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ORIGINAL ARTICLE

# Use of serum leptin and insulin hormones levels as predictors of pregnancy outcome in pregnant women with history of recurrent early pregnancy loss

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**KEYWORDS**

Recurrent pregnancy loss;
Leptin;
Insulin

**Abstract** *Aim:* To evaluate levels of leptin and insulin in cases of unexplained early RPL in comparison with cases of previous normal pregnancies and suggest these levels as prognostic factors for the continuation of pregnancy beyond the 20th week.

*Methods:* A prospective comparative controlled study was conducted at Obstetrics unit of Tanta University Hospital from Jan to Aug 2014 on 50 pregnant women who were divided into two groups: the study group included 25 cases with history of early RPL, and the control group included 25 cases with previous normal pregnancies. Serum levels of leptin and insulin were measured twice in both groups; at 5–8th and 10–12th week.

*Results:* Leptin levels in ng/ml in the first sample were 9.414 ± 3.183 and 30.559 ± 10.672 in the control and study groups respectively with significant difference. As for the second sample, it was 11.672 ± 2.611 and 29.733 ± 9.133 in the control and study groups respectively with significant

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difference. Insulin levels in μlU/ml in the first sample were 18.075 ± 5.845 and 32.502 ± 13.057 in the control and study groups respectively with significant difference. In the second sample, on the other hand, it was 20.237 ± 4.944 and 34.128 ± 12.677 in the control and study groups respectively with significant difference. Leptin showed higher accuracy than insulin in prediction of early pregnancy loss.

*Conclusion:* Higher levels of leptin and insulin were found in cases with early RPL especially in the aborted cases. The two hormones could be used as predictors of pregnancy continuation in these cases.



## 1. Introduction

Two or more failed clinical pregnancies before 20 weeks according to the American Society for Reproductive Medicine (ASRM) are defined as recurrent pregnancy loss (RPL). Before considering abortion, the biochemically diagnosed pregnancy must be documented by ultrasound and histological examination (1). Although there are different multiple etiologic factors for RPL, no apparent cause could be found in 50–75% of the cases (unexplained RPL) (2). There are only few evidence-based strategies for diagnosis and treatment of RPL. Intensive research for the cause behind RPL is pursued within immunological and genetic studies (3).

Most of the published studies emphasized on the causes and treatment of unexplained RPL with little effort done for founding a predictor of pregnancy continuation in these cases (4).

Leptin hormone was originally thought to be produced only by adipocytes to modulate satiety and energy (5). However, now it is known to be produced in many other tissues and is responsible for specific events in the reproductive maturity and fertility e.g. implantation, maternal physiological changes, regulation of conceptus development and fetal growth (6–8).

Insulin resistance (IR) and hyperinsulinemia are incriminated as potential causes of the high rate of pregnancy loss and have been linked to the metabolic and endocrine abnormalities associated with the pathphisiologyology of RPL (9,10). Some studies suggested the use of leptin and insulin as predictors for pregnancy continuation beyond 20 weeks in cases of RPL (11).

## 2. Aim of the study

The aim of this study was to evaluate levels of leptin and insulin in cases of unexplained early RPL in comparison with cases of previous normal pregnancies and to suggest these levels as prognostic factors for the continuation of pregnancy beyond the 20th week.

## 3. Patients and methods

This prospective comparative controlled study was conducted in Tanta University Hospital, Obstetrics and Gynecology Department from January 2014 to November 2014. Seventy pregnant women were selected for the study after getting the approval of the hospital ethical committee and full explanation of the study to the women who signed an informed written consent. Half of the selected women had previous two or more normal pregnancy and with no history of abortion, while the other half had a history of previous two or more consecutive first trimester miscarriage with the same partner, and all the previous pregnancy losses were documented by ultrasound and/or histological exam after uterine curettage. Cases of RPL were fully investigated and 35 cases were considered to have unexplained RPL based on the absence of apparent cause after the diagnostic workup (12) which included complete history taking & clinical examination, 2D & 4D ultrasound examination (for exclusion of anatomical malformation e.g. septum, fibroids, adenomyosis, polyps and intrauterine adhesions), hysterosalpingography and/or hysteroscopy, karyotypes of both partners, and the laboratory workup which included screening for diabetes, thyroid function tests, estimation of serum level of prolactin, basal FSH & LH, serum androgen, antiphospholipd antibodies, anticardiolipin antibodies, lupus anticoagulant, study of genetic thrombophilic mutations (factor V Leiden, prothrombin, methylenetetrahydrofolate reductase and Antithrombin III) and proteins C and S.

The inclusion criteria for both groups included age between 20 and 35 years and viable singleton pregnancy between 5 and 12 weeks.

The exclusion criteria for both groups included obesity, ectopic or molar pregnancy, patients with chronic diseases, and history of receiving any relevant hormonal treatment during or shortly before the current pregnancy, previous cervical cerclage and clinical evidence of genitourinary infection.

Each pregnant woman was subjected to the following: Complete history taking, general examination, abdomino-pelvic ultrasound, and routine laboratory investigations. Three ml of fasting venous blood samples was collected from patients in both groups under aseptic precautions by venipuncture, then it was put in a clean plain test tube, after centrifugation, the separated serum was stored at −20 °C until the use. Serum levels of leptin and insulin hormone were measured twice using enzyme-linked immunosorbent assay (ELISA) technique. The first sample was taken at the 5–8th weeks of gestations and the second sample at the 10–12th weeks.

Maternal serum leptin level was determined using the (DRG® Leptin ELISA (EIA-2395) kit which was a solid phase ELISA based on the sandwich principle. Maternal serum insulin level was determined using the (DRG® Insulin ELISA (EIA-2935) kit which was a solid phase ELISA based on the sandwich principle. Both were manufactured by DRG Instruments GmbH, Germany (13).