

Role of serum cancer antigen CA-125 in the First Trimester Threatened Miscarriage

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Abstract

Background: Threatened Obstetricians are quite concerned about miscarriage occurring during the first trimester. It is still a clinical problem to identify pregnant women at risk of miscarriage early on. One promising serum biomarker for the prediction of unfavourable pregnancy outcomes is CA-125. The purpose of this research was to determine if serum CA125 has a predictive role in threats of abortion during the first trimester and in the 20-week follow-up. Methods: A cross-sectional research was conducted with 90 participants, 45 of whom were pregnant normally (Group A) and 45 of whom were pregnant with a risk of miscarriage (Group B). Following a defined procedure, thorough clinical evaluations were carried out, which included obtaining medical history, doing physical exams, conducting laboratory investigations, performing transvaginal ultrasounds, and evaluating CA-125 levels. Up to the 20th week of pregnancy, patients were monitored. It was shown that the group experiencing a miscarriage had significantly higher serum CA-125 levels (77.55 ± 26.38 IU/ml vs. 42.97 ± 14.09 IU/ml, $p < 0.0001$). With a sensitivity of 91.7% and specificity of 86.4%, a CA-125 cut-off value of 31.87 was associated with a statistically significant increased risk of miscarriage. Results: There is a strong correlation between elevated blood CA-125 levels and certain clinical indicators and the risk of miscarriage during the first trimester.

Keywords: Risk of Miscarriage in the First Trimester, Transvaginal Ultrasound, and Early Pregnancy Evaluation with Serum CA-125.

1. Introduction

Abortion refers to the medical condition in which a pregnancy fails before the 20th week of gestation. Scarce, inevitable, incomplete, full, septic, and missed abortions are the many forms of spontaneous abortion. In the event of vaginal bleeding before to 20 weeks of gestation, a positive urine and/or blood pregnancy test, a closed cervical os, the absence of passage of products of conception, and the absence of signs of foetal or embryonic death are all necessary conditions for a threatened abortion. When a woman has bloody vaginal discharge or open bleeding during the early half of her pregnancy without cervical dilatation, the World Health Organization (WHO) considers this a hazard to abortion [1].

Approximately half of the pregnant women who have vaginal bleeding in the first two trimesters go on to miscarry their baby. In most cases, a threatened abortion will cause mild to moderate bleeding. Intermittent cramping, pain above the pubic area, pressure in the pelvis, or discomfort in the lower back are all possible symptoms of abdominal pain [2].

It is not always possible to pinpoint the precise cause of an abortion danger. At least half of all spontaneous abortions are likely caused by chromosomal abnormalities, and it is generally believed that this makes them completely preventable or modifiable [3].

Typical signs of a miscarriage include mild bleeding, a brownish-looking discharge (like

coffee grounds), spotting, bright red blood, tissue passing through the vagina, stomach discomfort or cramping, and a gradual waning of pregnancy symptoms including nausea and tenderness in the breasts [...].

CA-125 has the potential to be a marker for the future of pregnancy outcomes. Carbohydrate antigen 125, also known as cancer antigen 125, is a high molecular weight glycoprotein found on the surface of cells in embryonic coelomic and decidua tissue. Its primary source is the amnion, and it is present in high concentrations in human amniotic fluid [5].

An increase in the mother's CA 125 level during pregnancy may be an indicator of a future spontaneous abortion if the decidua or the foetal membrane's epithelial basement membrane is disrupted. During early pregnancy and just after delivery, its levels are higher than usual. This suggests that the tumour marker rise might be caused by the dissolution of the maternal decidua, which includes blastocyst implantation and placental separation [6].

The health care system is burdened and cost more by the several prior research that examined various US predictors and found varying predictive capacities for the continuation of the pregnancy after a first trimester threatening miscarriage. However, these studies all included repeated US scans. Urgent ultrasounds should be scheduled at intervals of 7 to 10 days under these conditions [7].

The purpose of this research was to determine if serum CA125 has a predictive role in threats of abortion during the first trimester and in the 20-week follow-up.

2. Patients and Methods

Patients:

This The 90 participants in this cross-sectional research were recruited from Benha University's Obstetrics and Gynecology clinics using a systematic random procedure. The research did not proceed until it had received approval from the Research Ethics Committee at Benha University's Faculty of Medicine. Every single participant gave their informed permission.

Individuals were divided into two categories: There were 45 women in Group A who had a healthy pregnancy, and 45 women in Group B who were at risk of abortion due to vaginal bleeding throughout the first trimester.

Women with a gestational age of 6–13 weeks, who were in their twenties to thirties, were eligible to participate. The study's participants were women who were expecting a single child, who were experiencing vaginal bleeding or spotting, and whose ultrasound results confirmed the pregnancy.

Women who were previously ectopic, had a history of uterine abnormalities, endometriosis, or twin pregnancies were not eligible to participate in the study. Neither were pregnant women who had a history of ectopic pregnancies.

Methods:

Every single subject who took part in the trial followed the exact same protocol:

Different groups were formed from the eligible subjects: Every pregnant woman in the control group was carrying a healthy baby. This group was continuously monitored during the trial. Participants who had problems throughout their pregnancy or vaginal bleeding were not included in the research. Those expecting a child who started bleeding vaginally in the first trimester were part of the case group (6-13 weeks).

Every participant was subjected to a thorough process that included:

Summarize the History: This required collecting detailed information, including demographics like name, age, parity, place of residence, profession, and health history (including smoking). Parity, Gravida, prior delivery information, abortion history, abortion frequency, history of sibling death, gestation time, and a complete pregnancy history were all part of the documentation. In addition to the present complaint, it included the patient's

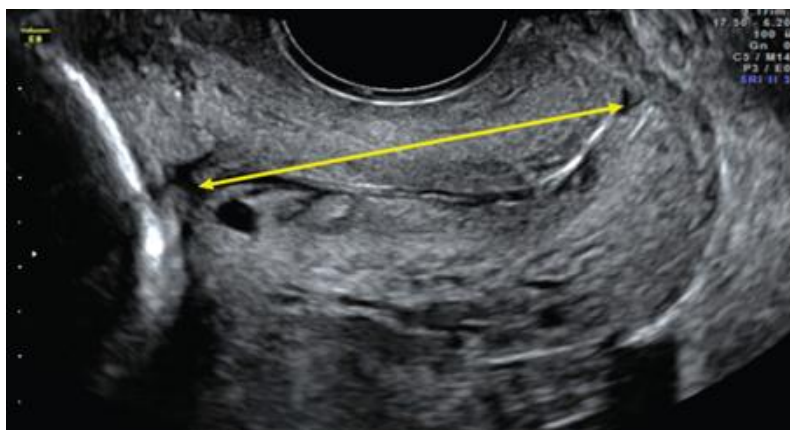
medical history (including diabetes, hypertension, anaemia, Preeclampsia, and any prior surgeries), medication sensitivity information, and the patient's current medical status.

Assessments of the Body: There were both systemic and regional checks performed as part of the physical examination. A thorough evaluation of the patient's vital signs, including temperature, pulse, respiration rate, blood pressure, and the presence or absence of pallor, cyanosis, jaundice, and enlarged lymph nodes; this evaluation may help rule out systemic disorders. An abdominal obstetric examination was performed to measure the uterus's fundal level and any scars from prior laparotomies. A digital and bimanual vaginal examination was used to measure the cervix, vaginal canal, and uterine size. Finally, a pelvic examination was performed to measure the uterine size and identify any exclusion criteria.

Laboratory investigations: This section covered the standard laboratory tests that are done on all patients upon admission, including complete blood count (CBC), erythrocyte sedimentation rate (ERT), C-reactive protein (CRP), liver and kidney function, PT, PTT, and INR tests, urinalysis, random blood sugar, ABO and Rh typing, and C-125 assessment.

Procedures for collecting and analysing blood samples: Each participant had a 3 ml venous blood sample taken. After being separated, the serum was promptly refrigerated at -80° C for analysis, which was completed within 3 months. The patients' serum samples and the quality control serum were tested using a commercially available ELISA kit. All of the tests were carried out precisely as directed by the manufacturer.

A missing miscarriage was diagnosed via a transvaginal ultrasound scan. When testing the viability and contents of an embryo, it was the method of choice. Seven days after the final misoprostol dosage, a transvaginal ultrasound is performed to confirm that the uterine contents have been fully evacuated. A transvaginal probe measuring 4-7 MHz was used to assess cervical length, which is defined as the distance between the internal and external os. We took three readings and utilised the lowest one as our baseline. Careful consideration was given to the image's orientation during the insertion of the transvaginal transducer. The distal vagina or the external cervical OS was where the probe was inserted. From one adnexa to the other, the probe was moved side to side to provide sagittal imaging.



Transvaginal ultrasonography measurement of cervical length Fig. (1).

The the results of the transvaginal ultrasound indicated that a missed miscarriage may have occurred: a crown-rump length of 7 mm or longer without a heartbeat, or a mean sac diameter of 25 mm or longer without an embryo visible in two separate ultrasounds taken at least seven days apart, or the failure to detect an embryo with a heartbeat two weeks or more following a scan that revealed a gestational sac without a yolk sac, or the failure to detect an embryo with a heartbeat eleven days following a scan that revealed a gestational sac with a yolk sac.

To conduct the biochemical experiments, venous blood samples (5 ml) were used, which will clot, and the sera were separated by centrifugation at room temperature for 10 minutes at 3,000 rpm. The measurement of serum CA-125 was measured. The sera were kept at a temperature of -80°C until the conclusion of the research, when they were examined. We used direct chemiluminometric technique with kits to quantify CA-125.

In order to determine which patients would have a miscarriage and which would continue into the second trimester, outcome measurements and follow-up were conducted until the patients reached 20 weeks of pregnancy. The next step was to compare the two groups (those who miscarried and those who completed the pregnancy) based on the ultrasound findings and CA-125 levels.

Data analysis: SPSS 26.0 for Windows was used for data collection, tabulation, and

statistical analysis (SPSS Inc., Chicago, IL, USA). The quantitative data was described using range (minimum and maximum values), mean, standard deviation, and median; the qualitative data was demarcated using percentages and figures. We used a two-tailed test in our analyses, where a significance level of $P\text{-value} < 0.05$ was considered, and a non-significant difference was indicated by a $P\text{-value} > 0.05$. A variety of tests were used, including the independent T-test to compare two groups with parametric quantitative data, Fisher's exact test to compare proportions of qualitative parameters, and the Chi-square (χ^2) test to compare proportions of quantitative parameters within a group.

3. Findings

There were 45 cases and 45 controls in the research. Cases and controls did not vary substantially with respect to age or body mass index. Cases were more likely to live in urban areas (53.33% vs. 33.33% in the control group), however this difference was not statistically significant (33.33 percent). In terms of gestational age, GA, prior procedures, and birth style, there was no statistically significant difference between the two groups. Nonetheless, compared to controls, cases had much higher rates of parity, prior abortion, and abortion frequency. There was no difference in the rate of sibling death between the control group and the cases. Listing 1

Data on demographics and basic features of the participants enrolled are shown in Table (1)

	Cases (N = 45)	Controls (N = 45)	P. Value
Age (Years)	25.16 \pm 3.45	24.11 \pm 2.82	0.119605
BMI (Kg/m^2)	23.64 \pm 1.55	23.4 \pm 1.37	0.439331
Residence			
• Urban	24 (53.33%)	15 (33.33%)	0.05647
• Rural	21 (46.67%)	30 (66.67%)	
Mode of previous delivery			
• CS	23 (51.11%)	21 (46.67%)	0.7465

• NVD	19 (42.22%)	20 (44.44%)	
Previous operations	11 (24.44%)	8 (17.78%)	0.44407
GA (Weeks)	9.31 ± 2.44	9.58 ± 2.17	0.58498
Primigravida	3 (6.67%)	4 (8.89%)	0.6939
Gravidity Frequency	3.47 ± 1.1	3.31 ± 1.08	0.50081
Parity Frequency	1.69 ± 1.41	3.09 ± 1.08	<0.0001*
Previous Abortion	37 (82.22%)	10 (22.22%)	<0.0001*
Abortion Frequency	1.78 ± 1.35	0.22 ± 0.42	<0.0001*
Sibling death	8 (17.78%)	7 (15.56%)	0.78028

CS: Cesarean section.

The Instances of lower abdomen discomfort, cramps, spotting, and vaginal bleeding were much more common in the cases compared to the controls. Particularly, 80% of patients had vaginal bleeding while the controls did not, and 66.67 percent of cases had cramps while the controls only had 11.11%. Cases also had a much greater incidence of lower abdomen discomfort and spotting compared to controls. Part 2 of the table

Signs and symptoms among the participants included in the study (Table 2)

	Cases (N = 45)	Controls (N = 45)	P. Value
Vaginal bleeding	36 (80%)	0 (0%)	<0.0001*
Spotting	9 (20%)	0 (0%)	0.00133*
Cramping	30 (66.67%)	5 (11.11%)	<0.0001*
Lower abdominal pain	27 (60%)	4 (8.89%)	<0.0001*

Cases had a noticeably higher systolic blood pressure than controls (122.29 ± 4.76 vs. 118.56 ± 5.26 mmHg, p=0.00066*). There was no significant difference in diastolic blood pressure between the two groups (81.33 ± 2.97 vs. 82.04 ± 3.57 mmHg, p=0.30739). Additionally, there was no significant difference in temperature between the cases and controls, although there was a little tendency towards a cooler temperature in the patients (37.48 ± 0.32 vs. 37.61 ± 0.28 °C, p=0.05431). Table 3:

Table (3) Important information about the participants:

	Cases (N = 45)	Controls (N = 45)	P. Value
Systolic Blood pressure (mmHg)	122.29 ± 4.76	118.56 ± 5.26	0.00066*
Diastolic blood pressure (mmHg)	81.33 ± 2.97	82.04 ± 3.57	0.30739
Temperature (°C)	37.48 ± 0.32	37.61 ± 0.28	0.05431

The Neither group showed a statistically significant difference in haemoglobin level, white blood cell count, urine specific gravity, pH, glucose, or protein levels. But there was a significant difference between the two groups in terms of platelet count (297.31 ± 61.99 vs. 255.09 ± 48.76 ×10⁹/L, p=0.00054*). In instances, the RBC count in urine was found to be lower (0.82 ± 0.78 vs. 1.16 ± 0.85 HPF, p=0.05565), however this trend was not statistically significant. With 129.24 ± 5.41 vs. 127.91 ± 3.96 mg/dL, p=0.18564, there was no significant difference in the random blood sugar level between the patients and controls. Cases had a substantially higher total bilirubin level (4.16 ± 1.21 mg/dL vs. 3.64 ± 1.11 mg/dL, p=0.03706*) compared to controls. Chapter 4

The participants who were examined in the laboratory are listed in Table (4)

	Cases (N = 45)	Controls (N = 45)	P. Value
CBC			
• Hemoglobin	10.08 ± 0.46	10.14 ± 0.47	0.52929
• WBC (×10 ⁹ /L) ²	10.19 ± 2.16	10.09 ± 2.21	0.84137
• Platelets (×10 ⁹ /L) ²	297.31 ± 61.99	255.09 ± 48.76	0.00054*
Urine Analysis			
• PH	6.16 ± 0.82	6 ± 0.74	0.34841
• Specific gravity	1017.33 ± 9.21	1016.31 ± 5.13	0.51724
• Glucose	0 (0%)	0 (0%)	-
• Protein	0 (0%)	0 (0%)	-
• RBCs (HPF)	0.82 ± 0.78	1.16 ± 0.85	0.05565
• Squamous epithelial cells	0 (0%)	0 (0%)	-
• Pus Cells	3 (6.67%)	4 (8.89%)	0.6939
Random blood sugar (mg/dL)	129.24 ± 5.41	127.91 ± 3.96	0.18564
Total Bilirubin	4.16 ± 1.21	3.64 ± 1.11	0.03706*

The Cases and controls vary significantly in terms of CA125 levels, abortion rate, and weeks of abortion, as shown in the table. Both the incidence of abortion and CA125 levels were much greater in cases than in controls. They were likewise well along in their pregnancies when they decided to terminate. Five-Area Table

Table (5) Results for the two groups' included subjects:

	Cases (N = 45)	Controls (N = 45)	P. Value
CA125 (IU/ml)	65.58 ± 25.84	38.81 ± 10.06	<0.0001*
Abortion	21 (46.67%)	3 (6.67%)	0.00001*
Week of abortion (Aborted cases)	13.86 ± 1.93	11.67 ± 1.15	0.07144

The The incidence of abortions and the number of abortions endured by women were much greater than those of non-aborted women. Women who had vaginal bleeding, cramps, and lower abdomen discomfort during an abortion were more likely to report these symptoms compared to those who did not. Abortion victims had much higher systolic blood pressure readings than non-aborted women. Sixth Table

Table (6) General assessment and baseline characteristics of subjects that had and did not have abortions.

	Aborted (N = 24)	Not Aborted (N = 66)	P. Value
Age (Years)	24.5 ± 3.2	24.68 ± 3.19	0.81186
BMI (Kg/m ²)	23.53 ± 1.53	23.52 ± 1.45	0.97851
Residence			
• Urban	11 (45.83%)	28 (42.42%)	0.77591
• Rural	13 (54.17%)	38 (57.58%)	0.77591
GA (Weeks)	9.58 ± 2.38	9.39 ± 2.29	0.7317
Gravidity	3.71 ± 1.04	3.27 ± 1.09	0.09323
Parity	1.96 ± 1.52	2.55 ± 1.38	0.08621
Previous Abortion	0.79 ± 0.41	0.42 ± 0.5	0.00176*
Abortion Frequency	1.75 ± 1.36	0.73 ± 1.12	0.00049*
Sibling death	8 (17.78%)	7 (15.56%)	0.20511
Mode of previous delivery			
• CS	13 (54.17%)	35 (53.03%)	0.92493
• NVD	11 (45.83%)	31 (46.97%)	0.92493
Previous operations	7 (29.17%)	12 (18.18%)	0.26381
Symptoms and Signs			
• Vaginal bleeding	17 (70.83%)	19 (28.79%)	0.00022*
• Spotting	4 (16.67%)	5 (7.58%)	0.20796
• Cramping	15 (62.5%)	20 (30.3%)	0.00522*
• Lower abdominal pain	13 (54.17%)	18 (27.27%)	0.01735*
Blood Pressure			
• Systolic Blood pressure	122.75 ± 5.02	119.58 ± 5.22	0.01161*
• Diastolic blood pressure	82.5 ± 2.8	81.39 ± 3.42	0.15916
Temperature	37.49 ± 0.31	37.56 ± 0.3	0.35567

Age, There was no significant difference between the two groups with respect to body mass index (BMI), residency, GA, gravidity, parity, previous delivery method, prior procedures, or temperature. The two groups' CA125 levels varied significantly from one another (aborted and not aborted). A p-value of less than 0.0001 indicates that the mean CA125 level among those who had an abortion (77.55 ± 26.38 IU/ml) was significantly greater than the mean CA125 level among those who did not have an abortion (42.97 ± 14.09 IU/ml). Picture 2

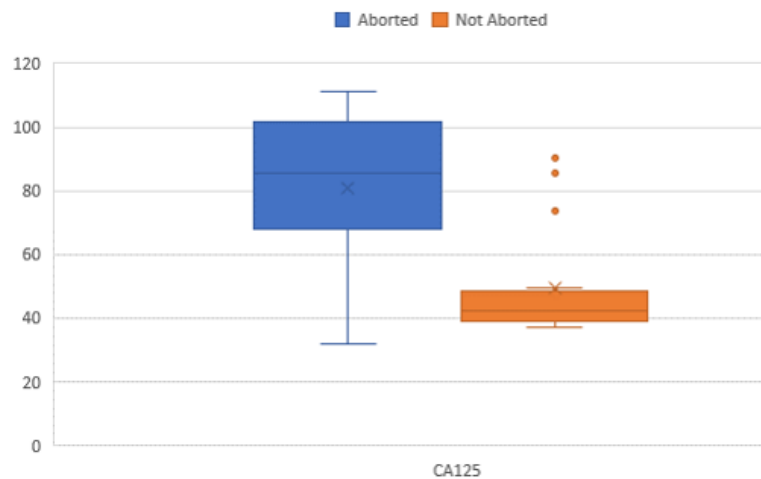
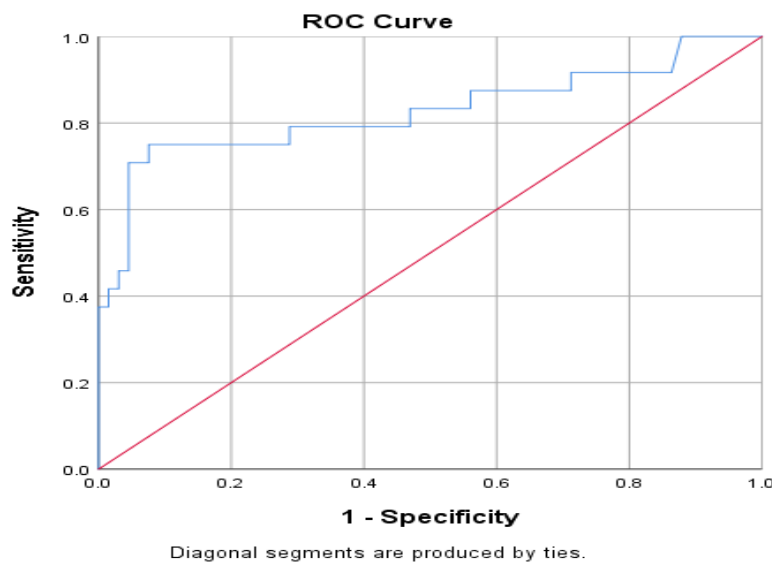


Fig. (2) CA125 as a function of whether or not the patient had an abortion.

There was a substantial connection between CA-125 and the incidence of abortion with a cut-off value of 31.87. A sensitivity of 91.7% and a specificity of 86.4% were recorded. Fig. 3



Abortion and CA-125 ROC curve study (Fig. (3)).

4. Discussion

The study's primary objective was to determine serum CA 125's predictive value in cases of imminent abortion during the first trimester and subsequent 20-week follow-up. One hundred and ten participants were chosen at random from the obstetrics and gynaecology clinics at Benha University for this cross-sectional research. There were 45 patients in the case group and 45 in the control group. Both the patients and controls did not vary substantially in terms of age or body mass index (BMI), according to our present investigation. Cases were more likely to live in urban areas (53.33% vs. 33.33% in the control group), however this difference was not statistically significant (33.33 percent). In terms of gestational age, GA, prior procedures, and birth style, there was no statistically

significant difference between the two groups. Nonetheless, compared to controls, cases had much higher rates of parity, prior abortion, and abortion frequency. There was no difference in the rate of sibling death between the control group and the cases.

Gidwani et al. (2019) sought to determine the cutoff values of maternal blood CA125 for predicting the pregnancy outcomes in patients with threatened abortion and to assess the predictive impact of serum CA125 in these patients. Our results corroborated their findings. One hundred and sixty people were included in the trial. A mean age of 24.23 ± 3.53 was recorded. With a p-value greater than 0.05, no statistical significance was found with respect to age, gravidity, or gestational age [8]. Our findings were in line with those of Oun et al. (2018), who sought to determine the

function of serum ca125 and ultrasonography in predicting the fate of a pregnancy where a first-trimester miscarriage was a possibility. We enrolled 110 participants in the trial. Their ages varied from twenty-five to thirty-five. In terms of age and gravidity, no statistical significance was found between the threatened group and the control group (p value >0.05) [9].

Similarly to Sudha & Sinha (2020), the goal of which was to determine if blood CA125 levels might foretell the result of a threatening abortion. At 20 weeks of pregnancy, 32 out of 100 pregnancies (or 32% of the total) terminated in abortion, while 68 out of 100 pregnancies (or 68% of the total) continued. The average age of all participants in the research was 24.87 ± 3.58 years. When comparing the two groups based on age, gestational age, and gravidity, no statistical significance was found (p value >0.05) [10].

Additionally, our findings were in agreement with those of Sherif et al. (2000), who contrasted the results from CA125 with those from ultrasonography in an effort to assess its usefulness as a tool for predicting the outcome of threatening abortions. Between the ages of 6 and 13 weeks into their pregnancies, 100 pregnant women participated in the research. Of these, 57 chose to prolong the pregnancy, 43 chose to abort, and the remaining women served as a control group (50 women). Considerations of age, abortion history, and gestational age did not provide statistically significant results (p value >0.05). [11].

Also in agreement with Mathur et al., (2022), the purpose of which was to investigate the function of serum CA125 in foretelling the possible result of early pregnancy haemorrhage. The 84 pregnant women who met the inclusion and exclusion criteria were recruited from the Obstetrics Outpatient Department of Santosh Medical College and Hospital. Their gestational age ranged from 7 to 14 weeks. Each participant was assigned to one of two groups: those exhibiting signs of an imminent abortion and those presenting with a seemingly normal pregnancy. Regarding gestational age, number of prior abortions, or gravidity, no statistical significance was found (p value >0.05). [12].

Our findings were in agreement with those of Adeku et al. (2019), who sought to determine if blood CA125 levels might predict the fate of a pregnancy in cases when a miscarriage was imminent. The research group had an average age of 29.5 ± 0.14 years, whereas the control group had an average age of 30.1 ± 0.14 years [13].

This is in keeping with the goals of Turgut et al. (2022), who set out to assess the usefulness of the systemic immune inflammation index in the prediction of miscarriage. The research group consisted of 709 pregnant women who had a miscarriage (defined as an intrauterine pregnancy that was not viable up to 20 weeks gestation) and 676 women who served as a control group. Age and gestational age did not show any statistical difference between the groups (p value >0.05). [14].

When comparing cases and controls, we find that cases are more likely to have vaginal bleeding, spotting, cramping, and lower abdomen discomfort. In particular, 30 individuals (or 80% of the total) reported cramps, whereas just 5 cases (or 0% of the control group) reported any vaginal bleeding. Cases also had a much greater incidence of lower abdomen discomfort and spotting compared to controls. Cases had a noticeably higher systolic blood pressure than controls (122.29 ± 4.76 vs. 118.56 ± 5.26 mmHg, $p=0.00066^*$). There was no significant difference in diastolic blood pressure between the two groups (81.33 ± 2.97 vs. 82.04 ± 3.57 mmHg, $p=0.30739$). Additionally, there was no significant difference in temperature between the cases and controls, although there was a little tendency towards a cooler temperature in the patients (37.48 ± 0.32 vs. 37.61 ± 0.28 oC, $p=0.05431$). There was no statistically significant difference between the two groups with respect to haemoglobin level, white blood cell count, urine specific gravity, pH, glucose, or protein in urine. But there was a significant difference between the two groups in terms of platelet count (297.31 ± 61.99 vs. $255.09 \pm 48.76 \times 10^9/L$, $p=0.00054^*$). In instances, the RBC count in urine was found to be lower (0.82 ± 0.78 vs. 1.16 ± 0.85 HPF, $p=0.05565$), however this trend was not statistically significant. With 129.24 ± 5.41 vs. 127.91 ± 3.96 mg/dL, $p=0.18564$, there was no significant difference in the random blood sugar level between the patients and controls. Cases had a substantially higher total bilirubin level (4.16 ± 1.21 mg/dL vs. 3.64 ± 1.11 mg/dL, $p=0.03706^*$) compared to controls.

Turgut et al. (2022) found no statistical significance between groups for haemoglobin, white blood cell, and platelet count (p value >0.05) [14], which contradicts our data. There were statistically significant variations in CA125 levels, abortion rates, and weeks of abortion between the cases and controls in the present research. Both the incidence of abortion and CA125 levels were much greater in cases than in controls. They were likewise

well along in their pregnancies when they decided to terminate.

There was a substantial reduction in hematoma in group (A) compared to group (B) (2.3 percent vs. 25.0 percent correspondingly) (p value<0.05), and our findings were in agreement with those of Oun et al. (2018), who found that 7.3% of the females investigated had hematomas. [9].

Patients in groups II and III who had vaginal bleeding had significantly higher blood CA125 levels compared to the control group, according to Fiegler et al. (2003). Patients who miscarried had much lower blood beta-hCG levels than those who carried the pregnancy to term, in contrast to CA125 [15].

There was no significant difference between the two groups with respect to age, body mass index (BMI), residency, gestational age (GA), parity, previous delivery method, prior procedures, temperature, or siblings' deaths. There was a statistically significant correlation between the number of abortions and the number of abortions sustained by women who had abortions. Women who had vaginal bleeding, cramps, and lower abdomen discomfort during an abortion were more likely to report these symptoms compared to those who did not. Abortion victims had much higher systolic blood pressure readings than non-aborted women. As far as the majority of laboratory examinations are concerned, there is little to no difference between the two groups. However, there may be a tendency towards significance, since the P value for RBCs in urine analysis is 0.05199.

There was no statistically significant difference between groups (A) and (B) (p value>0.05), and our findings corroborated those of Oun et al. (2018), who found that 82.7% of the women surveyed had never had an abortion, 13.6% had one, and 3.6% had two. With a p-value less than 0.05, there was a statistically significant reduction in reported pain in group (A) compared to group (B) (40 percent vs. 33.7% and 62.5%, respectively). [9].

In addition, our findings corroborated those of Turgut et al. (2022), who found no statistical difference between the groups when it came to the participants' abortion histories (p value>0.05). [14].

An analogous study by Shao et al. (2021) compared the platelet counts of 170 healthy pregnant women to those of 99 women who had a miscarriage between 5 and 10 weeks into their pregnancies. A high platelet count was shown to be independently related with an increased risk of miscarriage [16], and it was also considerably greater in pregnant women

who had miscarriages compared to healthy pregnancies.

The two groups' CA125 levels varied significantly from one another (aborted and not aborted). A p-value of less than 0.0001 indicates that the mean CA125 level among those who had an abortion (77.55 ± 26.38 IU/ml) was significantly greater than the mean CA125 level among those who did not have an abortion (42.97 ± 14.09 IU/ml).

Oun et al. (2018) found that CA125 levels varied from 8 to 77 IU/ml, and that group (A) (continued) had a significantly lower CA125 level than group (B) (aborted) (19.45 ± 5.57 vs 53.83 ± 9.48 respectively) [9]. Our results corroborated these findings.

In regards to maternal blood CA 125 levels (IU/ml), our findings corroborated those of Gidwani et al. (2019), who also found a very significant difference between the control and threatened groups. The researchers discovered a statistically significant rise in CA125 levels in individuals who had abortions compared to those who carried the pregnancy to term (48.36 ± 36.94 and 116.28 ± 81.04 respectively) [8].

The mean serum CA125 levels of aborted women were significantly higher (P<0.001) than those of the other two groups, as reported by Sherif et al. (2000) [11].

It is also comparable to what Adeku et al. (2019) found: a mean serum CA125 of 30.1 ± 1.1 IU/mL in the study group and 22.9 ± 1.2 IU/mL in the control group, with a p-value of 0.0001. On average, the blood CA125 level was 34.8 ± 1.4 IU/mL in women whose pregnancies were terminated, compared to 27.3 ± 1.2 IU/mL in women whose pregnancies were carried to term. P = 0.001 [13] indicates that this was significantly.

Furthermore, our findings corroborated those of Mohammed El Husseny (2019), who found that blood CA125 levels were significantly higher in women experiencing a threatened abortion compared to those in women experiencing a normal pregnancy [1].

Our findings corroborated those of Mathur et al. (2022), who found substantially greater blood CA125 levels in group I compared to group II. Moreover, it was noticeably greater among women who went on to have a miscarriage compared to those who were able to successfully carry the pregnancy to term (58.04 ± 12.56 vs 19.37 ± 5.7) (p value<0.001). [12].

In addition, our findings corroborated those of Zakaria et al. (2020), who sought to compare the predictive power of blood CA125 and serum progesterone in determining the likelihood of a miscarriage in women facing an

abortion during the first trimester. According to the study, there was a statistically significant difference in the mean levels of CA125 between the normal group (30.1±21.6) and the threatening group (42.3±19.1).

In addition, our findings were in line with those of Schmidt et al. (2001), who sought to determine the diagnostic utility of maternal CA125 in women experiencing symptoms during the first trimester of pregnancy and to compare the predictive power of CA125 to that of β -hCG in early pregnancies where the foetal heartbeat was intact and complications included vaginal bleeding. One hundred sixty-eight patients were recruited for the research. Patients at risk for abortion who have a viable pregnancy may benefit from using maternal CA125 levels as a very sensitive prognostic marker [18].

A substantial connection between CA125 and the incidence of abortion was shown in our present investigation with a cut-off value of 31.87. A sensitivity of 91.7% and a specificity of 86.4% were recorded.

Al Mohamady et al. (2016) found that blood CA125 levels were 54.28±11.4 IU/ml for the group that had a miscarriage, whereas the level was 18.81±8.02 IU/ml for the group that experienced a continuing danger of miscarriage. These findings are consistent with our own findings. It was a statistically significant difference. In addition, they noted that a cut-off level of 31.2 IU/ml of CA125 level attained a sensitivity of 96.2% and specificity of 100% when utilising a ROC curve for CA125 to predict the pregnancy outcome in threatening miscarriage instances. An overall accuracy of 99.4 percent was seen when the CA125 level was more than 31.2 IU/ml in predicting the incidence of miscarriage [19].

It is worth noting that Sudha & Sinha (2020) found different findings when using ROC graphs to predict the probability of abortion. They found a cutoff level of 60 IU/ml, with a sensitivity of 84.65%, specificity of 91.87%, PPV of 82.53%, NPV of 91.11%, and accuracy of 88%. This means that CA125 is clinically significant for predicting the fate of individuals who are threatened with abortion during the early stages of their pregnancies [10].

Additionally, at a threshold value of > 60 IU/ml, Gidwaniet al. (2019) found that CA125 had an 83.33 percent sensitivity and a 92.62% specificity for predicting abortion in the females they tested [8].

Also, according to Adeku et al. (2019), the diagnostic effectiveness (accuracy) was 79.4 percent, specificity was 83.3 percent, positive predictive value was 55.6 percent, negative

predictive value was 88.9 percent, and the sensitivity was 66.7 percent when using CA125 ≥ 36.2 IU/mL (mean value of serum CA125 among aborters + 1 standard deviation) as a threshold for intrauterine pregnancies that ultimately got aborted [13].

Also, contrary to what Turgut et al. (2022) found, our data show that serum CA125 level is not a reliable indicator of pregnancy loss when utilising ROC-curve analysis [14].

Further, Oun et al. (2018) found that CA125 has a sensitivity of 100% and specificity of 98.8% at a cutoff value greater than 35 IU/ml [9].

In addition, Ayaty et al. (2007) observed that they followed up on 50 women who were pregnant and 50 women who were threatened with abortion based on their CA125 levels. Normal pregnant women whose pregnancies proceed to term had an average CA125 level of 26.61±1.76 IU/mL, whereas patients who ultimately had abortions had an average level of 58.17±7.25 IU/mL. Women who were threatened but whose pregnancies progressed normally had a CA125 level of 30.89 IU/ml. A blood CA125 test may be a cheap, readily accessible, sensitive, and specific predictor of outcome in threatened abortion, leading to the loss of a pregnancy, according to their findings [20]. Furthermore, Fiegler et al. (2003) used a sensitivity level of 55% and a cut-off value of 66.5 IU/ml, which contradicts our findings [15].

Schmidt et al. (2001) also found a 50% sensitivity at 65 IU/ml, which they utilised as a cut-off value [18].

In addition, Yadav et al. (2021) found that a maternal blood CA125 cut off level of 61.64 U/ml had an 84.21 percent sensitivity, 96.77 percent specificity, 94.12% positive predictive value, and 90.91% negative predictive value when it came to predicting abortion [21].

Furthermore, progesterone, CA125, and Beta hCG are useful biochemical indicators for outcome prediction in women with threatening abortion, according to Maged and Al-Mostafa (2013). There were a total of 250 pregnant women included in the research, with 65 women in group I having abortions as a result of threats, 85 women in group II having their pregnancies continued despite the threats, and 100 women in group III having normal pregnancies. In terms of CA125, group I differed significantly from the other two groups. At 80 IU/mL, CA125 had an 80% sensitivity and a 78.3% specificity, according to [22].

5. Conclusion

In Our findings were in agreement with those of Oun et al. (2018), who found that 7.3% of the females in their study had a hematoma, and

that group (A) had a significantly lower hematoma rate than group (B) (2.3 percent vs. 25.0 percent, respectively) ($p < 0.05$). [9]. Additionally, Fiegler et al. (2003) found that compared to the control group, patients with vaginal bleeding (groups II and III) had significantly higher blood CA125 levels. Patients who had a subsequent miscarriage had much lower blood beta-hCG levels compared to CA125 [15].

Both groups were similar with respect to age, body mass index (BMI), place of residence, gestational age (GA), number of children, prior delivery method, number of procedures, temperature, and the number of siblings who passed away. Both the frequency and the number of abortions experienced by women who had abortions were far greater than those experienced by women who did not have abortions. Women who had abortions were more likely to experience vaginal bleeding, cramps, and lower abdomen discomfort compared to those who did not. Those who had abortions had much greater systolic blood pressure than women who did not. In the majority of laboratory tests, there was no discernible difference between the two sets of subjects. Unfortunately, RBCs in urine analysis had a P value of 0.05199, suggesting a possible trend towards significance.

Our findings are in line with those of Oun et al. (2018), who found that, when asked about prior abortions, 82.7% of the women surveyed had never had one, 13.6% had had one, and 3.6% had had two. They also found no statistically significant difference between groups A and B ($p > 0.05$). A substantial reduction in pain was seen in group (A) (33.7 percent vs. 62.5 percent, respectively) ($p < 0.05$), and 40 percent of the participants reported experiencing pain. [9].

According to Turgut et al. (2022), no statistical significance was found between the groups when it came to the history of past abortions ($p > 0.05$). Our results corroborated their findings. [14].

In a similar vein, Shao et al. (2021) compared the platelet counts of 170 healthy pregnant women to those of 99 women who had a miscarriage between 5 and 10 weeks into their pregnancies. Researchers discovered that pregnant women experiencing a miscarriage had much higher platelet counts compared to those in healthy pregnancies. Moreover, a high platelet count was revealed to be independently related with an increased risk of miscarriage [16].

The levels of CA125 are significantly different between the two sets of data (aborted and not aborted). The abortion group had a

substantially greater mean CA125 level (77.55 ± 26.38 IU/ml) compared to the non-aborting group (42.97 ± 14.09 IU/ml), with a p-value of less than 0.0001.

Based on the findings of Oun et al. (2018), who found CA125 levels to be 8–77 IU/ml, and a statistically significant drop in CA125 in group (A) (continued) compared to group (B) (aborted) (19.45 ± 5.57 vs 53.83 ± 9.48 respectively) [9], our results are in line with their findings.

Additionally, our findings corroborated those of Gidwani et al. (2019), who found a very significant difference in maternal blood CA 125 levels (IU/ml) between the control and threatened groups. Aborted patients had a significantly higher CA125 level (48.36 ± 36.94) compared to those who prolonged their pregnancy beyond 20 weeks (116.28 ± 81.04) [8].

In agreement with the findings of Sherif et al. (2000), who found that the average blood CA125 levels of abortion-related women were significantly higher ($P < 0.001$) than those of the other two groups (42.99 ± 18.38 vs 12.97 ± 5.34), we can say the same thing about our study [11].

The results were comparable to those of Adeku et al. (2019), who found a statistically significant difference between the study group and the control group in terms of serum CA125 levels, with the former measuring 30.1 ± 1.1 IU/mL and the latter measuring 22.9 ± 1.2 IU/mL ($P = 0.0001$). In women whose pregnancies ended in abortion, the average serum CA125 level was 34.8 ± 1.4 IU/mL, while in women whose pregnancies went to term, the average value was 27.3 ± 1.2 IU/mL. A p-value of 0.001 indicates statistical significance [13].

Mohammed El Husseny (2019) found that serum CA125 levels were significantly higher in women who were pregnant with a threat of abortion compared to women whose pregnancies were considered normal [1], and our findings corroborated his findings.

Mathur et al. (2022) found that serum CA125 was much higher in group I compared to group II, and our data corroborated that. A p-value of less than 0.001 indicates that it was substantially greater among women who went on to have a miscarriage compared to those whose pregnancies were successfully continued (58.04 ± 12.56 versus 19.37 ± 5.7). [12].

In a study comparing the predictive power of blood CA125 and serum progesterone in determining the likelihood of miscarriage in women facing a first-trimester abortion threat, our findings were in agreement with those of Zakaria et al. (2020). In the group that was

threatened, the average CA125 level was 42.3 ± 19.1 , whereas in the normal group it was 30.1 ± 21.6 , and this difference was statistically significant [17].

In a study conducted by Schmidt et al. (2001), the purpose was to compare the predictive power of CA125 versus β -hCG in early pregnancies with a healthy foetus and complications like vaginal bleeding, as well as to determine the diagnostic utility of maternal CA125 in patients experiencing symptoms during the first trimester of pregnancy. Six hundred eighty-eight patients were enrolled in the research. In women who are pregnant and at risk of having an abortion, maternal CA125 levels seem to be an extremely sensitive predictive indicator [18].

Our latest research demonstrated a statistically significant correlation between CA125 and the frequency of abortions at a cutoff value of 31.87. The specificity was 86.4% and the sensitivity was 91.7%.

We found that the levels of serum CA125 were 54.28 ± 11.4 IU/ml for the group that had a miscarriage, and 18.81 ± 8.02 IU/ml for the group that continued to have a threatened miscarriage, which is consistent with the findings of Al Mohamady et al. (2016). A statistical analysis revealed a noteworthy disparity. Furthermore, they noted that a sensitivity of 96.2% and specificity of 100% were attained using a cut-off level of 31.2 IU/ml of CA125 level while utilising a ROC curve for CA125 to forecast the pregnancy outcome in situations of impending miscarriage. There was a 99.4 percent overall accuracy in predicting the incidence of miscarriage when the CA125 level was more than 31.2 IU/ml [19].

Contrary to our findings, Sudha & Sinha (2020) found that a cutoff level of 60 IU/ml was associated with a sensitivity of 84.65%, specificity of 91.87%, PPV of 82.53%, NPV of 91.11%, and accuracy of 88.58% when using ROC graphs to predict the likelihood of abortion. Predicting the fate of patients with threatening abortion at an early stage of gestation is a therapeutically essential role for CA125 [10].

In addition, Gidwaniet al. (2019) found that at a threshold value of > 60 IU/ml, CA125 had an 83.33 percent sensitivity and a 92.62% specificity for predicting abortion in the females surveyed [8].

In addition, Adeku et al. (2019) found that tests for intrauterine pregnancies that ended in abortion had a sensitivity of 66.7%, specificity of 83.3%, positive predictive value of 55.6%, negative predictive value of 88.9%, and diagnostic effectiveness (accuracy) of 79.4%

when using CA125 ≥ 36.2 IU/mL (mean value of serum CA125 among aborters + 1 standard deviation) as a criterion [13].

Additionally, our findings contradict those of Turgut et al. (2022), who said that blood CA125 level was (62.6 percent sensitivity, 62% specificity) for miscarriage [14] according to their ROC-curve study.

In addition, Oun et al. (2018) found that CA125 has a sensitivity of 100% and specificity of 98.8% at a cutoff value greater than 35 IU/ml [9].

Furthermore, Ayaty et al. (2007) discovered that when they followed 50 pregnant women with healthy pregnancies and 50 pregnant women who were faced with abortion based on CA125 levels, they found that the former group fared better. In patients who had their pregnancies terminated, the average CA125 level was 58.17 ± 7.25 IU/mL, whereas in women who carried their pregnancies to term, it was 26.61 ± 1.76 IU/mL. Among pregnant women who were threatened but chose not to abort, the level of CA125 was 30.89 IU/ml. As a consequence, they came to the conclusion that blood CA125 measurement may be a cheap, readily accessible, sensitive, and specific predictor of outcome in threatened abortion, leading to the loss of pregnancy [20].

Furthermore, Fiegler et al. (2003) used a sensitivity level of 55% and a cut-off value of 66.5 IU/ml, which contradicts our findings [15].

In addition, a sensitivity of 50% was found for a cut-off value of 65 IU/ml by Schmidt et al. (2001) [18].

Additionally, it was shown by Yadav et al., (2021) that at a cutoff level of 61.64 U/ml, maternal serum CA125 is 84.21% sensitive, 96.77% specific, and has a positive predictive value of 94.12% and a negative predictive value of 90.91% in predicting abortion [21].

Furthermore, for women who are facing an abortion danger, CA125, Beta hCG, and progesterone are useful biochemical indicators for outcome prediction (Maged and Al-Mostafa 2013). One hundred and fifty pregnant women in their first trimester were separated into three groups for this study: those whose pregnancies ended in abortion (group I), those whose pregnancies terminated in abortion (group II), and those whose pregnancies ended normally (group III). When comparing CA125 levels across the three groups, group 1 stood out statistically. With an 80 IU/mL concentration of CA125, the sensitivity was 80.2% and the specificity was 78.3% [22].

References

- [1] A.M. El Hussiney, S.A. El-Sayed, M.F. Abo Hashim, B.S. Abd-Elhameed. Assessment of Uterine Artery Blood Flow

- in Threatened Miscarriage by 2D Doppler Ultrasound. *The Egyptian Journal of Hospital Medicine*;88:4085-9. 2022
- [2] L. Xu, Q. Tu, F. Wang, D. Yan, B. Li, P. Sun. Zishen yutai pill as an adjuvant therapy in threatened Miscarriage:A meta-analysis of 23 randomized controlled trials. *Heliyon*;9:e16213. 2023
- [3] A.G. Kanmaz, A.H. İnan, E. Beyan, A. Budak. The effects of threatened abortions on pregnancy outcomes. *Ginekol Pol*;90:195-200. 2019
- [4] S.L. Chen, S.M. Chang, P.L. Kuo, C.H. Chen. Stress, anxiety and depression perceived by couples with recurrent miscarriage. *Int J Nurs Pract*;26:e12796. 2020
- [5] P. Charkhchi, C. Cybulski, J. Gronwald, F.O. Wong, S.A. Narod, M.R. Akbari. CA125 and Ovarian Cancer: A Comprehensive Review. *Cancers (Basel)*;12. 2020
- [6] M. Anter, A. Shabana, H. Ellakwa, H. Hamza, M. Omar. Role of CA-125 and ultrasound in early prediction of outcome of threatened miscarriage. *Menoufia Medical Journal*;33:1258-63. 2020
- [7] A.H. Shaamash, H.A. Aly, M. Abdel-Aleem, S.N. Akhnowkh. Clinical and Ultrasound Evaluation of Early Threatened Miscarriage to Predict Pregnancy Continuation up to 28 Weeks: A Prospective Cohort Study. *J Ultrasound Med*;39:1777-85. 2020
- [8] C. Gidwani, B. Meena, M.L. Meena, G. Rashma. Role of serum CA125 levels in predicting the outcome of threatened abortion. *International Journal of Clinical Obstetrics and Gynaecology*;3:14-8. 2019
- [9] A.-E.M. Oun, E.M. Ibrahim, M. Elaziz. Role of both serum CA125 and ultrasound in prediction of pregnancy outcome in first trimester threatened miscarriage. *Int J Life Sci*;7:79-84. 2018
- [10] D.K.S. Sudha. Evaluation of serum marker CA125 and its role in determining the outcome of threatened abortion. *European Journal of Molecular & Clinical Medicine (EJMCM)*;7:2020. 2020
- [11] L.S. Sherif, A.G. El-Metwaly, H. Shalan, A.M. Badawy, E. Abu-Hashem. Can a single serum CA125 assay predict the outcome of threatened abortion? *J Obstet Gynaecol*;20:65-7. 2000
- [12] S. Mathur, A. Agrawal, M. Gupta, N. Agarwal. ROLE OF SERUM CA-125 IN PREDICTING THE OUTCOME OF THREATENED ABORTION. *Journal of Pharmaceutical Negative Results*;833-7. 2022
- [13] M.A. Adeku, O. Adegbola, G.O. Ajayi. The predictive value of serum cancer antigen 125 (CA125) levels on pregnancy outcome in threatened miscarriages. *J Perinat Med*;47:704-9. 2019
- [14] E. Turgut, M. Yildirim, B. Sakcak, S.G. Ayhan, O.M. Tekin, D. Sahin. Predicting miscarriage using systemic immune-inflammation index. *J Obstet Gynaecol Res*;48:587-92. 2022
- [15] P. Fiegler, M. Katz, K. Kaminski, G. Rudol. Clinical value of a single serum CA-125 level in women with symptoms of imminent abortion during the first trimester of pregnancy. *J Reprod Med*;48:982-8. 2003
- [16] X. Shao, D. Wang, Y. Xu, L. Guo, H. Yang, J. Zhou, et al. The high platelet counts as predictor for early foetal demise. *Ann Med*;53:1502-8. 2021
- [17] A.E.-M. M. Zakaria, F. A. Al-Omda, M. Abd El-Moneim, B. S. Mohamed. Predictive value of serum CA-125 versus serum progesterone in predicting risk of pregnancy loss in cases of first trimester threatened abortion. *Al-Azhar Medical Journal*;49:59-68. 2020
- [18] T. Schmidt, D.T. Rein, D. Foth, H.W. Eibach, C.M. Kurbacher, P. Mallmann, et al. Prognostic value of repeated serum CA 125 measurements in first trimester pregnancy. *Eur J Obstet Gynecol Reprod Biol*;97:168-73. 2001
- [19] M. Al Mohamady, G.A. Fattah, E. Elkattan, R. Bayoumy, D.A. Hamed. Correlation of Serum CA-125 and Progesterone Levels with Ultrasound Markers in The Prediction of Pregnancy Outcome in Threatened Miscarriage. *Int J Fertil Steril*;9:506-11. 2016
- [20] S. AYATI, R.F. VAHID, F. TAVASOLI. CA-125 in normal pregnancy and threatened abortion. 2007
- [21] K. Yadav, P. Ojha, A. Chopra. Comparison of maternal serum CA-125 and ultrasonography findings as a prognostic marker in threatened abortion. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*;10:2253-9. 2021
- [22] A.M. Maged, W.A. Mostafa. Biochemical and ultrasonographic predictors of outcome in threatened abortion. *Middle East Fertility Society Journal*;18:177-81. 2013