

# PREDICTIVE VALUE OF SERUM CA-125 VERSUS SERUM PROGESTERONE IN PREDICTING RISK OF PREGNANCY LOSS IN CASES OF FIRST TRIMESTERIC THREATENED ABORTION

By

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## ABSTRACT

**Background:** Pregnancy misfortune happens in 0.5-1% of ladies. The etiology is frequently vague and might be multifactorial, with much debate in regards to determination and treatment.

**Objective:** Investigating the relationship between serum progesterone and CA-125 distinguishing successful from unsuccessful pregnancy outcome during the first trimestic cases of threatened abortion.

**Patients and Methods:** This clinical trial included 80 cases of confirmed intrauterine pregnancies between 6-12 weeks with demonstrable embryonic pulsation 40 asymptomatic patients and 40 cases complicated with vaginal bleeding. All cases were selected from Obstetrics and Gynecology Department, Al-Hussein and Sayed Galal Hospitals, Al-Azhar University, from December, 2018 to August, 2019. All patients showed an evidence of embryonic cardiac activity. CA-125 serum levels ware measured and compared with progesterone levels.

**Results:** The mean level of CA.125 was 42.3±19.1 in threatened group and was 30.1±21.6 in normal group respectively. There was a statistically difference between the two groups regarding serum CA125. On the other hand, there was no statistically difference between the two groups regarding progesterone. ROC curve analysis showed 80.55% sensitivity and 100% specificity of CA125, and 78.65% sensitivity and 98.04% specificity of progesterone for prediction of the occurrence of miscarriage.

**Conclusion:** Serum CA-125 seemed to be a promising biomarker for the early prediction of miscarriage

**Key Words:** Normal pregnancy; serum CA 125; progesterone; threatened miscarriage.

## INTRODUCTION

Pregnancy misfortune happens in 0.5-1% of ladies. The etiology is frequently vague and might be multifactorial, with much debate in regards to determination and treatment. Sensibly acknowledged etiologic causes incorporate hereditary qualities, anatomical, endocrine and

hormonal issues. Other basic elements incorporate certain irresistible components; smoking, liquor utilization, presentation to ecological hazard factors, mental injury and unpleasant life occasions just as certain coagulation and immunoregulatory protein surrenders (*Li et al., 2012*).

Progesterone is valuable in enabling pregnancy to arrive at its physiologic term. At adequate level on myometrium, progesterone acts to obstruct the oxytocic impact of prostaglandin F2a. Common Progesterone is free of any irritating teratogenic, metabolic, or homodynamic impact (*Di Renzo et al., 2016*).

Analyzed maternal serum groupings of CA-125 during the early first trimester of ordinary and unusual pregnancies. In ordinary pregnancies, the CA-125 levels expanded altogether from the principal week after the missed menses up to the third week. After the third week, the mean CA-125 serum focuses leveled, till part of the arrangement. The mean CA-125 focuses were accounted for to be essentially higher in ordinary pregnancies than in ectopic developments.

*Sweed et al. (2016)* assessed the wellspring of maternal serum CA-125 during the principal trimester of pregnancy and showed that in non-reasonable pregnancies with euploid babies, an expansion in maternal serum CA-125 levels was discovered uniquely in nearness of decidual interruption related to vaginal dying.

They demonstrated that, despite the fact that there was a clear connection found between height of CA-125 and unconstrained premature birth, the higher levels happened right off the bat in the principal trimester, while most of premature births do not happen until some other time, after fetal feasibility was set up.

The present work aimed to investigate the relationship between serum progesterone and CA-125 distinguishing successful from unsuccessful pregnancy

outcome during the first trimester cases of threatened abortion.

## PATIENTS AND METHODS

**Study setting:** The investigation had been led at Obstetrics and Gynecology Department, Al-Hussein and Sayed Galal Hospitals, Al-Azhar University from December, 2018 to August, 2019.

**Type of study and study population:** This study included 80 instances of affirmed intrauterine pregnancies between 6-12 weeks with obvious embryonic throb, i.e. 40 asymptomatic patients and 40 cases convoluted with vaginal dying

### Inclusion criteria:

All patients had the following criteria:

1. Age: From 20-40 years.
2. Gestational age: From 6-12 weeks.

### Exclusion criteria:

Women with cursed ovum or twinning incubation, ectopic pregnancy, origination by helped regenerative strategies incendiary condition, and those not accessible to be reached for follow-up were rejected in the examination.

### All patients had been divided into two groups:

**Group 1:** Forty asymptomatic first trimester pregnant ladies.

**Group 2:** Forty first trimester patients with vaginal seeping with gestational age between 6 to 12 weeks

All patients showed an evidence of embryonic cardiac activity.

### Methods: Each case in the study was subjected to the following:

1. Explanation of the procedure.

2. Verbal consent was taken.
3. Detailed obstetric and gynaecological history was fulfilled.
4. Clinical examination was done.
5. Gestational age was determined according to the last menstrual period and ultrasound findings.
6. Transvaginal ultrasound assessment was performed preceding choosing the patients so as to survey the nearness of a gestational sac and a practical fetus in the uterine cavity.
7. CA-125 serum levels were estimated and contrasted and progesterone levels. Blood was acquired from an antecubital vein and the serum was isolated and solidified at - 70°C until tested.
8. The rule of estimating progesterone level by the Electrochemiluminescence Immunoassay (ECLIA) was planned for use on Elecsys and Cobase immunoassay analyzers.
9. CA-125 was estimated by the Electrochemiluminescence

Immunoassay (ECLIA) expected for utilized on Elecsys and Cobase the immunoassay analyzers.

10. The estimations of progesterone and serum CA-125 were thought about between the control group and the investigation group.

11. Samples were taken before exgerous progesterone application.

Patients were followed until 20 weeks of pregnancy.

Data were gathered from the beginning of time, essential clinical assessment, research center examinations and result measures coded, entered and broke down utilizing Microsoft Excel programming. Information were then brought into Statistical Package for the Social Sciences (SPSS variant 20.0) (Statistical Package for the Social Sciences) programming for investigation. Data were represented as number, percentage, mean  $\pm$  SD and correlation was by Pearson's correlation or Spearman's. P value was considered significant at  $<0.05$

## RESULTS

There were no statistically significant differences between the two groups regarding maternal age and parity, but there was a significant statistical

difference between the two groups regarding number of previous abortions (**Table 1**).

**Table (1): Comparison between demographic characteristics of control group and those with threatened miscarriage**

Parameters \ Groups	Threatened		Normal		p.value
	No	%	No	%	
Age/year mean± SD	24.2±4.9		23.9±3.1		> 0.005
Parity	No	%	No	%	> 0.005
<b>P0</b>	20	50%	22	55.00%	
<b>P1</b>	6	15%	14	35.00%	
<b>P2</b>	14	35%	2	5.00%	
<b>P3</b>	4	10.00%	0	0.00%	
<b>P4</b>	0	0.00%	2	5.00%	0.002
Abortion	No	%	No	%	
<b>0</b>	32	80%	40	100%	
<b>1</b>	10	25%	0	0%	

There was no statistically significant difference among control group and

patients with threatened miscarriage regarding gestational age/week (**Table 2**).

**Table (2): Gestational age in women with normal pregnancy and those with threatened abortion**

Pregnancy \ Groups	Threatened	Normal	p.value
	Mean ±S.D	Mean±S.D	
Gestational age (week)	8.1±1.09	8.4±1.03	> 0.005

Among the 40 patients who presented with threatened miscarriage (group I) 70 % continued their pregnancy and 30% had miscarriage. On the other hand, among

control group (group II), 85% continued their pregnancy and 15 % had miscarriage (**Table 3**).

**Table (3): Incidence of miscarriage in group I and group II**

Pregnancy \ Groups	Threatened		Normal		Total
	No	%	No	%	
Continued	28	70%	34	85%	62
Aborted	12	30%	6	15%	18
Total	40	100%	20	100%	80

The mean level of CA.125 was 42.3±19.1 in threatened group, and in normal group was 30.1±21.6. Also, there was a statistically difference between the

two groups regarding serum CA125 (P<0.05). On the other hand, there was no statistically difference between the two groups regarding progesterone (Table 4).

**Table (4): Comparison between group I and group II regarding mean value of CA125 and progesterone**

Parameters \ Groups	Threatened Mean ±S.D	Normal Mean ±S.D	p. value
CA.125	42.3±19.1	30.1±21.6	0.01
Progesterone	34.9±31.1	49.7±51.7	> 0.005

There were statistically differences between the two groups regarding CA125 (P<0.05) but there was no statistically

difference between the two groups regarding Progesterone (Table 5).

**Table (5): CA125 and progesterone in group I women who continued pregnancy and those with miscarriage**

Biomarkers \ Groups	Continued Mean±S.D	Aborted Mean±S.D	p.value
CA.125	32.1±14.1	60.4±15.13	0.012
Progesterone	43.5±10.2	5.4±2.6	0.01

## DISCUSSION

Undermined Miscarriage is characterized as pregnancy misfortune at a phase when the incipient organism or baby is not fit for free survival and that is before the time of suitability (Osmanagaoglu et al., 2014).

The maternal serum level of CA125 rises unassumingly in the primary trimester of pregnancy, at that point drops during the second and third trimesters to the range found in non-pregnant ladies the most extreme estimation of 550 IU/mL

has been accounted for in the principal trimester. There is higher convergence of CA125 in human amniotic liquid, as contrasted and maternal or fetal blood (Sweed et al., 2016).

A few examinations have demonstrated that degrees of CA125 can be utilized to forecast result of pregnancies convoluted with undermined unnatural birth cycles (Revankar et al., 2015) while other did not. A meta-investigation study has anyway demonstrated that estimation of CA125 and progesterone levels are

valuable in segregating ectopic and intrauterine fruitless from typical pregnancies (*Abdul-Hussein et al., 2012*). There is at present no all-around acknowledged cut-off an incentive for CA125 for forecasting pregnancy result, diverse cut-off qualities have been utilized in various investigations.

Progestogens have been utilized, starting in the principal trimester of pregnancy, trying to avoid unconstrained unnatural birth cycle. Their utilization is especially normal with helped conceptive innovations (*Maggio et al. 2014*).

We directed the present work to explore the connection between serum progesterone and CA-125 indistinguishing effective from fruitless pregnancies during the main trimester.

In this work, there were 80 instances of affirmed intrauterine pregnancies between 6-12 weeks with obvious embryonic throb, first group of 40 patients complaining of vaginal draining and the second group of 40 asymptomatic patients. All patients were seen at Obstetrics and Gynecology Clinic in Al-Hussein and Sayed Galal Hospitals, Al-Azhar University.

All patients demonstrated proof of embryonic heart action.

The present examination demonstrated that among the 40 patients who gave undermined unsuccessful labor (group I), 70 % proceeded with their pregnancy and 30% had unnatural birth cycle. Among control group (group II), 85% proceeded with their pregnancy and 15 % had premature delivery.

*Adeku et al. (2019)* who study Serum CA-125 for Early Prediction of

Miscarriage revealed that 25% occurred in created unnatural birth cycle, while 75% proceeded with their pregnancy till 20 weeks. Also, 10% quiet just created premature delivery and 90% proceeded with their pregnancy.

In the present investigation, there were no measurably critical contrasts between the two groups with respect to maternal age and equality. Yet, there was noteworthy factual distinction between the two groups in number of past premature births. These were in concurrence with *Adeku et al. (2019)*.

An ongoing methodical audit and meta-investigation proposed serum CA-125 to have a high prescient incentive in distinguishing pregnancies that are prone to proceed. It even recommended it to be clinically better than the ordinarily utilized biochemical markers as -HCG and progesterone in anticipating the result of a pregnancy with sound embryo (*Pillai et al. 2015*).

There were factually contrasts between patients who gave compromised unnatural birth cycle and control group with respect to serum CA125, but no factually distinction between the two groups with respect to progesterone.

These discoveries were reliable with *Sweed et al. (2016)* who expressed those CA125 serum level increments during first trimester of pregnancy than those in non-pregnant ladies. Additionally, serum CA-125 demonstrated a factually critical distinction between group I and II. Furthermore, it varied essentially between ladies who proceeded with their pregnancy and the individuals who created premature delivery. The same contrast was seen between ladies who

finished their pregnancy till 20 weeks and the individuals who created unnatural birth cycle inside each group.

*Adeku (2019)* stated that the mean CA125 level was fundamentally higher in the examination group when contrasted with the control group. This abnormal state mirrors a conceivable tropho-decidual birthplace for CA125. This examination additionally uncovered that the more elevated amount of serum CA125 found in aborters contrasted and the non-aborters was factually huge after effects of this investigation. Serum CA-125 indicated fundamentally higher levels in ladies giving seeping than those with typical pregnancy, and this backing the possibility of CA-125 being discharged auxiliary to decidual disturbance which was proposed by a few different investigations (*Sweed et al. 2016*). Utilizing ROC bend examination with affectability of 80% and explicitness 100%, this investigation discovered ideal cut-off criteria of CA-125 > 40.16 IU/ml would be utilized for expectation of event of premature delivery.

*Revankar et al. (2015)* demonstrated that the serum CA-125 level assurance is significant in the ladies with side effects of undermined fetus removal and it might be a shabby, touchy and explicit expectation in the instances of compromised premature birth and pregnancy misfortune.

*Haas and Ramsy (2008)* assessed the adequacy and security of progesterone supplementation as a deterrent treatment against undermined fetus removal. They didn't bolster the standard utilization of serum progesterone test to anticipate danger of pregnancy misfortune in

instances of first trimesteric compromised fetus removal.

*Adeku et al. (2019)* investigated the connection between serum progesterone and practicality of the pregnancy during the principal trimester. The mean serum progesterone of the considered populace was fundamentally high in suitable pregnancy group contrasted with non-practical pregnancy group.

In this investigation; 6.7% of suitable pregnancies had serum progesterone level >10 ng/ml, while 20.7% of non-feasible pregnancies had serum progesterone level <10 ng/ml, the serum progesterone cut off level 10 ng/ml was 79.3% delicate to analyze non-reasonable pregnancy and was 93.3% explicit to analyze practical pregnancy.

Additionally, in this investigation, 1.1% of feasible pregnancies had serum progesterone level <20 ng/ml, while 4.8% of non-suitable pregnancies had serum progesterone level >20 ng/ml, the serum progesterone at cut off level 20 ng/ml was 95.1% touchy to analyze non-reasonable pregnancy and was 98.9% explicit to analyze practical pregnancy.

*Seong (2016)* concluded that serum progesterone is a solid marker for early pregnancy disappointment and single examine of its serum level can separate among reasonable and non-practical pregnancies.

*Adeku et al. (2019)* in their examination, found no noteworthy distinction between levels of CA125 between ladies with undermined premature deliveries and those with ordinary intrauterine pregnancies. This distinction might be on the grounds that

patients utilized in their investigation had a background marked by fruitlessness or routine premature births. There is a likelihood that such a populace contrasts from an ordinary prolific populace utilized in our examination concerning CA125 levels. An investigation done by *Mahdi et al. (2010)* demonstrated that CA125 levels in compromised premature deliveries are higher than ordinary intrauterine pregnancies. This was anyway factually inconsequential. This might be because of contrasts in the test strategy for CA125 levels. Radioimmunoassay was utilized in their investigation while an ELISA was utilized in this examination.

Our examination stated that 80.55% affectability and 100% particularity of CA125 and 78.65% affectability and 98.04% explicitness of progesterone for expectation of the event of unnatural birth cycle.

These discoveries were steady with *Sweed et al. (2016)* who expressed that Using Receiver-working trademark (ROC) bend investigation with affectability of 80% and explicitness 100%, an ideal cut-off basis of CA-125 > 40.16 IU/ml would be utilized for expectation of event of unnatural birth cycle. While, ideal cut-off criteria of CA-125 > 58 IU/ml for expectation of event of unsuccessful labor in patients with compromised unnatural birth cycle) group I) would be set up with affectability of 78 % and particularity 97%). Likewise in group II, with affectability of 80% and particularity 100%, ideal cut-off criteria of CA1-25 > 28.45 IU/ml was found for expectation of event of unnatural birth cycle

A few cutoff esteems for serum CA125 level were proposed to segregate among feasible and non-reasonable incubations at time of vaginal dying. Utilized a 125 IU/ml as a cutoff esteem and announced a 100% affectability and particularity. *Abdul-Hussein. (2012)* used a 65 IU/ml as a cutoff esteem and revealed affectability half for this level. *Han et al. (2012)* used a cutoff estimation of 66.5 IU/ml with affectability of 55%.

## CONCLUSION

Serum CA-125 is a promising biomarker for the early prediction of miscarriage.

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## القيمة التنبؤية من قياس الأنتيجين السرطاني 125 مقابل قيمة البروجستيرون في الدم لتوقع خطر فقدان الحمل في حالات الاجهاض المنذر في الثلاث شهور الأولى من الحمل

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**خلفية البحث:** الإجهاض يحدث في حوالي 5,0-1% من النساء الحوامل . وغالباً ما يكون سبب الإجهاض غير معلوم، وقد يكون بسبب عدة عوامل مع وجود العديد من النقاش حول تحديد السبب وطرق العلاج.

**الهدف من البحث:** تحقيق العلاقة بين هرمون البروجسترون في الدم و CA-125 التمييز الناجح من حالات الحمل غير الناجحة خلال الأشهر الثلاثة الأولى.

**المرضي وطرق البحث:** شملت الدراسة 80 حالة من حالات الحمل المؤكدة داخل الرحم بين 6-12 أسبوعاً: منها نبض جنيني مثبت في اربعين حالة بدون أعراض (المجموعة الاولى )، واربعين حاله مع نزيف مهلي ودليل على نشاط القلب الجنيني (المجموعة الثانية). وقد تم اختيار جميع الحالات من قسم أمراض النساء والولادة بمستشفى الحسين وسيد جلال بجامعة الأزهر، وذلك في المده من ديسمبر 2018 إلي أغسطس 2019. وقد ظهر في جميع المرضى نبضاً جنينياً، وتم قياس نسبة CA125 بالمقارنة بنسبة البروجستيرون.

**نتائج البحث:** كان المستوي المعياري ل CA 125 (42.3±19.1) في حالات الاجهاض المنذر، (21.6±30.1) في الحالات الطبيعيه . كان هناك إختلافاً إحصائياً بين المجموعتين بخصوص CA125 و علي الجانب الآخر، لم يكن هناك إختلافات إحصائية بين المجموعتين بخصوص نسبة البروجستيرون وقد أظهر تحليل منحدر ROC 80.55% حساسيه ، 100% خصوصيه لتوقع نسبة 78.65% CA125، حساسيه ، 98.04% خصوصيه لتوقع نسبة البروجستيرون لحدوث الاجهاض.

**الاستنتاج:** نسبة CA125 من التحاليل الواعده للتوقع المبكر للإجهاض.