

Serum leptin level in the first trimester in ectopic versus normal pregnancies

Zahra Kamyabi, MD, Ghazaal Mansouri, MD, Fatemeh Azizzian, MD.

ABSTRACT

الأهداف: التحقق من احتمال اختلاف مستويات هرمون اللبتين في الحمل الطبيعي والحمل خارج الرحم.

الطريقة: أُجريت هذه الدراسة المقطعية في قسم النساء والولادة بمركز أفزاليبور الطبي، كرمان، إيران وذلك خلال الفترة من يناير 2009م إلى فبراير 2010م، وقد تم تقسيم المشاركات في الدراسة إلى مجموعتين وهما: مجموعة الحمل الطبيعي وتضم 47 مشاركة (أ)، ومجموعة الحمل خارج الرحم وتضم نفس العدد من المشاركات (ب). ولقد تم استثناء المشاركات اللاتني لديهن الصفات التالية: وجود تاريخ سابق بالإجهاض أو الحمل خارج الرحم، واستخدام الأدوية خلال فترة الحمل باستثناء الفيتامينات وحمض الفوليك، والتعرض لحالة غير مستقرة تستدعي فتح البطن، والتدخين، وإذا كان مؤشر كتلة جسم المشاركات يساوي أو أكثر من 25 كغ/م² أو يساوي أو أقل من 19 كغ/م². لقد صل الحد الأقصى لفترة الحمل إلى 8 أسابيع في كلتي المجموعتين، وتم تحديد مستويات هرمون اللبتين في مصل الدم من خلال المقاييس المناعية الإنزيمية، وبعد ذلك تم تحليل نتائج الدراسة باستخدام تحليل التباين أحادي الاتجاه.

النتائج: أشارت الدراسة إلى عدم وجود اختلاف واضح بين المجموعتين وذلك عند اعتبار العوامل التالية: العمر، ومدة الحمل، ومؤشرة كتلة الجسم. وكانت مستويات هرمون اللبتين في المجموعة (ب) (الوسيط: 30.93، ويتراوح ما بين 14.8-84.2) أعلى من المجموعة (أ) (الوسيط: 32.74، ويتراوح ما بين 8.4-8.61).

خاتمة: أثبتت الدراسة أن قياس مستويات هرمون اللبتين في الثلث الأول من الحمل قد يكون مؤشراً دالاً عند تشخيص الحمل خارج الرحم.

Objectives: To determine whether maternal serum leptin level is different or not in ectopic and normal pregnancy.

Methods: In this cross sectional study, we included 47 women with normal pregnancy (group A), and 47 women with ectopic pregnancy (group B) attending the Department of Obstetrics and Gynecology,

Afzalipour Medical Centre, Kerman, Iran from January 2009 to February 2010. Previous history of miscarriage or ectopic pregnancy, body mass index equal to or more than 25 and equal or less than 19 kg/m², using drugs during pregnancy except for multivitamin and folic acid, unstable conditions requiring emergency laparotomy, and cigarette smoking were considered as exclusion criteria. The maximum gestational age in both groups was 8 weeks. Maternal serum leptin level was determined using enzyme-linked immunosorbent assay kit. Data were analyzed using one-way analysis of variance.

Results: There were no statistically significant differences between the 2 groups in maternal age, gestational age, and body mass index. Women in group B (median [range]: 30.93 [14.8-84.2]) showed significantly higher serum leptin level in comparison with group A (median [range]: 32.74 [8.4-8.61]).

Conclusion: Serum leptin level in the first trimester of pregnancy may be a useful marker in the differential diagnosis of ectopic pregnancy.

Saudi Med J 2011; Vol. 32 (4): 376-378

From the Department of Obstetrics and Gynecology, Afzalipour Medical Centre, Kerman University of Medical Sciences, Kerman, Iran.

Received 15th September 2010. Accepted 24th January 2011.

Address correspondence and reprint request to: Dr. Zahra Kamyabi, Department of Obstetrics and Gynecology, Afzalipour Medical Centre, Kerman University of Medical Sciences, Kerman 7616913911, Iran. Tel. +98 (341) 3222250 Ext. 306. Fax. +98 (341) 2456269. E-mail: zkamyabi@yahoo.com

Leptin is a 167 amino-acid protein that is basically secreted by adipocytes. It affects the hypothalamic centers that are responsible for the regulation of body weight homeostasis. Leptin has also an important role in reproduction, in a way that lack of it causes infertility in mice, and it has been reported that the administration of recombinant leptin can solve this problem.^{1,2} According

to previous studies, this effect is exerted through an interaction with the hypothalamic-pituitary-gonad axis, and modulation of luteinizing hormone and follicle-stimulating hormone production.² Leptin level is higher in women compared to men, especially during the luteal phase of the menstrual cycle. Ovarian granulosa and theca cells contain leptin receptors, and leptin decreases the production of steroids by these cells. Recently, it has also been reported that both leptin and its receptors are present in the endometrium.² Trophoblastic cells also secrete leptin causing an elevated leptin concentration during pregnancy reaching to its peak at the twenty-eighth week of gestation, and it almost remains constant after that immediately decrease after parturition.² According to some researchers, abnormal leptin levels are associated with poor prognosis in pregnancy, that is, while low leptin levels have been seen in intrauterine growth retardation.³ High leptin levels have been reported in pre-eclampsia cases.^{2,4,5} Since alteration of leptin level can be results from abnormal development of fetoplacental unit, it is thought that spontaneous miscarriage is associated with altered leptin levels.⁶⁻⁸ There are some differences in the results of previous studies in regard to the relationship between abortion and serum leptin.^{4,8} Makrydimas et al⁶ in their study on the role of leptin in pregnancy failure in the first trimester, observed higher leptin level in coelomic fluid in missed abortion compared to normal pregnancies. They attributed this increase to the impaired oxygenation of placenta leading to an increase in leptin production.⁹ Since in ectopic pregnancy, blastocyst implantation is in places other than endometrial lining of the uterine cavity, we aimed to determine whether there is a difference between ectopic and normal pregnancies with regard to maternal serum leptin levels.

Methods. Maternal serum leptin levels were measured in 2 groups of pregnant women attending the Department of Obstetrics and Gynecology, Afzalipour Medical Centre, Kerman, Iran from January 2009 to February 2010. Group A consisted of 47 women with normal pregnancy and maximum gestational age of 8 weeks, without any general or pregnancy-related pathology. Group B consisted of 47 women with ectopic pregnancy, and the same gestational age as group A. All patients were at stable condition and the diagnosis of ectopic pregnancy was according to serum β -human chorionic gonadotropin (HCG) levels and vaginal ultrasonography. Group A followed by

term for any other complications such as threatened abortion, preeclampsia, intrauterine growth restriction and if there was a previous history of miscarriage or ectopic pregnancy, body mass index equal to or more than 25 and equal or less than 19 kg/m², using drugs during pregnancy except for multivitamin and folic acid, unstable conditions requiring emergency laparotomy, and cigarette smoking were considered as exclusion criteria. The body mass index (BMI [by determining height and weight]), the last menstrual date, and general, as well as obstetric history were recorded at admission time in the clinic, or the Obstetric Ward of Afzalipour Hospital. Then, transvaginal ultrasound scan were carried out to confirm the diagnosis of ectopic and intrauterine pregnancy. Consent forms were filled out by the 2 groups. Blood samples were collected from the antecubital vein, and serum leptin levels were determined using a specific human leptin enzyme-linked immunosorbent assay (ELISA) kit. Conduction of this study was approved by the Research Ethics Committee of Kerman University of Medical Sciences.

Data were analyzed using Statistical Package for Social Sciences version 17 software (SPSS Inc, Chicago, IL, USA). One-way analysis of variance (ANOVA) was used to compare the mean level of leptin and BMI in the 2 groups. A $p < 0.05$ was considered statistically significant.

Results. The mean maternal age was 25.4 ± 4.36 years in group A, and 27.80 ± 3.6 years in group B. Mean gestational age was 7.05 ± 0.69 weeks in group A, and 6.62 ± 0.93 weeks in group B. The BMI was 22.77 ± 1.77 in group A, and 23.17 ± 1.73 in group B. No significant difference was observed between the 2 groups with regard to maternal age, gestational age, and BMI. In group B, the most frequent clinical symptom was vaginal bleeding and abdominal pain (78.7%), and group A had no symptoms and they had been referred just for routine check up. Median (range) serum leptin level in group A was 32.47 (confidence interval [CI]: 28.79-36.19), and in group B, it was 39.93 (CI: 36.22-43.64). Group B had significantly higher serum leptin level in comparison with group A ($p = 0.045$) (Figure 1).

Discussion. It is believed that leptin has an important role in reproduction. Since leptin is produced by trophoblastic placenta cells, its concentration increases during pregnancy reaching to a maximum at approximately the twenty-eighth week, and remains constant after that. Immediate decrease of leptin concentration after parturition shows that most of maternal leptin is of placental source.^{1,2} Many studies have reported high maternal leptin concentrations in the second trimester of pregnancy in women with preeclampsia.⁵ While low concentration of maternal leptin is associated

Disclosure. This study was funded by Kerman Medical University, Kerman, Iran (No. 88/87).

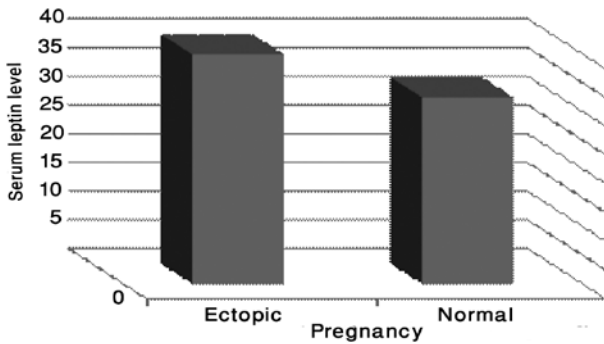


Figure 1 - Serum leptin level in group A (normal) was 32.47 (confidence interval [CI]: 28.79-36.19), and in group B (ectopic) was 39.93 (CI: 36.22-43.64). Group B had significantly higher serum leptin level in comparison with group A ($p=0.045$)

with sub-optimal pregnancy outcomes,^{3,8} fetal birth weight is correlated with neonatal cord blood leptin concentration.^{1,2,9} According to Giovanni et al,⁸ there is no difference in leptin levels in the first trimester of threatened abortion cases, even those that led to complete abortion, and normal pregnancy. Laird et al's⁸ study on women with previous recurrent abortion showed leptin levels significantly lower in miscarried pregnancies in comparison to term pregnancies. The limitation of this study was the maternal serum concentration reflect not only the trophoblast-derived leptin, but the additional contribution from adipocytes. Also, leptin metabolism and clearance maybe different in any woman.

In our study, it had been hypothesized that ectopic pregnancy due to being an abnormal pregnancy may show alterations of leptin level, so we measured the concentration of leptin in blood of women with normal and ectopic pregnancies during the first trimester (until the eighth weeks of gestational age), and based on the obtained results, there was a significant increase of leptin level in ectopic pregnancy compared to normal

pregnancy. This fact can be due to the impairment of placental oxygenation that stimulates production of leptin.

In conclusion, in this present study, leptin level can be considered as a useful marker in the diagnosis of ectopic pregnancy but more studies with larger samples are suggested to confirm this conclusion.

References

1. Cunningham F, Leveno K, Bloom S, Hauth J, Gilstrap L, Wenstrom K, editors. Chapter 9-10. In: Williams Obstetrics. 22nd ed. New York: McGraw Hill; 2005. p. 232-236 & 254-260.
2. Speroff L, Fritz MA. Clinical Gynecology, Endocrinology and Infertility. Baltimore (MD): Lippincott Williams & Wilkins; 2005. p. 663-683.
3. Pighetti M, Tommaselli GA, D'Elia A, Di Carlo C, Mariano A, Di Carlo A, et al. Maternal serum and umbilical cord blood leptin concentrations with fetal growth restriction. *Obstet Gynecol* 2003; 102: 535-543.
4. Laird SM, Quinton N, Anstie B, Li TC, Blakemore AIF. Leptin and leptin binding activity in recurrent miscarriage women; correlation with pregnancy outcome. *Human Reproduction* 2001; 16: 2008-2013.
5. Teppa RJ, Ness RB, Crombleholme WR, Roberts JM. Free leptin is increased in normal pregnancy and further increased in preeclampsia. *Metabolism* 2000; 49: 1043-1047.
6. Baban RS, Ali NM, Al-Moayed HA. Serum Leptin and Insulin Hormone Level in Recurrent Pregnancy Loss. *Oman Medical Journal* 2010; 25: 203-207.
7. Berek JS, editor. Berek & Novak's Gynecology. 14th ed. Baltimore (MD): Lippincott Williams & Wilkins; 2007. p. 1056-1057.
8. Tommaselli GA, Di Spiezio Sardo A, Di Carlo C, Bifulco G, Cerrota G, Cirillo D, et al. Do serum leptin levels have a role in the prediction of pregnancy outcome in case of threatened miscarriage? *Clin Endocrinol (Oxf)* 2006; 65: 772-775.
9. Makrydimas G, Vandecruys H, Sotiriadis A, Lakasing L, Spencer K, Nicolaides KH. Coelomic fluid leptin concentration in normal first-trimester pregnancies and missed miscarriages. *Fetal Diagn Ther* 2005; 20: 406-409.

Related topics

Al-Atawi FS, Addar MH, Wasy AS, Babay ZA. Leptin concentration during different trimesters of pregnancy and its relation to other pregnancy hormones. *Saudi Med J* 2004 Nov;25(11):1617-22.

Babay ZA, Wasy AS, El-Hazmi MA, Addar MH. Leptin level in pregnant mothers at term and cord blood and the effect of newborns gender. *Saudi Med J* 2004 Feb;25(2):212-4.