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Serum Progesterone Hormone Level and Threatened Miscarriage with Its Predictive Value for Viability

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Abstract

Background and objectives: Serum progesterone hormone is essential for pregnancy development and progression. Thus, this study aimed to assess the level of serum progesterone in normal pregnancy and threatened miscarriage with its predictive value for viability.

Methods: This case-control study was held in outpatient clinics in the Emergency Departments of Erbil Maternity Teaching Hospital, Erbil, Iraq, from the 1st June 2022 to 31st May 2023 on 75 pregnant women with threatened miscarriages and 75 healthy pregnant women as controls. Diagnosis of threatened miscarriage was made through clinical features, investigations and ultrasonography. Then, the blood samples were collected to assess the serum progesterone level as a predictor for threatened miscarriage and viability of early pregnancy.

Results: Most participants (44%) were young (20-29 years old), had low economic status, gave birth to 1-3 children and had a gestational age of >9.0 weeks with no significant difference between both groups ($p>0.05$). A highly significant association ($p<0.001$) was observed between pregnant women with threatened miscarriage and non-viability of fetuses. The mean serum progesterone level was obviously decreased in females with threatened miscarriage. The mean serum progesterone hormone level of 20.5 nmol/L was a significant predictor of threatened miscarriage with acceptable validity findings. The mean serum progesterone hormone level of 11.8 nmol/L was a significant predictor of non-viability in pregnant women with threatened miscarriage and acceptable validity findings.

Conclusions: The serum progesterone level is an appropriate predictor of threatened miscarriage and fetal viability in early pregnancy.

Keywords: Early pregnancy, Fetal viability, Outpatients, Serum progesterone, Threatened miscarriage

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Introduction

Miscarriage generally is a frequent pregnancy complication which is presented as a spontaneous gestational loss before the 20th week of gestational age. The threatened miscarriage is affecting ongoing pregnancy accompanied by vaginal bleeding, regardless of abdominal pain.[1] It is regarded as an emergent obstetrical complication affecting generally 15% to 20% of pregnant women, which leads to spontaneous type in 25% of these pregnancies.[2,3] Multiple diagnostic efforts are directed to predict the spontaneous type among those women, and the assumption for initial risk evaluation is helpful in prevention and management plans that decrease the chance of spontaneous miscarriage.[4] Miscarriage is not only leading to gestation loss but it may also be complicated by anxiety, depression and other mental health problems.[5] Till now, no fixed treatment regimen has been able to prevent loss of gestation in pregnant women with threatening abortion except progesterone in women with recurrent miscarriages.[6] Common maternal-associated risks predicting spontaneous abortion were increased maternal age with low body mass index, in addition to the impact of serum biological markers in the prediction of spontaneous miscarriage.[7,8] Progesterone is the essential hormone required in the development and maintenance of pregnancy. It is vital in endometrial maturation, and good immune circumstances are required for early embryonic development. Low progesterone level was shown frequently among women with recurrent miscarriage and among pregnancies, which subsequently ended in miscarriage, however, it is unclear if low progesterone level was only a predictor of miscarriage or if it is causative for this miscarriage.[9-11] Nowadays, the National Institute for Health and Care Excellence (NICE) guidelines recommend conservative treatment for threatened miscarriage.[12] Multiple authors recognized the decline of serum progesterone among women with symptoms of threatening miscarriage compared to women with normal gestation.[13] Specifically, declined progesterone level was detected in women presented with a spontaneous abortion that was not affected by gestational duration. Otherwise, pregnant women with high progesterone levels showed a low risk of miscarriage.[9] Consequently, progesterone might help predict a spontaneous miscarriage in women with threatening miscarriage.[12] For that, serum progesterone hormone level is applied nowadays for early diagnosis of miscarriage with a cutoff value of ≤35 nmol/L with acceptable validity outcomes.[4, 14] Therefore, this study aimed to assess the level of serum progesterone in normal pregnancy and threatened miscarriage with its predictive value for viability.

Patients and methods

A case-control study was done in outpatient clinics and the Emergency Departments of Erbil Maternity Teaching Hospital, Erbil City, Kurdistan Region, Iraq, from the 1st June 2022 to 31st May 2023. Inclusion criteria were women with single intrauterine pregnancy confirmed by ultrasound examination, <13 weeks of gestation with positive fetal heart rate, complaining of vaginal bleeding and remarkable serum beta-human chorionic gonadotropin (b-HCG) hormone. Exclusion criteria were multiple pregnancies, unavoidable miscarriages, ectopic or molar pregnancies, previous progesterone hormone treatment for vaginal bleeding and in vitro fertilization. The ethics of this study were agreed upon with the Ethical Committee of the Kurdistan Higher Council for Medical Specialties (KHCMS). Samples of 75 pregnant women with threatened miscarriage were recruited, and 75 healthy pregnant women were selected as controls. The researcher collected information on women directly using

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questionnaires that covered participants' properties, symptoms, clinical history, pregnancy outcome, and serum progesterone level. The definition of threatened miscarriage was acquired by remarkable serum b-HCG level, proved gestation by ultrasonography with vaginal hemorrhage till the 20th week of pregnancy. No viability of pregnancy was proved through ultrasonography, which showed an emptied gestational sac and no fetal heart rate. This is mainly due to genetic abnormality rather than reduced progesterone level. Serum progesterone hormone level was assessed by collecting blood samples from study participants, which were sent to the Laboratory of Maternity Teaching Hospital for analysis. Statistical analysis was conducted using the Statistical Package for Social Sciences (SPSS, Chicago, USA, Version 25) program. The Chi-square and Fishers' exact tests were used to determine correlations between categorical variables and an independent sample t-test was used for continuous variables. Receiver Operating Curve (ROC) was done in the assessment of progesterone prediction for threatened miscarriage and viability of pregnancy. A p-value of ≤0.05 was considered a significant difference, while p≤0.001 was set as highly significant.

Results

Regarding the sociodemographic characteristics, most participants in both groups (44%) were young (aged 20-29 years old) had low economic status and normal body weight. Consequently, no significant differences were found between women in both groups regarding sociodemographic characteristics (p>0.05). Concerning the clinical characteristics, most participants in both groups gave birth to 1-3 children and had a gestational age of >9.0 weeks. Accordingly, there were no significant discrepancies between women in both groups regarding general characteristics (p>0.05), as shown in Table (1).

Table (1): Sociodemographic and clinical characteristics of the study groups.

Variable	Study groups				p-value
	Threatened miscarriage (n=75)		Controls (n=75)		
	No.	%	No.	%	
Age groups (Years)					
<20	18	24	7.0	9.3	0.07
20-29	33	44	33	44	
30-39	22	29.3	33	44	
40	2.0	2.7	2.0	2.7	
Socioeconomic status					
Low	47	62.7	45	60	0.9
Middle	20	26.7	22	29.3	
High	8.0	10.7	8.0	10.7	
Parity					
Nulliparous	25	33.3	18	24	0.4
Para 1-3	44	58.7	49	65.3	
Para ≥4	6.0	8.0	8.0	10.7	
Body Mass Index (BMI, Kg/m^2)					
Underweight (<18.50)	1.0	1.33	0.0	0.0	0.75

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Normal weight (18.50 - <24.90)	35	46.6	36	48	
Overweight (≥25–29.9)	25	33.33	20	26.66	
Obese (≥30)	14	18.66	19	25.33	
Mean gestational age (Weeks)	9±2.4		9.2±2.3		0.6

There was a highly significant association between pregnant women with threatened miscarriage and controls regarding hemorrhage symptoms ($p<0.001$), as no one had symptoms of bleeding among controls. Also, a significant correlation was observed between both studied groups regarding travel history ($p=0.004$), as no one in the controls had a history of travelling. Simultaneously, there were no significant discrepancies between women in both groups regarding past histories of early miscarriage, trauma, heavy work, diabetes mellitus and thyroid diseases ($p>0.05$), as shown in Table (2). A highly significant association was observed between pregnant women with threatened miscarriage and controls regarding fetus viability ($p<0.001$). Mean serum progesterone level declined among pregnant women with threatened miscarriage than control groups, with a highly significant association between both groups ($p<0.001$), as shown in Table (3).

Table (2): Symptoms and clinical history of the study groups.

Variable	Study groups				p-value
	Threatened miscarriage		Controls		
	No.	%	No.	%	
History of early miscarriage					
Positive	17	22.7	9.0	12	0.08
Negative	58	77.3	66	88	
Symptoms					
Bleeding	57	76.0	0.0	0.0	<0.001**
Bleeding & pain	18	24.0	0.0	0.0	
Asymptomatic	0.0	0.0	75	100	
History of trauma					
Positive	5.0	6.7	3.0	4.0	0.40
Negative	70	93.3	72	96	
History of travel					
Positive	8.0	10.7	0.0	0.0	0.004*
Negative	67	89.3	75	100	
History of heavy work					
Positive	8.0	10.7	7.0	9.3	0.78
Negative	67	89.3	68	90.7	
History of diabetes mellitus					
Positive	3.0	4.0	6.0	8.0	0.3
Negative	72	96	69	92	
History of thyroid diseases					
Positive	4.0	5.3	3.0	4.0	0.69
Negative	71	94.7	72	96	

*Significant difference **Highly significant difference

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Table (3): Fetal outcome and progesterone hormone in study groups.

Variable	Study groups				p-value
	Threatened miscarriage		Controls		
	No.	%	No.	%	
Outcome					
Viable	52	69.3	70	93.3	<0.001**
Non-viable	23	30.7	5.0	6.7	
Serum progesterone					
Mean±SD (nmol/L)	16.8±5.8		25.2±5.7		<0.001**

**Highly significant difference

Additionally, the mean serum progesterone level was significantly decreased in women with threatened miscarriage who had non-viable gestation (p<0.001), as shown in Figure (1). Moreover, a progesterone level of 20.5 nmol/L was a significant predictor of threatened miscarriage with acceptable validity findings (90.7% sensitivity, 72% specificity and 80% accuracy), as shown in Figure (2). Whereas progesterone level of 11.8 nmol/L was a significant predictor of non-viability in pregnant women with threatened miscarriage with acceptable validity findings (98.1% sensitivity, 95.7% specificity and 97% accuracy), as shown in Figure (3).

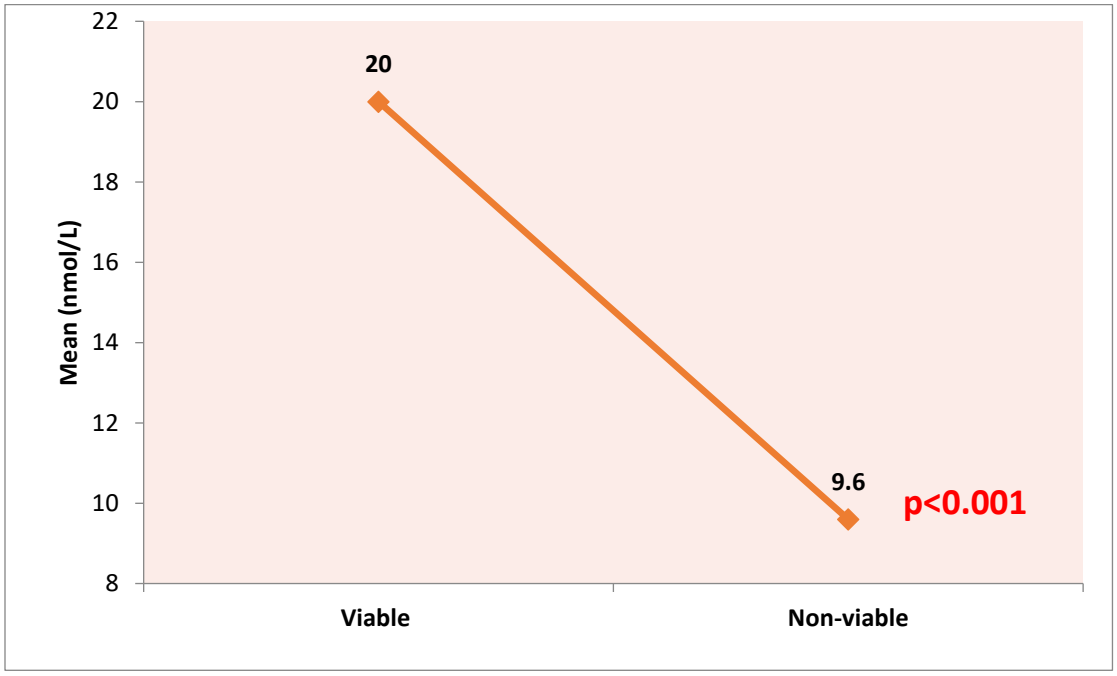

Figure (1): Progesterone hormone regarding pregnancy viability.

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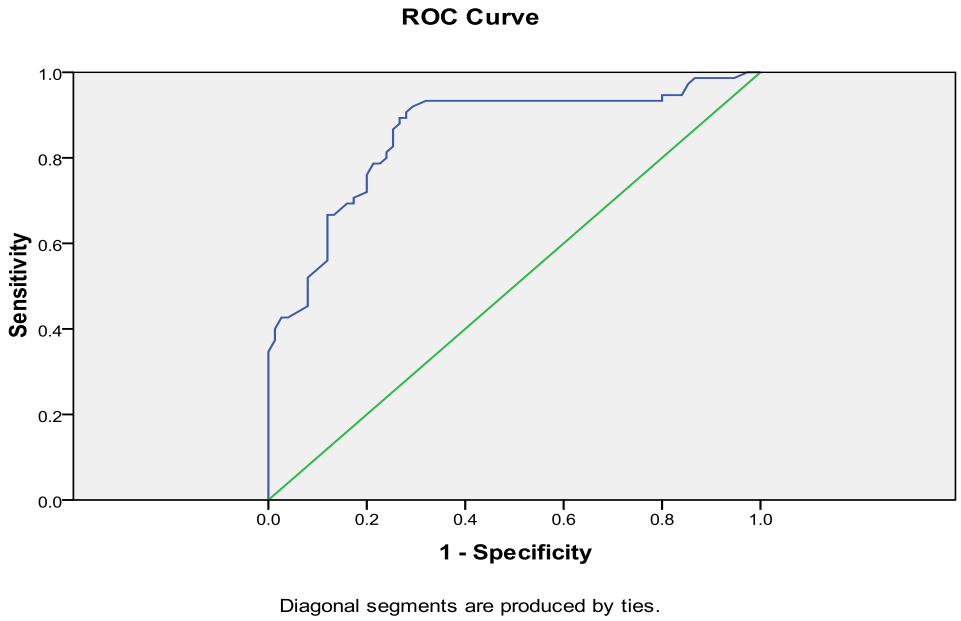

Figure (2): ROC of progesterone hormone in prediction of threatened miscarriage (AUC=0.85). AUC: Area under curve; ROC: Receiver Operating Curve

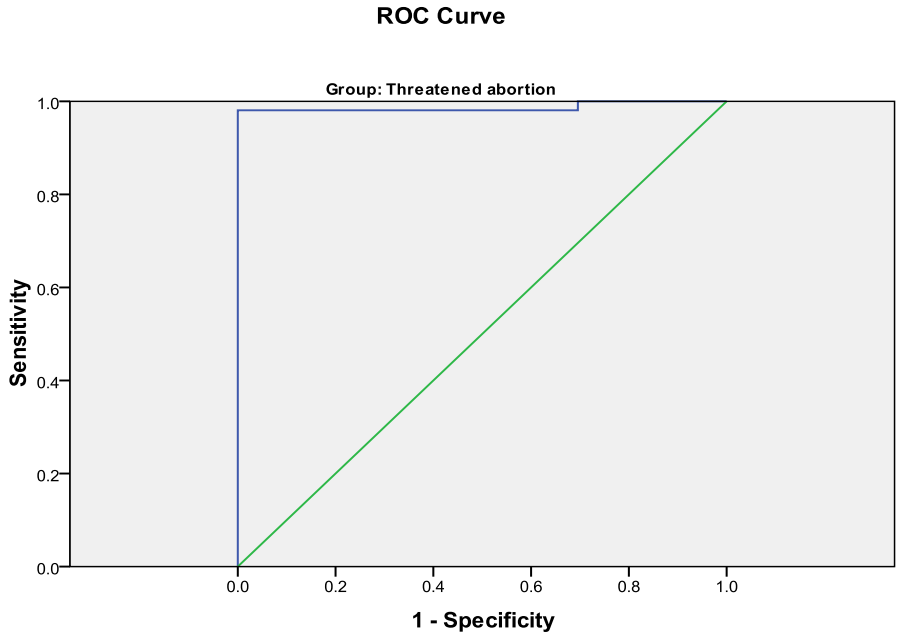

Figure (3): ROC of progesterone in the prediction of fetal viability in pregnant women with threatened miscarriage (AUC=0.98). AUC: Area under curve; ROC: Receiver Operating Curve

Discussion

In the current study, hemorrhage symptoms were predominant for women with threatened miscarriage. Akpan et al. retrospective cohort study stated that the main symptom of threatened miscarriage was hemorrhage. [15]

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Also, in this study, travel history (by land) with a duration of 2.0 to 3.0 hours among women with threatened miscarriages was significantly higher (10.7%) than controls. Coffey et al. stated that a positive travelling history for pregnant women at early pregnancy was related to a high chance of threatened miscarriage. [16] In the present study, the threatened miscarriage was related to the non-viability of fetuses, as 30.7% of women had non-viable pregnancies. However, this data is lower than that reported in a recent survey conducted in Kurdistan Region/Iraq by Saeed et al. on 113 pregnant women with early vaginal hemorrhage that found non-viable pregnancy constituted 67.3%. [18] Also, Ahmed et al. in a retrospective case-control study found a significant relationship between threatened miscarriage and non-viability of pregnancies. [17] The current study found a decline in progesterone hormone levels among women with threatened miscarriages. This finding is similar to the results of many literatures.[13,19] Previous Iraqi prospective studies revealed that serum progesterone measurement is a reliable biochemical test in establishing the diagnosis of early pregnancy failure and a predictive test for pregnancy continuation.[20] The present study also found lower mean serum progesterone hormone levels in pregnant women with threatened miscarriages and non-viable fetuses. This finding coincides with the results of Bucuri et al. prospective case-control study. [21] Blavier et al. reported that serum progesterone levels may have the ability to predict threatened miscarriage and viability of pregnancy. [22] Our study showed that a serum progesterone level of 20.5 nmol/L significantly predicted threatened miscarriage with acceptable validity findings (90.7% sensitivity, 72% specificity and 80% accuracy). These findings are close to the results of the Lek et al. prospective cohort study, which reported that a serum progesterone cutoff value of <35 nmol/L is a significant predictor of threatened miscarriage among pregnant women at early pregnancy with an accuracy of 87%. [4] Our study also showed that a serum progesterone level of 11.8 nmol/L) was a significant predictor of fetal non-viability in pregnant women with threatened miscarriage with acceptable validity findings (98.1% sensitivity, 95.7% specificity and 97% accuracy). These findings are close to the results of the Muttalib et al. prospective studies in the Kurdistan Region/Iraq, which reported that a serum progesterone cutoff value of 13.68 nmol/L predicts a non-viable pregnancy (78.9% sensitivity, 82.5% specificity and 80.4% accuracy). [23]

Conclusions

Serum progesterone level is an appropriate predictor for threatened miscarriage and viability in early pregnancy. The bleeding and history of travel also help in the prediction of threatened miscarriage. This study recommended implementing measurement of serum progesterone level with ultrasound examination for women with abnormal vaginal bleeding at early pregnancy.

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Conflict of interest

The authors declared no conflict of interest related to this study.

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