# Serum CA 125, Progesterone, and βHCG Levels in the Differential Diagnosis of Abortion and Ectopic Pregnancy

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*ABSTRACT*

*This study aimed to investigate the role of serum cancer antigen (CA) 125, progesterone, and beta-human chorionic gonadotropin (βHCG) levels in the differential diagnosis of intrauterine pregnancy, complete or incomplete abortion, and extrauterine pregnancy.*

*This study was carried out in a teaching and research hospital between 2007 and 2009. A total of 175 patients with abortion, tubal ectopic pregnancy, and healthy pregnancy were recruited into the study. Pre- and post-treatment blood levels were compared among the groups.*

*Serum βHCG levels were higher in cases of normal healthy pregnancy than in cases of abortion and ectopic pregnancy. No difference was observed between serum βHCG levels of abortion and ectopic pregnancy cases. The levels of serum CA 125 in abortions were found to be higher compared with the other two groups. The levels of serum progesterone in cases of ectopic pregnancy were found to be lower compared with the other two groups.*

*The utilization of the serum βHCG level in the differential diagnosis of normal/abnormal pregnancies and serum CA 125 and progesterone levels in the differential diagnosis of abortion and ectopic pregnancies are alternative parameters.*

*Key Words: CA 125, complete/incomplete abortion, ectopic pregnancy, βHCG, progesterone*

## INTRODUCTION

In early pregnancy, it is very difficult to distinguish the clinical and laboratory values of normal pregnancies, complete or incomplete abortions, and ectopic pregnancies (1). Late diagnoses can cause troubles that may result in maternal deaths (2). Ectopic pregnancies are still responsible for 10% of maternal deaths in the Western world and are the leading cause of maternal mortality in the first trimester (3). Therefore, they should be diagnosed as soon as possible so treatment can begin.

The solution to this problem is limited to the interpretation of ultrasonography and blood values. While an ultrasonography is dependent on factors such as the experience of the technician and the quality of the device, unlike subjective parameters, blood parameters can increase correct diagnosis rates (4).

The estimation of gestational wellness using one or more hormonal parameters in early pregnancy has been the subject of many studies about the discrimination of normal and abnormal pregnancies. It has been observed that these blood parameters show differences between these groups of patients. The levels of beta-human chorionic gonadotropin (βHCG), cancer antigen (CA) 125, and progesterone in these patients are controversial in the literature (5). The aim of this study was to determine the role of serum βHCG, CA 125, and progesterone levels in the differential diagnosis between abortion and ectopic pregnancies.

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TABLE 1: Demographic characteristics of groups.

|  | Control group (*n*=50) | Abortus group (*n*=50) | Ectopic pregnancy (*n*=75) | *p* |
|---|---|---|---|---|
| Age (year) | 23.6±3.7 (17–34) | 26.5±5.6 (18–41) | 30.5±5.2 (21–43) | <0.001 |
| Gravidity | 1 (1–4) | 2 (1–8) | 3 (1–7) | <0.001 |
| Mean pregnancy week | 7.1 (5-10.4) | 7.3 (5–12) | 5.4 (4–9) | <0.001 |

## MATERIALS AND METHODS

This study was carried out in a teaching and research hospital between 2007 and 2009, and it was approved by the Institutional Review Board. A total of 175 patients suffering from pelvic pain or vaginal bleeding, with complete/incomplete abortion (*n* = 50), tubal ectopic pregnancy (*n* = 75), and healthy intrauterine pregnancy (*n* = 50) were included in the study. Serum βHCG, CA 125, and progesterone levels were compared between these three groups.

The patients were chosen among the intrauterine pregnancies that were proved by ultrasound and resulted in a complete or incomplete abortion less than 12 weeks and tubal ectopic pregnancies that were proved by ultrasound. The control group consisted of patients having an intrauterine pregnancy with a fetal heart rate below 12 weeks. Demographic characteristics, gynecological and obstetric history, and ultrasonographic findings were recorded in the patient evaluation form following the informed consent of the patients. All patients in the study group were assessed by vaginal and ultrasonographic examinations, whereas the patients in the control group were evaluated only by ultrasonography.

Ruptured ectopic pregnancies, pregnancies after infertility treatment, pregnancies with other pathologic conditions that would increase the CA125 level, and pregnancies with progesterone treatment due to abortus imminence were excluded. Since serum βHCG levels could be affected by the gestational week, βHCG levels were corrected according to the gestational week.

At the time of admission, 10 mL of peripheral blood samples were taken from the antecubital vein for βHCG, CA125, and progesterone levels. Repeat samples were taken for βHCG, CA125, and progesterone measurement on days 4 and 7 of single-dose methotrexate therapy for ectopic pregnancies as well as 24 h after revision curettage that resulted in abortion. The samples were assessed on the same day without waiting. Serum measurements of the three parameters were performed by the radioimmunoassay method with a Rosh E 170 Modular Instrument at the nuclear medicine laboratory of the hospital.

## Statistical Analyses

Data were analyzed using SPSS Software for Windows version 11.5 (SPSS, IL, USA). The Shapiro–Wilk test was used to determine whether the distribution of continuous variables was close to normal. Descriptive statistics were expressed as mean ± standard deviation for age and as median (minimum–maximum) for gravida, gestational week, CA125, progesterone, and βHCG. In the case of a large number of parameters, the receiver operator characteristics (ROC) curve was used to assess the diagnostic importance of each.

## RESULTS

The demographic characteristics of the patients, such as age, gravidity, and gestational week, are given in Table 1. A significant difference was found between the groups in terms of age (*P*<0.001). The mean age of the ectopic pregnancy group was significantly higher than that of the control and abortion groups (*P*<0.001 and *P*<0.001). Moreover, the mean age of the abortion group was also higher compared with the control group (*P*=0.013). Mean gravida was different between the groups (*P*<0.001). The gravidity of the abortion and ectopic pregnancy groups was higher than that of the control group (*P*=0.012 and *P*<0.001). No difference was observed between the abortion and ectopic pregnancy groups in terms of mean gravida (*P*=0.073). A significant difference was found between the groups in terms of gestational week (*P*<0.001). The gestational week of the ectopic pregnancy group was lower than that of the control and abortion groups (*P*<0.001 and *P*<0.001). No difference was noted between the control and abortion groups in terms of mean gestational week (*P*=0.952).

A significant difference was observed in terms of CA 125 levels (*P*<0.001). CA 125 levels were significantly higher in the abortus group than in the control and ectopic pregnancy groups (*P*<0.001 and *P*<0.001). No significant difference was found between the control and ectopic pregnancy groups in terms of CA 125 levels (Table 2).

| | Control | Abortion | Ectopic pregnancy | P |
|---|---|---|---|---|
| **TABLE 2: Comparison of CA125, progesterone and ßhcg levels between groups.** | | | | |
| | Median (min-max) | Median (min-max) | Median (min-max) | |
| CA 125 | 27.2 (6.5–64.2) | 53.6 (18.6–743) | 21.1 (3.2–223) | <0.001 |
| Progesterone | 23.1 (8.7–46.5) | 12.6 (3.1–31.4) | 3.8 (0.6–12.3) | <0.001 |
| ßhcg | 25958.8 (2223–182642) | 852.5 (26–33077) | 1400 (178–12169) | <0.001 |

A significant difference was observed between the groups in terms of progesterone levels ($P<0.001$). The progesterone levels of the ectopic pregnancy group were significantly lower than those of the control and abortion groups ($P<0.001$ and $P<0.001$). At the same time, the progesterone level of the abortion group was also significantly lower than that of the control group ($P<0.001$).

Significant differences were also found between the groups in terms of βHCG levels ($P<0.001$). βHCG levels of the abortion and ectopic pregnancy groups were lower than those of the control group ($P<0.001$ and $P<0.001$). No significant difference was observed between the ectopic pregnancy and abortion groups in terms of βHCG level ($P=0.144$). Because βHCG levels were clinically affected by the gestational week, βHCG levels of the ectopic pregnancy and abortus groups remained lower compared with the control group when the effect of the gestational week was ruled out ($P<0.001$ and $P<0.001$).

It was seen that CA125 was a significant determinant when distinguishing the abortion group from the control and ectopic pregnancy groups. The area under the curve of CA125 (95% confidence interval) was 0.892 (0.840–0.944). The best cut-off point was 39.77. The sensitivity, selectivity, and positive and negative predictive values for this point were, respectively, 86%, 87.2%, 72.9%, and 94% (Figure 1).

When corrected according to the gestational week, the sensitivity, selectivity, and positive and negative predicted values at the cut-off points determined for the βHCG level were not changed while distinguishing the ectopic pregnancy and abortion groups from the control group.
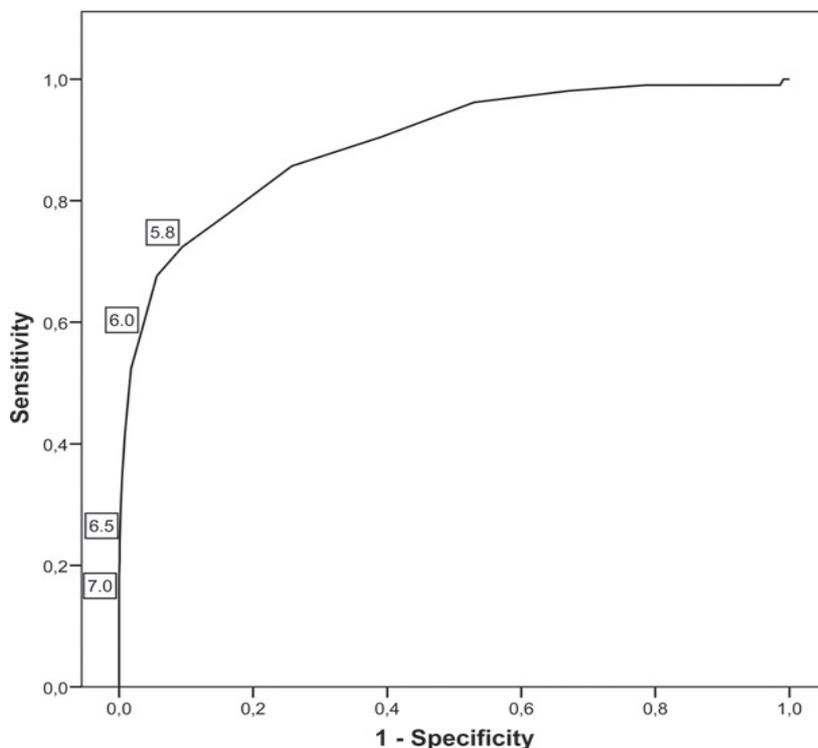


FIGURE 1: ROC curve of serum CA 125 level with ectopic pregnancies.

A significant decrease was found in CA125, progesterone, and βHCG levels after revision curettage within the abortion group, according to the admission ($P<0.001$, $P<0.001$, and $P<0.001$, respectively).

In the ectopic pregnancy group, after single-dose methotrexate treatment, a statistically significant difference was observed in recurrent CA125, progesterone, and βHCG levels ($P<0.001$, $P<0.001$, and $P<0.001$). A statistically significant decrease was detected in CA125, progesterone, and βHCG levels on the fourth and seventh days compared with the levels on admission ($P<0.001$). A statistically significant decrease was detected in CA125, progesterone, and βHCG levels on the seventh day compared with the levels on the fourth day ($P<0.001$).

## DISCUSSION

Abdominal pain and other gynecologic causes of vaginal bleeding should be considered in the differential diagnosis of ectopic pregnancies, one of which is an intrauterine abortion. An anamnesis, physical examination, and ultrasonography are often inadequate in distinguishing these two clinical situations, and some biochemical and hormonal parameters such as serial measurements of βHCG level can be used for a differential diagnosis (6).

Despite variations according to age and gravida, no difference was found between the groups. It is assumed that the situation did not affect the results of the study because it is known that no age-related changes in the examined parameters exist among the patients appropriate for pregnancy.

The gestational week was found to be higher during the first evaluation in the control group because abortion and ectopic pregnancies were detected more frequently in the early weeks of gestation, and the pregnancies were normal in the control group. The βHCG was corrected to fit the gestation week of patients with abortion and ectopic weeks.

The serum βHCG levels of the abortion and ectopic pregnancy groups were significantly lower than those of the control group in this study ($P<0.001$, $P<0.001$). No significant difference was observed between the ectopic and abortion groups ($P=0.144$).

βHCG is a valuable biochemical marker in pregnancy. It is known that first-trimester serial βHCG measurements may be a good parameter to distinguish whether the trophoblastic function isnormal (7). Lower levels than those in the gestational week are important for the diagnosis of ectopic pregnancy (8). Serial βHCG measurements are reported to be more valuable than one βHCG measurement, despite publications that advocate a reversal (9).

Below-normal βHCG measurements in the first trimester predict a spontaneous abortion (10).

Statistically significant differences were observed between groups in terms of CA125 in this study ($P<0.001$). CA 125 levels of the abortion group were statistically higher than those of the control and ectopic pregnancy groups ($P<0.001$, $P<0.001$). No statistically significant difference was found between the control and ectopic pregnancy groups in terms of CA125 levels ($P=0.05$).

The source of serum CA125 levels in pregnant women is the endometrial glands in the decidua (8). Maternal serum CA125 levels may vary during pregnancy. They increase markedly in the first trimester and then decrease to a normal level in the second and third trimesters (11). Studies have shown that events causing damage to decidua and fetal membranes lead to an increase in maternal serum CA 125 levels (12). Maternal serum CA125 levels may guide determining the prognosis of pregnancy, as well as the degree of damage of the decidual and fetal membranes (13). This describes the increase in CA125 due to the damage in fetal membranes and endometrium in abortions. The literature showed that CA 125 increased in abortions according to normal pregnancies and the relative increase in CA 125 levels because of the lack of fetal membrane and endometrial destruction in normal pregnancy and extrauterine pregnancies until rupture (11). A similar result was found in the present study. On the contrary, other researchers found no difference between abortions and ectopic pregnancies and discerned low levels of CA 125 in relation to normal pregnancies (14). In another study, the CA 125 level was highest in abortions, less in normal, and least in ectopic pregnancies (15). It is thought that this divergence between the studies is due to the difference in the number of pregnancies, the volume of the pregnancy, and damaged tissue volume.

The other parameter in the present study, progesterone hormone, is secreted from the corpus luteum until the seventh week of pregnancy. The placenta starts secreting progesterone with the corpus luteum between the seventh and tenth weeks and continues producing it alone after the tenth week. Low progesterone levels are usually associated with abnormal pregnancies (abortive, ectopic) (16). However, the specific level determining abnormal pregnancy is not known. Serum progesterone levels in ectopic pregnancies are below 15 ng/mL, and this level does not coincide with the levels in normal pregnancies (17). The level in the present study was found to be similar to the mean level of 3.8 ng/mL, and values less than 5 ng/mL showed nonviability. Serum progesterone levels were below 15 ng/mL in 81% of ectopic pregnancies, while serum progesterone levels were below 11 ng/mL in 11%

of normal pregnancies (1). Similar results were obtained in the present study. If the cut-off value is taken as 25 ng/mL, 95% of the cases above this level showed that the pregnancy was normal (18). The present study results were found to be similar to those described in the literature. Some studies showed that it was normal in abortion (19), and some showed that the progesterone level had no prognostic significance (20). It seems that different studies in the literature provide divergent results about the importance of progesterone. Also, the serum βHCG, CA125, and progesterone levels were re-evaluated on the fourth and seventh days of single-dose methotrexate treatment in ectopic pregnancies and at the 24th hour after revision curettage in abortion cases. A statistically significant decrease in post-treatment values was observed according to the values at the time of admission ($P<0,001$, $P<0,001$). Similar results were reported in the literature (21).

Therefore, it is thought that these parameters have a prognostic value in the evaluation of the response to treatment.

Consequently, the present study investigated the prognostic significance of serum βHCG, CA125, and progesterone levels in differentiating ectopic pregnancies from intrauterine abortions. Serum βHCG levels have prognostic significance in discriminating between normal and abnormal pregnancies. However, it is not an effective and reliable parameter to distinguish abnormal pregnancies. The serum CA125 level can be used as an alternative parameter in discriminating ectopic pregnancies and abortions because it is significantly higher in abortion cases compared with ectopic pregnancy and normal pregnancies. The serum progesterone level has a prognostic value in discriminating ectopic pregnancies and abortions; however, further research is needed on cut-off values.

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