables as independent (explanatory) variables:

	Unstandardized partial regression coefficient	P	Standardized partial regression coefficient
(Constant)	-186.136	0.29[NS]	
Newborn weight for age z score	-2.943	0.45[NS]	-0.096
Newborn male gender compared to females	5.107	0.55[NS]	0.068
Parity	-3.946	0.32[NS]	-0.18
Body mass index (Kg/m2)	7.805	<0.001	0.507
Maternal age (years)	0.158	0.9[NS]	0.022
Gestational age at birth (weeks)	0.496	0.9[NS]	0.015

P (Model)=0.006

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