

**Role of CA 125 Levels in Predicting the Outcome of Threatened Abortion**Shahnaz Parveen<sup>1</sup>, Mohammad Monis Khan<sup>2</sup>, Kamal Aziz<sup>3</sup><sup>1</sup> Assistant Professor, Dept. of Pathology, Al Falah School of Medical Science & Research Centre, Faridabad<sup>2</sup> Assistant Professor, Dept. of Physiology, Al Falah School of Medical Science & Research Centre, Faridabad<sup>3</sup> Radiologist & Director, DKI&D Centre, Jamia Nagar, New Delhi - 110025

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**Abstract:**

**Background:** A higher CA-125 level could be caused by genital or non-genital causes. Its levels rise early in pregnancy and shortly after delivery, suggesting that the maternal decidua and amnion have disintegrated. This suggests that any damage to the decidua or the basement membrane of the fetus would result in an increase in maternal CA-125 and indicate a subsequent miscarriage. We undertook the current study with this objective in mind in order to assess the prognostic role of CA-125 in predicting the pregnancy outcome in cases of threatening abortion.

**Methods:** From June 2021 to May 2022, this prospective hospital-based observational study was carried out at the Obstetrics and Gynecology department of a tertiary care hospital in New Delhi. 160 pregnant women (20–40 years old) with gestational ages ranging from 7 to 14 weeks participated in the study and reported vaginal bleeding. All of the patients' features, including their age, gravidity, gestational period, and ultrasonographic findings, were identified, and information was gathered. The women in the study group were tracked prospectively from their initial session until gestational outcome and patients were classified into 2 groups Group (A): Abortion (cases) and Group (B): Delivered (controls). Each patient had 5 ml of venous blood drawn to measure the serum level of CA-125. The data was entered into an MS Excel spreadsheet and used there for analysis.

**Results:** Out of 160 pregnant women, 68 (42.5%) were cases of abortions and remaining 92 (57.5) were cases of delivery. The baseline characteristics of the cases and controls were comparable as difference in age, BMI, gestational age at presentation, gravida, parity and previous abortions were non-significant ( $p > 0.05$ ). In cases the mean CA-125 levels were higher  $101.23 \pm 63.81$  IU/mL when compared with the controls  $37.33 \pm 23.76$  IU/mL and this difference was statistically significant ( $p < 0.05$ ). We also, derived the cut off for the CA-125 levels to predict the risk of abortion and cut derived was 63.21 IU/mL at the sensitivity and specificity of 85.21% and 91.43% respectively, with an accuracy of 90.65%.

**Conclusion:** Every pregnant woman who has bleeding in the early stages of her pregnancy may find it perplexing; up to 50% of such pregnancies are typically lost. We were able to distinguish better between pregnancies with a positive result and those without attributable to the analysis of maternal serum CA-125 levels.

**Keywords:** Pregnancy, CA-125, fetus, ROC, period of gestation

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**Introduction**

The loss of a pregnancy before the fetal viability age, or at a point when the embryo or fetus is unable to survive on its own, is referred to as an abortion. According to the WHO, an abortion is the ending of a pregnancy before 20 weeks of pregnancy or the delivery of a fetus that weighs less than 500 grams. [1]

The signs and symptoms of a threatened abortion include vaginal bleeding during the first trimester of pregnancy, no cervical dilatation, and normal fetal heart activity on an ultrasound. [2] According to reports, it affects roughly one-fifth of pregnancies,

causes miscarriage in 3–16% of cases, and places a heavy emotional and financial strain on the mother and her family. It is difficult for the doctor to predict the outcome of a threatened abortion because of the lack of clarity in doing so. [3]

Although numerous studies have been conducted, the outcomes of threatening abortions have not been satisfactorily predicted using ultrasonographic and biochemical markers. Biochemical markers include CA-125, serum beta-HCG, progesterone, HPL, and AFP are frequently investigated. The mucin family of

glycoproteins, which includes CA-125, is found in tissue generated from embryonic coelom. [4] A higher CA-125 level could be caused by genital or non-genital causes. High quantities of CA-125 are seen in human amniotic fluid, with amnion being the main source. [5] Its levels rise early in pregnancy and shortly after delivery, suggesting that the maternal decidua and amnion have disintegrated. This suggests that any damage to the decidua or the basement membrane of the fetus would result in an increase in maternal CA-125 and indicate a subsequent miscarriage. [6]

Therefore, it is urgent to determine whether CA-125 can be employed as a biochemical marker to forecast pregnancy outcomes in cases where abortion is threatened. We undertook the current study with this objective in mind in order to assess the prognostic role of CA-125 in predicting the pregnancy outcome in cases of threatening abortion.

### Materials and Methods

From June 2021 to May 2022, this prospective hospital-based observational study was carried out at the Obstetrics and Gynecology department of a tertiary care hospital in New Delhi. 160 pregnant women (20–40 years old) with gestational ages ranging from 7 to 14 weeks participated in the study and reported vaginal bleeding. The cases were from the obstetrics and Gynecology unit's inpatient and outpatient departments. The study excluded pregnant women having a history of endometriosis, chronic pelvic infection, gynecological disease, uterine abnormalities, history of recurrent miscarriages, or pregnancy induced by assisted reproductive technology. The participants gave their written consent after receiving complete information. All of the patients' features, including their age, gravidity, gestational period, and ultrasonographic findings, were identified, and information was gathered. They underwent thorough systemic, general, and obstetric exams as well as a thorough history and physical examination. Their blood was drawn, and samples submitted for tests on their liver, kidneys, and ABO Rh, viral markers, and serum CA 125 levels. Sonographic testing was done on all participants to determine gestational age, fetal viability, and intrauterine single gestation. The women in the study

group were tracked prospectively from their initial session until gestational outcome and patients were classified into 2 groups Group (A): Abortion (cases) and Group (B): Delivered (controls). The hospital records were consulted for outcome information, which was then verified, if necessary, via telephone follow-up. Each patient had 5 ml of venous blood drawn to measure the serum level of CA-125. After the blood sample had clotted, the serum was extracted using a sterile pipette within an hour after collection by centrifugation after being separated from the cells. The samples were held refrigerated at 2-8 °C. Using the ADVIA Centaur, chemiluminescent immunometric analysis of serum CA-125 levels was performed.

### Statistical Analysis

The data was entered into an MS Excel spreadsheet and used there for analysis. While nominal/categorical variables were summarised as a proportion (%), continuous variables were presented as mean and standard deviation. Continuous variables were compared using the unpaired t test, whereas nominal or categorical values were compared using the Chi square test. Moreover, ROC curve analysis was performed to determine the proper serum CA 125 cutoff to distinguish between abortion cases and delivered controls. P values under 0.05 were considered significant.

### Results

In our study, we followed the 160 pregnant women presenting with complaints of vaginal bleeding till the outcome as abortion (cases) or delivery (controls). Out of 160 pregnant women, 68 (42.5%) were cases of abortions and remaining 92 (57.5) were cases of delivery. The mean gestational age at time of presentation was 10.82±1.58 weeks for cases and was 10.73±1.52 weeks for controls. The mean age of cases was 26.16±4.59 years and for controls it was 27.03±4.68 years. History of previous abortion was reported in 38.2% of cases and 30.4% of controls. The baseline characteristics of the cases and controls were comparable as difference in age, BMI, gestational age at presentation, gravida, parity and previous abortions were non-significant (p>0.05) (Table 1).

**Table 1: Baseline characteristics of the study subjects**

Variables	Frequency (%) / Mean ± SD		P value
	Cases (n=68)	Controls (n=92)	
Age (in years)	26.16±4.59	27.03±4.68	0.243
BMI (kg/m <sup>2</sup> )	24.35±5.21	24.63±5.01	0.732
Gestational age at presentation (in weeks)	10.82±1.58	10.73±1.52	0.716
Gravida			
1	39 (57.4)	42 (45.7)	0.342
2	17 (25.0)	29 (31.5)	

3 or more	12 (17.6)	21 (22.8)	
Parity			
0	28 (41.2)	38 (41.3)	0.085
1	14 (33.6)	37 (40.2)	
2 or more	17 (25.0)	17 (18.5)	
Previous abortions			
No	42 (61.8)	64 (69.6)	0.302
Yes	26 (38.2)	28 (30.4)	

In cases the mean CA-125 levels was higher 101.23±63.81 IU/mL when compared with the controls 37.33±23.76 IU/mL and this difference was statistically significant ( $p<0.05$ ). We also, derived the cut off for the CA-125 levels to predict the risk of abortion and cut derived was 63.21 IU/mL at the sensitivity and

specificity of 85.21% and 91.43% respectively, with an accuracy of 90.65%. So, 73.5% of cases were having cut off level of >60 IU/mL, and only 14.1% of controls were having cut off level of >60 IU/mL ( $p<0.05$ ) (Table 2).

**Table 2: Comparison of CA-125 levels and period of Gestation with the outcome in the study subjects**

Variables	Frequency (%) / Mean ± SD		P value
	Cases (n=68)	Controls (n=92)	
CA-125 (IU/mL) levels	101.23±63.81	37.33±23.76	< 0.0001
CA-125 (IU/mL) cut off			
60 or less	18 (26.5)	79 (85.9)	< 0.0001
>60	50 (73.5)	13 (14.1)	
Period of gestation at delivery			
<37 weeks	65 (95.6)	22 (23.9)	< 0.0001
37 weeks or more	3 (4.4)	70 (76.1)	

## Discussion

Predicting the outcomes of patients whose threatening abortions occur in the early stages of gestation is critical from a clinical standpoint. In order to use as a predictor of impending abortion, specific biomarkers had been studied. In the current study, we used serum CA-125 measurement to predict the outcome of a threatened abortion. In our study, patients in the threatened abortion group had mean serum CA-125 levels that were higher than those of patients in the normal pregnancy group at the same gestational weeks ( $p<0.0001$ ). Many research explored the value of maternal serum CA-125, but the outcomes were conflicting.

Recent studies have shown that individuals who miscarried had serum CA-125 levels that were considerably greater than those of patients who had a successful outcome. [6] Fiegler et al. found that in 200 women with threatened miscarriage, a single CA-125 concentration of at least 43.1 IU/mL was associated with a higher risk of abortion, and that high CA125 concentration was a strong predictor of threatened miscarriage. [7] Witt et al., observed higher levels in the serum of symptomatic individuals who had abortions and lower serum CA 125 levels in asymptomatic pregnant patients. [8] According to Kamiski et al., patients with threatened abortions had higher CA125 values

than patients in the control group. The women with the highest CA-125 levels later had abortions. [9]

In our study, among the cases the mean CA-125 levels were higher (101.23±63.81 IU/mL) when compared with the controls (37.33±23.76 IU/mL) and this difference was statistically significant ( $p<0.05$ ). In a prospective study involving 80 pregnant women, Hamed et al., found that the level of CA-125 was 19.37±1.64 IU/mL in those who carried their pregnancy to term, compared to 41.04±7.55 IU/mL in those who those who had an abortion ( $p<0.01$ ). The results of their study indicated that serum CA-125 measurements are not only diagnostic but also have good predictive value for pregnancy outcome. [10] In a case-control study involving 167 pregnant women between 6 and 12 weeks along, Mohammed et al., found that the level of CA-125 in women who were at risk of miscarriage was 51.2±22.9 IU/mL and the level in the control group was 22.3±6.7 IU/mL. When compared to the control group, it was discovered that the threatened miscarriage group had significantly higher serum levels of CA-125 ( $p<0.001$ ). [11]

In our study, we also, derived the cut off for the CA-125 levels to predict the risk of abortion and cut derived was 63.21 IU/mL at the sensitivity and specificity of 85.21% and 91.43% respectively, with an accuracy of 90.65%. According to a study conducted by

Yadav et al., on 200 pregnant women, maternal serum CA-125 has a cutoff level of 61.64 IU/mL that is 84.21% sensitive and 96.77% specific for predicting abortion. [12]

Some other previous research determined that the mean CA-125 level of patients with favourable outcomes was significantly higher than that of patients who aborted. [13,14] Schmidt et al., demonstrated in patients with symptomatic first-trimester pregnancy that single measurements of CA-125 failed to distinguish between spontaneous miscarriage and ectopic pregnancies from normal conditions. They did, however, demonstrate that in these patients, sequential measurements of serum CA-125 were a very sensitive prognostic marker. [15] However, some studies propose that CA-125 assessment in the first trimester cannot effectively predict pregnancy outcomes due to the vast overlap of ranges. [16]

### Conclusion

Every pregnant woman who has bleeding in the early stages of her pregnancy may find it perplexing; up to 50% of such pregnancies are typically lost. We were able to distinguish better between pregnancies with a positive result and those without attributable to the analysis of maternal serum CA-125 levels. Because it would enable tighter prenatal surveillance, earlier diagnosis, and quicker interventions, accurate first-trimester prediction of abortion has the potential to enhance pregnancy outcomes. To validate the results and broaden the application of the CA-125 prognostic tool in threatened pregnancies, clinician researchers must now decide on likely various cut off levels of serum CA 125.

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