Al-Azhar International Medical Journal

Volume 5 | Issue 7 Article 53

7-31-2024

Value of Serum Estradiol, Progesterone and Beta-Human Chorionic Gonadotropin in Prediction of 1st Trimester Miscarriage within 9 weeks of Gestation

Wael Solaiman Taha
Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Mohamed Ahmed Abd El-Moaty
Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Mohamed Gamal Abd El-Salam
Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt,
mohamed.elbermawy9@gmail.com

How to Cite This Article

Taha, Wael Solaiman; Abd El-Moaty, Mohamed Ahmed; and Abd El-Salam, Mohamed Gamal (2024) "Value of Serum Estradiol, Progesterone and Beta-Human Chorionic Gonadotropin in Prediction of 1st Trimester Miscarriage within 9 weeks of Gestation," *Al-Azhar International Medical Journal*: Vol. 5: Iss. 7, Article 53.
DOI: https://doi.org/10.58675/2682-339X.2571

ORIGINAL ARTICLE

Value of Serum Estradiol, Progesterone and Beta-Human Chorionic Gonadotropin in Prediction of 1st Trimester Miscarriage within 9 weeks of Gestation

Wael S. Taha, Mohamed A. Abd El-Moaty, Mohamed G. Abd El-Salam *

Department of Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Abstract

Background: ***One in five women experience the emotional toll of a threatened miscarriage.***

Aim and objectives: ***To forecast the probability of a miscarriage occurring within the first nine weeks of pregnancy, an assessment of serum estradiol, progesterone, as β-human chorionic gonadotropin (β-HCG) levels is conducted within the same time frame.***

Patients and methods: ***This was a prospective cross-sectional study conducted on eighty-six pregnant women in the first trimester at Obstetrics & Gynecology department of Sayed Galal Hospital, Al-Azhar University.***

Results: ***At cutoff point <420, serum estrogen at 5–6-week gestation has 96.6% sensitivity and 92.6% specificity as a predictor for Miscarriage, at cutoff point <18.5, serum Progesterone at 5–6-week gestation has 96.6% sensitivity and 96.3% specificity as predictor for Miscarriage, at cutoff point <657.5, serum HCG at 5–6-week gestation has 94.9% sensitivity and 96.3% specificity as predictor for Miscarriage. At cutoff point <733, serum estrogen at 8–9-week gestation has 98.3% sensitivity and 96.3% specificity as a predictor for Miscarriage; at cutoff point <21.5, serum Progesterone at 8–9-week gestation has 78% sensitivity and 77.8% specificity as predictor for Miscarriage, at cutoff point <2116, serum HCG at 8–9-week gestation has 98.3% sensitivity and 81.5% specificity as predictor for Miscarriage.***

Conclusion: ***Regarding hormonal profile at 8-9 gestational weeks, there was statistically significant lower Estrogen, progesterone, and HCG levels in Miscarriage than in the Ongoing pregnancy group.***

Keywords: Serum estradiol; Beta-human chorionic gonadotropin; Miscarriage

1. Introduction

Around 20 percent of women experience threatened Miscarriage, which is linked to considerable emotional suffering. The ambiguity surrounding the prognosis of impending Miscarriage presents an equally difficult challenge for healthcare practitioners. Past research has examined different biochemical indicators to forecast the outcome of impending Miscarriage.[1]

The incidence of loss of pregnancy is roughly fifteen to twenty-five percent. It remains the prevailing pregnancy problem that has a significant impact on the physical and mental well-being of women. The repetitive clinical evaluations, as well as interventions for threatening abortion, impose both financial and psychological hardships on patients. However, no dependable clinical sign is available to forecast it accurately in its early stages.[2,3] Diminished levels and sluggish development rates of estradiol and β-human chorionic gonadotropin likely suggest an unfavorable pregnancy outcome. HCG, a crucial endocrine factor, can suppress T cell activation and prevent aberrant stimulation of T lymphocyte response, protecting the embryo from potential harm. Low initial HCG levels, an abnormal HCG ratio, & a slow increase in HCG levels during early pregnancy may suggest the possibility of a miscarriage or ectopic pregnancy.[4]

Estrogen promotes the growth of the endometrium & increases the thickness of the myometrium. It also improves blood flow and strengthens uterine contractions. Research indicates that estradiol plays a crucial role in sustaining early pregnancy.[5]

This study aimed to predict miscarriage outcomes within nine weeks of gestational age by evaluating values of serum estradiol, progesterone, and β-human chorionic gonadotropin (β-HCG) within nine weeks of gestation.

Accepted 21 July 2024.
Available online 31 July 2024

* Corresponding author at: Obstetrics and Gynecology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt.
E-mail address: mohamed.elbermawy9@gmail.com (I. G. M. Abdulmageed).

https://doi.org/10.58675/2682-339X.2571

2. Patients and methods

This prospective cross-sectional study was conducted on 86 pregnant women in the initial trimester at the Obstetrics and Gynecology department of Sayed Galal Hospital, Al-Azhar University.

Inclusion criteria: Pregnant females in the first trimester, no gestational complications, and no medical disorders.

Exclusion criteria: Individuals with a history of recurrent Miscarriage & thyroid autoimmunity. Pregnancies are attained using artificial assisted reproductive technology (ART), for example, intracytoplasmic sperm injection (ICSI) or intrauterine insemination (IUI).

Sample size justification

The calculations for sample size were performed using the MedCalc® version 12.3.0.0 program, located in Ostend, Belgium. The statistical calculator utilized a 95% confidence interval as well as a research power of 95%, with α error of 5%. Based on a prior investigation[6], they indicated that measuring blood levels of estradiol at 7-9 weeks can accurately predict Miscarriage. The area under the ROC curve (AUC) was discovered to be 0.866 (95% CI 0.793-0.938, P=0.000). The diagnostic cutoff value was determined to be 576pg/ml, with a sensitivity of 0.804 and specificity of 0.829. Therefore, given this assumption, the sample size was 78 cases, the minimum number required for this investigation, given a dropout rate of 10%. Thus, based on the computation, the sample size comprised 86 ladies.

Methods

All participants underwent

Entire history taking: Personal history, Present history, menstrual history. Menstrual Cycle Details: Age at menarche, duration of their menstrual cycle, frequency of periods, date of the last menstrual period, regularity of cycles, Presence of clotting or spotting between periods, and any changes in menstrual patterns over time. Menstrual Pain or Discomfort: Any menstrual pain, any other menstrual-related symptoms, gestational age, expected date of delivery, obstetric history for each previous delivery, Presence or absence of prior pregnancy complicated by FGR, medical history, and Past Surgical history

Estradiol, progesterone, and β-HCG measurement

Chemiluminescence was employed to determine serum estradiol, progesterone, and β-HCG levels on a Roche Elecsys 2010 device. The changes across the batches were 6.4 percent, whereas the variances within the batches were 6.0 percent.

Radiological investigation

The same proficient attending physician did the transvaginal ultrasound scans. The patient was positioned on the examination table in the lithotomy position, similar to a pelvic examination. Provide a drape or sheet for privacy. Frequency: Typically, transvaginal ultrasound uses a frequency range of 5-9 MHz to provide high-resolution images. Depth: Adjust the depth setting based on the area of interest. Standard depth settings range from 4 to 10 cm. The average pregnancy category was identified through ultrasound screening utilizing the GE V730 Ultrasonic instrument, with confirmation of fetal viability at twelve weeks of gestational age. Miscarriage was diagnosed with ultrasonic criteria[7]: A crown-rump length of seven millimeters or more without a heartbeat, a mean sac diameter of 25 millimeters or greater without an embryo, the absence of an embryo with a heartbeat for at least two weeks following a scan that revealed a gestational sac without a yolk sac, and the absence of an embryo with a heartbeat for at least 11 days after a scan that revealed a gestational sac with a yolk sac.

Ethical considerations

The research protocol received approval from the Ethical Committee of the Faculty of Medicine of AL Azhar University, specifically the Ethical Committee of the Obstetrics & Gynecology Department. Before the study, everyone involved was provided with a clear description of its goal and procedures, and their consent was obtained verbally and in writing. The trial assumed confidentiality and privacy at all levels.

3. Results

Neither group differed significantly from the other in terms age & BMI p= 0.333, 0.635 respectively

Table 1. Demographic data of patients

	MISCARRIAGE N=27		ONGOING PREGNANCY N=59		INDEPENDENT STUDENT T TEST	
	Mean	SD	Mean	SD	t	P-value
AGE (YEARS)	28.52	1.34	28.86	1.87	-0.975	0.333
BMI	28.80	1.55	28.61	2.01	0.477	0.635

Regarding fetal US, there was statistically in significant change amongst the 2 groups as regard the CRL and Mean sac diameter p>0.05.

Table 2. CRL and Mean sac diameter of the studied population

	MISCARRIAGE N=27		ONGOING PREGNANCY N=59		INDEPENDENT STUDENT T TEST	
	Mean	SD	Mean	SD	t	P-value
CRL	24.15	4.32	24.64	3.74	-0.515	0.609
MSD	30.30	3.07	29.90	2.45	0.592	0.557

Regarding hormonal profile at 5-6 gestational week, there is statistically significant lower Estrogen, progesterone and HCG level in Miscarriage than Ongoing pregnancy group p= 0.0001.

Table 3. hormonal profile of the studied population at 5-6 gestational week

	MISCARRIAGE N=27		ONGOING PREGNANCY N=59		INDEPENDENT STUDENT T TEST	
	Mean	SD	Mean	SD	t	P-value
ESTROGEN	351.59	43.57	484.54	30.21	-14.354	0.0001
PROGESTERONE	16.89	1.12	20.78	1.22	-14.53	0.0001
HCG	514.22	49.52	711.54	45.42	-17.593	0.0001

Regarding hormonal profile at 8-9 gestational week, there was statistically significant lower Estrogen, progesterone and HCG level in Miscarriage than Ongoing pregnancy group p= 0.0001.

Table 4. hormonal profile of the studied population at 8-9 gestational week

	MISCARRIAGE N=27		ONGOING PREGNANCY N=59		INDEPENDENT STUDENT T TEST	
	Mean	SD	Mean	SD	t	P-value
ESTROGEN	590.85	50.40	1177.20	119.76	-31.933	0.0001
PROGESTERONE	20.22	2.29	22.83	1.63	-5.327	0.0001
HCG	2010.67	120.38	2730.20	166.60	-22.672	0.0001

At cutoff point <420, serum estrogen at 5–6-week gestation has 96.6% sensitivity and 92.6% specificity as predictor for miscarriage, at cutoff point <18.5, serum Progesterone at 5–6-week gestation has 96.6% sensitivity and 96.3% specificity as predictor for miscarriage, at cutoff point <657.5, serum HCG at 5–6-week gestation has 94.9% sensitivity and 96.3% specificity as predictor for miscarriage. (Table 5)

Table 5. sensitivity and specificity of hormonal profile at 5–6-week gestation as predictor for miscarriage

	CUTOFF POINT	AREA UNDER CURVE	STD. ERROR	SENSITIVITY%	SPECIFICITY%	ASYMPTOTIC 95% CI	
						Lower Bound	Upper Bound
ESTROGEN	420	0.984	0.01	96.60%	92.60%	0.964	1.000
PROGESTERONE	18.5	0.992	0.006	96.60%	96.30%	0.981	1.000
HCG	657.5	0.981	0.012	94.90%	96.30%	0.956	1.000

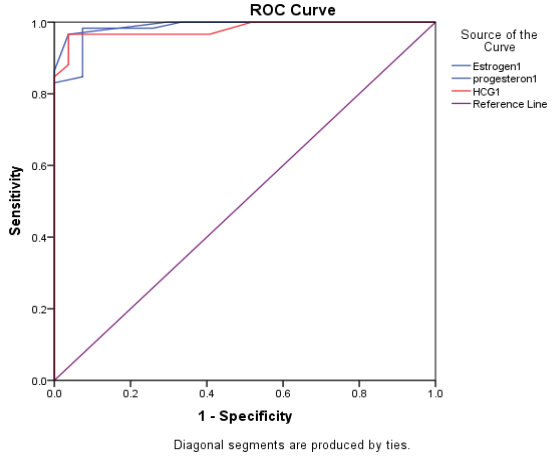

Figure 1. ROC curve for hormonal profile at 5-6 week gestation as predictor for miscarriage

At cutoff point <733, serum estrogen at 8–9-week gestation has 98.3% sensitivity and 96.3% specificity as predictor for miscarriage, at cutoff point <21.5, serum Progesterone at 8–9-week gestation has 78% sensitivity and 77.8% specificity as predictor for miscarriage, at cutoff point <2116, serum HCG at 8–9-week gestation has 98.3% sensitivity and 81.5% specificity as predictor for miscarriage. (Table 6)

Table 6. sensitivity and specificity of hormonal profile at 8–9-week gestation as predictor for miscarriage

	CUTOFF POINT	AREA UNDER CURVE	STD. ERROR	SENSITIVITY%	SPECIFICITY%	ASYMPTOTIC 95% CI	
						Lower Bound	Upper Bound
ESTROGEN	733	0.999	0.002	98.30%	96.30%	0.995	1.000
PROGESTERONE	21.5	0.831	0.055	78%	77.80%	0.724	0.938
HCG	2116	0.994	0.006	98.30%	81.50%	0.982	1.000

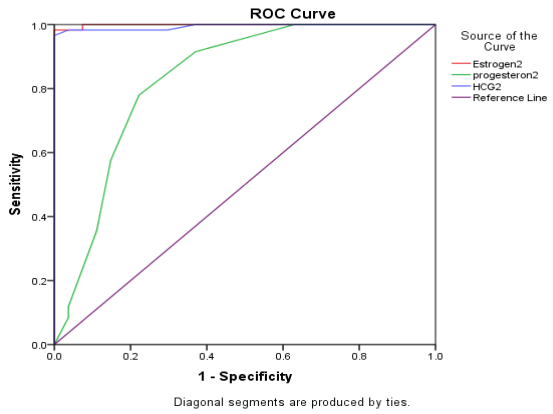

Figure 2. ROC curve for hormonal profile at 8-9 week gestation as predictor for miscarriage

4. Discussion

Around between 15 and 25% of pregnancies end in Miscarriage. It continues to be the leading cause of psychological and physiological problems among pregnant ladies.[8]

The main results of our study were as follows:

Our study showed that, regarding age distribution, the mean age in the Miscarriage group was 28.52±1.34 years, the mean age in Ongoing pregnancy was 28.68±1.87 years, and the mean BMI in the Miscarriage group was 28.8±1.55, the mean age in Ongoing pregnancy was 28.61±2.01. There was statistically significant variance among the two groups concerning age and BMI.

Jha et al. Their prospective study was carried out on a cohort of 125 women, aged between twenty and thirty-five years, who had a history of recurrent pregnancy loss. The cases were categorized into three distinct groups. Group A is the control group, including 45 healthy pregnant women who have not experienced any miscarriages in the past. Group B comprised 40 individuals who had experienced two or more instances of pregnancy loss during the first trimester. Group C consisted of forty females who experienced pregnancy termination for the first time during the research before completing the first trimester.[9]

We found that regarding hormonal profile at 5-6 gestational weeks, there was statistically significant lower Estrogen, progesterone, and HCG levels in the Miscarriage group than in the Ongoing pregnancy group. The current study showed that regarding hormonal profile at 8-9 gestational weeks, there was statistically significant lower Estrogen, progesterone, and HCG levels in the Miscarriage group than in the Ongoing pregnancy group.

Our results are supported by Deng et al.[6], who reported a significant change among the studied groups regarding Estrogen and progesterone within nine weeks of gestation. They also demonstrated that there was no significance between the studied groups regarding HCG.

As well, Duanet al. revealed that the average levels of progesterone, as well as β-HCG among females with inevitable miscarriages, were significantly reduced (13.76 ± 5.52 ng/ml, 3,647.00 ± 2,123.00 mIU/ml, respectively) compared to ongoing pregnancies (25.47 ± 6.18 ng/ml, 8,492.00 ± 2,389.00 mIU/ml, respectively) and normal intrauterine pregnancies (31.67 ± 5.86 ng/ml, 13,437.00 ± 6,256.00 mIU/ml, respectively) (P under 0.001). In addition, the levels of these markers among women with continuing pregnancies were markedly lower than those observed in normal intrauterine pregnancies (P under 0.001).[10]

According to our results, at cutoff point <420, serum estrogen at 5–6-week gestation has 96.6% sensitivity and 92.6% specificity as a predictor for Miscarriage, at cutoff point <18.5, serum Progesterone at 5–6-week gestation has 96.6% sensitivity and 96.3% specificity as predictor for Miscarriage, at cutoff point <657.5, serum HCG at 5–6-week gestation has 94.9% sensitivity and 96.3% specificity as predictor for Miscarriage.

Regarding our results, at cutoff point <733, serum estrogen at 8–9-week gestation has 98.3% sensitivity and 96.3% specificity as a predictor for Miscarriage, at cutoff point <21.5, serum Progesterone at 8–9-week gestation has 78% sensitivity and 77.8% specificity as predictor for Miscarriage, at cutoff point <2116, serum HCG at 8–9-week gestation has 98.3% sensitivity and 81.5% specificity as predictor for Miscarriage.

Jha et al. revealed that blood beta HCG exhibited a sensitivity of 100%, a specificity of 55.9%, a positive predictive value of 52.7%, and a negative predictive value of 100%. The sensitivity of Serum progesterone was 37.42%, with a specificity of 82.34%, a positive predictive value of 54.91%, and a negative predictive value of 80.53%.[9]

Research has demonstrated that monitoring progesterone levels is crucial for predicting early normal development throughout pregnancy.[11,12]

4. Conclusion

Regarding hormonal profile at 8-9 gestational weeks, there was statistically significant lower Estrogen, progesterone, and HCG levels in the Miscarriage than in the Ongoing pregnancy group. At cutoff point <733, serum estrogen at 8–9-week gestation has 98.3% sensitivity and 96.3% specificity as a predictor for Miscarriage; at cutoff point <21.5, serum Progesterone at 8–9-week gestation has 78% sensitivity & 77.8% specificity as predictor for Miscarriage, at cutoff point <2116, serum HCG at 8–9-week gestation has 98.3% sensitivity and 81.5% specificity as predictor for

Miscarriage.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

Funding

No Funds : Yes

Conflicts of interest

There are no conflicts of interest.

References

1. Pillai RN, Konje JC, Tincello DG, Potdar N. Role of serum biomarkers in the prediction of outcome in women with threatened miscarriage: a systematic review and diagnostic accuracy meta-analysis. Hum Reprod Update. 2016;22(2):228-239.
2. Kanmaz AG, İnan AH, Beyan E, Budak A. The effects of threatened abortions on pregnancy outcomes. Ginekol Pol. 2019; 90(4):195-200.
3. RYCHIK, Jack. Evaluation and management of the child and adult with Fontan circulation: a scientific statement from the American Heart Association. Circulation, 2019, 140.6: e234-e284.
4. Turesheva A, Aimagambetova G, Ukybassova T, et al. Recurrent Pregnancy Loss Etiology, Risk Factors, Diagnosis, and Management. Fresh Look into a Full Box. J Clin Med. 2023;12(12):4074.
5. Verma P, Verma R, Nair RR, et al. Altered crosstalk of estradiol and progesterone with Myeloid-derived suppressor cells and Th1/Th2 cytokines in early miscarriage is associated with early breakdown of maternal-fetal tolerance. Am J Reprod Immunol. 2019;81(2):e13081.
6. Deng W, Sun R, Du J, et al. Prediction of miscarriage in first trimester by serum estradiol, progesterone and β-human chorionic gonadotropin within 9 weeks of gestation. BMC Pregnancy Childbirth. 2022;22(1):112.
7. Doubilet PM, Benson CB, Bourne T, et al. Diagnostic criteria for nonviable pregnancy early in the first trimester. N Engl J Med. 2013;369(15):1443-1451.
8. Wang L, Jiang Y, Shen H, et al. Independent value of serum β-human chorionic gonadotropin in predicting early pregnancy loss risks in IVF/ICSI cycles. Front Immunol. 2022; 13:992121. Published 2022 Sep 29.
9. JHA, Ela; JHA, Arun Kumar; SAMUEL, Annie. Prognostic Value of Biochemical Markers-Ca 125, Serum Beta HCG And Serum Progesterone in Cases of Recurrent Pregnancy Loss In The First Trimester of Pregnancy.2019 April; 18: 2279-0861.
10. Duan L, Yan D, Zeng W, Yang X, Wei Q. Predictive power progesterone combined with beta human chorionic gonadotropin measurements in the outcome of threatened miscarriage. Arch Gynecol Obstet. 2011;283(3):431-435.
11. Day A, Sawyer E, Mavrelos D, Tailor A, Helmy S, Jurkovic D. Use of serum progesterone measurements to reduce need for follow-up in women with pregnancies of unknown location. Ultrasound Obstet Gynecol. 2009;33(6):704-710.
12. Al-Sebai MA, Kingsland CR, Diver M, Hipkin L, McFadyen IR. The role of a single progesterone measurement in the diagnosis of early pregnancy failure and the prognosis of fetal viability. Br J Obstet Gynaecol. 1995;102(5):364-369.