



# CA-125 levels in threatened abortion, ectopic, and normal pregnancy

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## ABSTRACT

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**Background:** Determination of the best diagnostic methods for ectopic pregnancy (EP) and threatened abortion is important specially to improve the final prognosis. The aim was to determine the CA-125 level in cases of EP and threatened abortion in comparison with control subjects.

**Materials and Methods:** In this descriptive cross-sectional study, 90 consecutive women attending to Shohada-e-Tajrish and Mahdiah Hospitals in Tehran including those with EP and threatened abortion and control subjects were enrolled where CA-125 level was determined and compared across the three groups.

**Results:** CA-125 level was significantly different across the groups ( $P < 0.005$ ) and in paired comparisons it was higher in threatened abortion cases versus control subjects ( $P < 0.003$ ). However, it was not significantly different between the other groups ( $P > 0.05$ ).

**Conclusion:** Overall, it was found that the serum CA-125 level was higher in threatened abortion cases but not significantly in EP cases. Hence, use of this marker may be helpful in diagnosis of threatened abortion.



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## INTRODUCTION

Ectopic pregnancy (EP) is a leading cause of maternal morbidity. This high risk condition has an occurrence of 2% in reported pregnancies; a fivefold increase from the 1970s. EP is responsible for pregnancy-related mortality in the first trimester and has a negative effect on future pregnancies since less than half the affected can conceive later [1-3].

Today, early intervention is key to reducing morbidity and saving lives. Meanwhile, 4% to 10% of pregnancy related mortality is caused by ectopic pregnancy which leads to a high incidence of ectopic site gestations in subsequent pregnancies [4, 5]. EP predominantly occurs among 35-44 year-old females [6]. If ultrasound was not capable of visualizing an ectopic pregnancy, diagnosis can be a challenge [1]. Currently not many early diagnostic methods have been found; therefore, the use of serum biomarkers is being investigated to enhance the speed and accuracy of detecting EP and differentiating it from a threat to abortion.

An affected individual produces a serum biomarker which can be detected in serum indicating the disease status. Early diagnosis and prognosis prediction for EP is possible with a specific biomarker for EP. The only biomarker available in clinical practice is human chorionic gonadotropin ( $\beta$ -HCG) [1, 7].

Several studies have recently been conducted on the level of CA-125 in mothers' serum to assess pregnancy and especially early detection of EP and abortion. In most studies, it has been concluded that the level of CA-125 in EP has been significantly higher than in intrauterine pregnancy and abortion threat cases. Since the comparison of CA-125 levels in intrauterine pregnancy and EP had not been accurately investigated in our country, this study examined the level of CA-125 in women in our region.

## MATERIALS and METHODS

This descriptive cross-sectional study was performed on 90 participants including 30 patients with ectopic pregnancy, 30 patients with abortion, and 30 with normal pregnancies in Shohada-e-Tajrish and Mahdih hospitals in Tehran in 2017. All women under study were aged 25-35 and were between 6-8 weeks of gestation. The 30 patients with ectopic pregnancy were diagnosed through HCG serum and ultrasonography, and definitive diagnosis was made by surgery or laparoscopy. Thirty patients with abortion threats were women with gestational age of 6 to 8 weeks with uterine and cervical bleeding with normal  $\beta$ -HCG levels, visible gestational sac in the uterus, and fetal heart using ultrasonography. Cases in the control group were chosen from women who attended for routine pregnancy checkups. These cases had a similar gestational age and maternal age as all others in our study. Then, their CA-125 levels were measured and they were followed up for 20 weeks for continued normal pregnancy. All pregnancies were singleton and occurred spontaneously.

Exclusion criteria for this study included all elements that increased CA-125. Therefore, all pregnant women who had a history of severe pelvic infection, ovarian cyst, endometriosis, uterine and endometrial myoma, and subjects with kidney, lung and liver disease were excluded.

The information about each patient was recorded in the ques-

tionnaire, including patient characteristics such as maternal age, gestational age, parity, gravidity, and abortion. All patients with an abortion risk were monitored for 20 weeks for continued pregnancy. On the other hand, patients with perforated and unperforated ectopic pregnancy were separated and the serum CA-125 level was measured by radio-immunoassay method.

Data analysis was executed using SPSS version 24 software. The tests used included Pearson regression, ANOVA, Tukey, and T-test. The significance level was considered to be 0.05. This study was approved by the ethics committee of Shahid Beheshti University of Medical Sciences.

## RESULTS

A total of 90 individuals were participated in this cross-sectional study. They were divided into three equal groups: normal pregnancy, ectopic pregnancy, and abortion. The mean age and standard deviation (SD) for each group is presented in Table 1.

Table 1. Mean age and SD for three groups under study

Group	Mean age $\pm$ SD
Normal pregnancy	29.47 $\pm$ 3.0
Ectopic pregnancy	29.50 $\pm$ 3.3
Abortion	29.57 $\pm$ 3.1

Gravidity, parity, abortion, and gestation were not significantly different between the three groups (Table 2).

Table 2. Mean $\pm$ SD of gravidity, parity, abortion, and GA in normal and ectopic pregnancy and abortion. GA = Gestational Age.

Group	Gravidity	Parity	Abortion	GA*
Normal pregnancy	1.67 $\pm$ 0.661	0.30 $\pm$ 0.466	0.33 $\pm$ 0.547	7.00 $\pm$ 0.743
Ectopic pregnancy	1.80 $\pm$ 0.761	0.33 $\pm$ 0.547	0.40 $\pm$ 0.621	6.93 $\pm$ 0.740
Abortion	1.73 $\pm$ 0.785	0.40 $\pm$ 0.621	0.33 $\pm$ 0.606	6.93 $\pm$ 0.691
P-Value	0.819	0.898	0.868	0.920

The mean CA-125 was 18.3 $\pm$ 5.5 for normal pregnancy group, 22.4 $\pm$ 12 for ectopic pregnancy group, and 26.7 $\pm$ 9.9 for abortion group. However, CA-125 levels were significantly different between the three groups ( $P < 0.005$ ). The mean CA-125 was significantly higher in abortion group compared to the normal group (26.7 vs. 18.3,  $P < 0.003$ ). On the other hand, the mean level of CA-125 in ectopic pregnancy group was higher than in normal pregnancy group (22.4 vs. 18.3,  $P = 0.23$ ), though this difference was not statistically significant. The mean level of CA-125 in abortion group was higher compared to ectopic pregnancy group (26.7 vs. 22.4,  $P = 0.197$ ), yet this difference was not statistically significant either (Fig. 1).

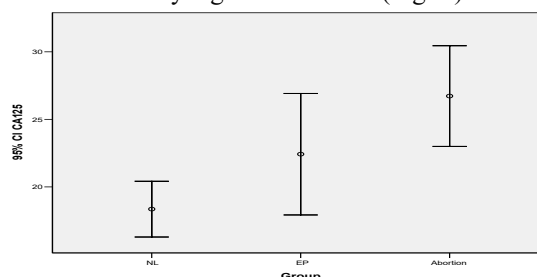


Fig. 1. Comparison of the levels of CA-125 between the three groups. (NL=Normal, EP=Ectopic Pregnancy)



## DISCUSSION

The results of this study indicated that women with abortion had a significantly higher level of CA-125 compared to women with normal pregnancy. CA-125 level was higher in women with abortion compared to ectopic pregnancy group as well as in ectopic pregnancy group compared to normal group; however, these differences were not statistically significant.

The importance of CA-125 in diagnosis of ectopic pregnancy and abortion has been evaluated by other studies. Katsikis et al. conducted a study in Greece in 2006 on 40 EP patients and 20 patients with intrauterine abortion and 20 normal pregnancies. All cases of abortion and ectopic pregnancy were confirmed by surgery. The levels of progesterone and CA-125 were measured at visit time and 24 hours later. This study suggested that in cases of abortion, the CA-125 level was clearly higher [8]. Schmidt et al., showed in their study in Greece in 2001, that measuring CA-125 alone in symptomatic patients in the first trimester of pregnancy cannot distinguish between spontaneous abortion, intrauterine, and ectopic pregnancy. However, it can predict the risk of abortion in intrauterine pregnancy [9]. These results are consistent with the findings of our research. Further, the study conducted by Condous et al. showed that the level of CA-125 in combination with serum  $\beta$ -HCG contributes greatly to the differentiation of intrauterine pregnancy from a high-risk EP case. In this study, 153 cases of abortion and 116 normal pregnancies as well as 28 EP cases were investigated. They found that CA-125 levels help differentiate intrauterine pregnancy from abortion, yet that is not the case in differentiating EP from abortion [10]. In our study, we also concluded that there was no significant difference between CA-125 in EP groups and the risk of abortion.

In a study by Butler et al. in 2013 in London, 175 normal pregnancy, 175 abortion, and 26 EP cases were chosen. It was concluded that a cutoff point of 41/98 u / ml for CA-125 levels in intrauterine abortion is able to distinguish EP from abortion with sensitivity of 100% and specificity of 43% [11], which is in line with our findings.

Fiegler et al. concluded in a 2003 study that based on the level of CA-125, pregnancies with risk of abortion can be distinguished from normal pregnancies [12]. These results are compatible with ours.

On the contrary, an analytical study by Predanic et al. in 2000 in the United States, after evaluation of 26 pregnant women, reported that serum CA-125 marker levels in EP cases were significantly higher than in normal pregnancies [13]. However, in our research, this difference was not significant. These results were similar to the findings of a study conducted by Meena M et al. in 2011. In this study, CA-125, progesterone, estradiol, and  $\beta$ -HCG levels were measured in 40 symptomatic EP patients and 24 intrauterine pregnant women at 4-10 weeks in Baghdad Hospital. It was shown that CA-125 is significantly higher in ectopic pregnancy than in normal pregnancy [14]. These results contradict our findings since we observed this value as insignificant.

Furthermore, another study on 188 pregnant women suggested that abortion cannot be determined using CA-125 levels [15].

## Conclusion

Overall, it is recommended that further studies be conducted to confirm the findings of this study with a larger sample size. Also, further studies on other diagnostic methods for EP and abortion threats should be considered in the future.

It was ultimately attained that the level of CA-125 is elevated in cases of abortion; however, in cases of ectopic pregnancy, this increase is not significant. Accordingly, it is recommended to use it for detecting the risk of abortion and distinguishing it from other pathological conditions.

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