

Relation Between Maternal Serum Leptin Levels and Fetal Umbilical Artery Doppler Values in Normal and IUGR Pregnancies

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Abstract

Aim: To investigate the relation between umbilical artery Doppler values and maternal serum leptin levels in pregnant women having normal fetus and with intrauterine growth restriction

Materials and Methods: This study was carried out in Firat University Obstetrics and Gynecology Department on 16 healthy pregnant women having intrauterine growth restriction (IUGR) and 15 healthy pregnant women having normal fetus in the third trimester of pregnancy. Pregnant women with normal fetus were allocated to group I and those with fetus that had IUGR were allocated to group II. Maternal serum leptin levels and umbilical artery pulsatility index (PI), resistance index (RI) systole/diastole rates (S/D) of all cases were determined twice, at 01.00-02.00 a.m. and 10.0-11.00 a.m.

Results: Mean maternal serum leptin levels were significant in group I diurnal change ($p<0.05$), while the difference between day and night was not significant in group II ($p>0.05$). The highest values in gravida with group I were obtained at 01.00-02.00 a.m. at night. The correlation between umbilical artery Doppler values and serum leptin values in pregnant women group II was significant, but in the group I was not.

Conclusion: The clinical use of maternal leptin levels in IUGR has not been documented yet. However, maternal serum leptin levels' loss of their diurnal pattern in IUGR and the correlation between maternal leptin values and umbilical artery Doppler changes in these fetuses may be important as a marker that may be used in the diagnosis and follow-up of IUGR and may offer new perspectives on etiology.

Keywords: maternal serum leptin, IUGR, umbilical artery Doppler

Özet

Normal ve IUGR'li Gebeliklerde Maternal Serum Leptin Düzeyleri ve Umbilikal Arter Doppler İndeksleri Arasındaki İlişki

Amaç: Normal ve intrauterin gelişme geriliği fetuslara sahip gebelerde umbilikal arter Doppler değerleri ile maternal leptin düzeyleri arasındaki ilişkinin araştırılması.

Materyal ve Metot: Bu çalışma Firat Üniversitesi Kadın Hastalıkları ve Doğum ABD'da 16 intrauterin gelişme geriliği (IUGR) ve 15 sağlıklı üçüncü trimester gebe kadın üzerinde yapıldı. Normal fetusa sahip gebeler Grup I, IUGR'li fetusa sahip gebeler Grup II olmak üzere iki gruba ayrıldı. Tüm olguların gece saat 01:00-02:00 ve gündüz 10:00-11:00 aralığında olmak üzere iki kez serum leptin düzeyleri, umbilikal arter pulsatilite İndeks(PI), Rezistans İndeks(RI) ve sistol/diastol oranları (S/D) oranları belirlendi.

Sonuçlar: Ortalama maternal serum leptin düzeylerinin diurnal değişimi normal gebelerde anlamlı bulunurken ($p<0.05$), IUGR'ye sahip gebelerde gece gündüz arasındaki fark anlamlı bulunmadı ($p>0.05$). Normal fetusa sahip gebelerde maternal serum leptin düzeyleri gece saat 01:00-02:00 arasında en yüksek değerlerde bulundu. IUGR gebelerde umbilikal arter Doppler değerleri ile leptin değerleri arasındaki korelasyon anlamlı iken normal fetusa sahip olgularda anlamlı bulunmadı.

Tartışma: Maternal Leptin düzeyinin IUGR'nin klinik takibinde herhangi bir kullanımı henüz yoktur. Bununla birlikte, Maternal serum leptin düzeylerinin IUGR'de diurnal patternini kaybetmiş olması ve bu fetuslarda maternal leptin değerleri ile umbilikal arter Doppler değişimleri arasındaki korelasyon gerek IUGR'nin tanı ve takibinde bir marker, gerekse etiyolojiye daha farklı görüş açıları getirmesi bakımından olabilir.

Anahtar sözcükler: maternal serum leptin, IUGR, umbilikal arter Doppler

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Introduction

Many pathological factors in nutritional, genetic, idiopathic or placental vascular structures have long been held responsible for intrauterine growth restriction (IUGR) (1-3). Recently, it was found that fetal leptin levels were correlated with fetal growth and it was claimed that leptin could be a growth factor in fetal development (4, 5). This phenomenon was confirmed in studies conducted on fetuses of twin gravida with discordance and it was demonstrated that fetus that were smaller according to gestational age had lower leptin levels (6). It was established in several later studies that leptin levels markedly decreased in IUGR and lower leptin levels were held responsible as an additional etiological cause of IUGR (7, 8).

Maternal serum leptin levels display a progressive increase from the first trimester until the 28th gestational week (9). Likewise, it is known that fetal blood flow begins to increase in the first trimester and continues to do so until the third. It was shown in both human and rat studies that leptin was effective on vascular reactivity and had vasodilator influence (10). When evaluated together, all this information suggests that one of the effects of leptin on fetal growth may be associated with its effect on fetal blood flow. As far as we know, the relation between maternal leptin levels, which were shown to be closely related with fetal growth, and umbilical artery blood flow has not been discussed until now.

In this study, it was planned to examine the relation between umbilical artery Doppler indices and maternal serum leptin levels.

Materials and Methods

This study included 16 healthy pregnant women having fetus with IUGR and 15 healthy pregnant women having normal fetus, in the third trimester of pregnancy, who presented at Obstetrics and Gynecology Department of Firat University. The study included informed, voluntary gravida, whose written consents were taken after they were informed about the study. Pregnant women in the study were allocated to two groups, group I being composed of healthy pregnant women having normal fetus and group II of those with IUGR. IUGR was diagnosed as the abdominal perimeter being below 2.5 percentile by ultrasonography and the expected fetal weight's being less than 10 percentile (11).

Serum leptin levels and umbilical artery systole/diastole rates of all cases were determined twice, at 01.00-02.00 a.m. and 10.00-11.00 a.m. Women in group II were selected from inpatients, who were admitted to hospital for follow-up, and outpatients and group I were selected from those who presented for some complaint, but found to be normal after examinations. Healthy pregnant women having normal fetus were asked to come to hospital again the next day at the indicated hours after Doppler examinations and blood collection. Fetal biophysical profiles, our routine follow-up procedure, were prepared for all IUGR fetuses.

Umbilical artery Doppler indices were determined in Hitachi EUB 525 ultrasound instrument using 3.5 MHz convex probe. All sonographic examinations were made while the patients were in semi-recumbent position. Doppler evaluations were made at the free central part of the umbilical artery, in the absence of fetal movements, respiratory and cardiac arrhythmia (12).

About 3 ml of venous blood was collected from each patient in order to determine maternal serum leptin levels. The collected blood samples were centrifuged at 5000 rotations. The serums obtained were stored at -80°C. After all serums were collected, they were studied in EL X 800 micro-elisa equipment, using DRG leptin kit (DRG, international, inc. USA) according to ELISA method.

All women in the study were selected from among pregnant women with BMI between 22 and 26. The pregnant women who were chronic hypertensive, had preeclampsia, diabetes or any acute or chronic disease, had pregnancy complications, smoked cigarettes or had a condition that could affect serum leptin levels were excluded from the study.

For the statistical analysis, Wilcoxon rank test was used in dependent and Mann Whitney U test in the independent groups and spearman correlation analysis was employed in correlation analyses (p,r,n). Values for which p<0.05 were considered significant.

Results

Throughout the study none of the fetuses with IUGR, who were followed up specifically, had any impairment in the fetal condition that could require termination of pregnancy. Biophysical profile of all fetuses with IUGR in the study was above 6. Clinical, laboratory and socio-demographic data about women in the study and control groups are presented in Table 1.

	Group I (n:15)	Group II (n:16)	P value
Age (year)	27.1±5.2	26.8±4.3	>0.05
Gestational age (week)	32.2±4.5	31.2±5.3	>0.05
Parity (number)	2.6±1.2	2.3±0.9	>0.05
Body mass Index (BMI)	24.4±0.9	23.8±1	>0.05
Hemoglobine (Hb)	12.2±1.6	11.9±0.8	>0.05
Glucose	90.1±26.3	88±23.7	>0.05

Table 2. Maternal serum leptin changes at 10:00-11:00 a.m. and 01.00-02.00 a.m. in groups

	Maternal serum leptin (ng/ml)		P value
	10:00-11:00 a.m.	01:00-02:00 a.m.	
Group I (n:15)	8.9±2.2	9.9±1.8	0.017*
Group II (n:16)	7.5±1.1	7.6±0.8	0.87

*: statistically significant

Table 3. Umbilical artery pulsatility index (PI), resistance index (RI) and systole/diastole (S/D) changes at 10:00-11:00 a.m. and 01.00-02.00 a.m. in groups (mean ± standard deviation)

	Umbilical artery PI, RI, S/D			P value
		13:00-14:00 a.m.	01:00-02:00 a.m.	
Group I (n:15)	PI	0.84 ±0.04	0.83 ±0.05	p>0.05
	RI	0.60±0.02	0.61±0.09	p>0.05
	S/D	2.47±0.24	2.37±0.22	p>0.05
Group II (n:16)	PI	1.11±0.18	1.12±0.20	p>0.05
	RI	0.78±0.08	0.79±0.07	p>0.05
	S/D	3.3±1.31	3.2±1.36	p>0.05

Diurnal and nocturnal differences in maternal serum leptin levels were found significant in group I ($p<0.05$), but insignificant in group II ($p>0.05$). Mean maternal serum leptin levels were the highest at 01.00-02.00 a.m. and the lowest at 10:00-11:00 a.m (Table 2).

Umbilical artery S/D values were significantly higher in group II. There was no significant difference between diurnal and nocturnal umbilical artery S/D values in any group ($p>0.05$) (Table 3).

The correlation between umbilical artery Doppler values (PI,RI,S/D) and maternal serum leptin values was found significant in group II ($p:0.01$, $r:621$, $n:16$ – $p:0.01$, $r:647$, $n:16$ – $p:0.02$, $r:611$, $n:16$, respectively), but insignificant in group I ($p:0.10$, $r:388$, $n:15$ – $p:0.18$, $r:423$, $n:15$ – $p:0.16$, $r:397$, $n:15$, respectively) (Figure 1, 2 and 3).

Discussion

In this study, maternal serum leptin levels in pregnant women with normal fetus were found higher than those in pregnant women having fetus with IUGR. Although there are studies reporting increased maternal serum leptin levels in pregnant women with normal fetus, in comparison to fetus with IUGR, the literature information on this topic is contradictory. Pighetti et. al. reported that maternal serum leptin levels in fetus with IUGR were higher than those in normal fetus (13), while Yıldız et. al. found that the levels were lower in the former than in the latter (14). Aslan et al., on the other hand, could not find a difference between the two (15). These dif-

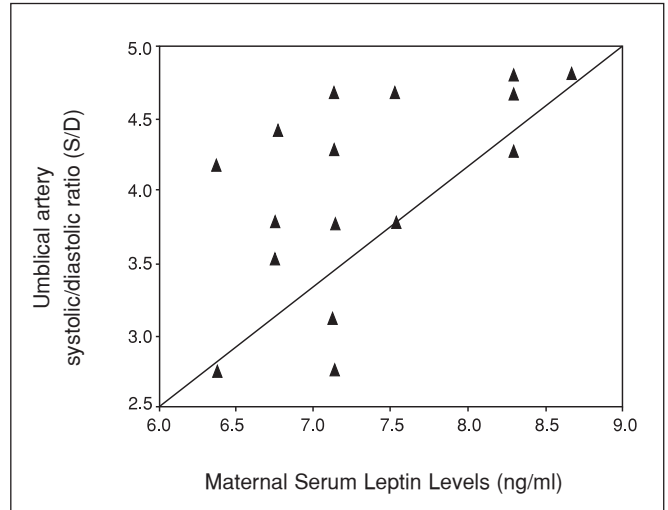


Figure 1. The correlation between umbilical artery S/D rates and maternal serum leptin levels in group II.

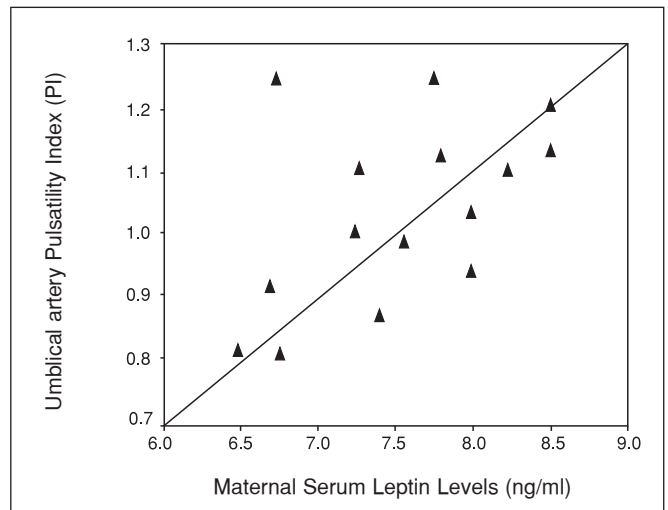


Figure 2. The correlation between umbilical artery PI and maternal serum leptin levels in group II.

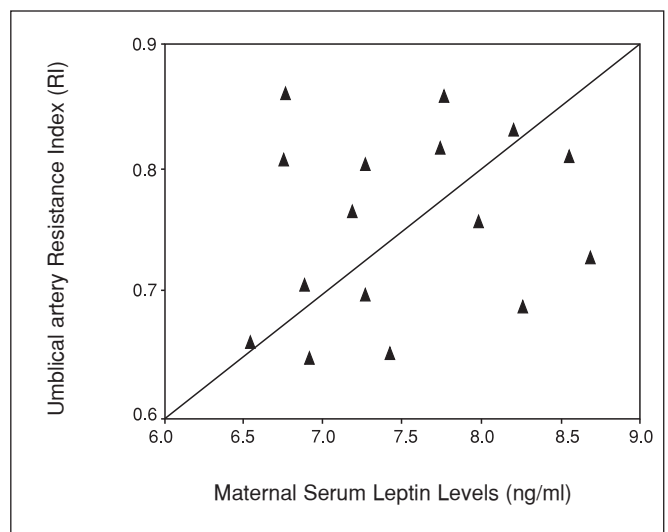


Figure 3. The correlation between umbilical artery RI and maternal serum leptin levels in group II.

ferences may be attributed to determination of leptin levels in fasting or satiety and at different hours of the day.

Leptin levels in both women and men are subject to diurnal and ultradian changes and the highest levels are reached at 01.00-02.00 a.m. Leptin levels also display ultradian patterns during the day (16). This opinion of ours is based upon the diurnal changes found in serums of pregnant women with normal fetus. The same change could not be established in serums of women whose fetus had IUGR. This finding was not seen in the studies reporting leptin levels in pregnancy.

Another significant finding of this study is the positive correlation between maternal leptin levels and umbilical artery Doppler changes in fetus with IUGR. No correlation was found between maternal serum leptin levels and Doppler values in pregnant women with normal fetus. Besides, the diurnal changes observed in maternal leptin levels could not be obtained in umbilical artery Doppler indices.

The correlation between maternal leptin levels of mothers whose fetus had IUGR and umbilical artery Doppler changes can be partially explained by some pieces of literature information. One of these can be found in both human and rat studies that show that leptin affected vascular reactivity and had vasodilator effect (10, 17). Another explanation comes from studies which report that leptin levels increased in placental failure conditions that lead to hypoxia (18, 19). When this literature information and our findings are evaluated together, it can be said that the positive correlation between maternal leptin levels and Doppler indices in fetus with IUGR can result from a compensation mechanism.

However, it is not possible for the time being to draw certain conclusions about the cause and effect relation of this correlation with the available findings and information. Further and more detailed studies should be conducted about the effect of maternal leptin levels on vascular structures.

In conclusion, maternal leptin level is not used in any way in the clinical follow-up of IUGR, yet. Nevertheless, loss of diurnal rhythm in IUGR and the correlation between maternal leptin values and umbilical artery Doppler changes are important both as a marker in the follow-up of IUGR and in bringing different perspectives to etiology.

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