

Use of single serum progesterone level measurement as a predictor of the fetal viability during the first trimester

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Abstract

Background and objective: Approximately one in third of pregnant women experience discomfort, pain and or vaginal bleeding during the first trimester of pregnancy. Ultrasound is known to be a useful tool in detecting and diagnosing the viability of the fetus but it is sometimes inconclusive. In cases in which pregnant women experience symptoms of discomfort, serum progesterone may be admitted to the patient for counseling and prediction of the continuity of pregnancy. This study aimed to estimate the relation between single serum progesterone level and the viability of the fetus during the first trimester.

Method: A prospective study was carried out in Maternity teaching hospital-Erbil city to estimate the accuracy of single serum progesterone measurement for the prediction of fetal viability at the end of the first trimester. All the cases have been detected by ultrasound device that has been for women who attended the hospital and reported the feeling of discomfort, pain and bleeding early in the first trimester of pregnancy, serum progesterone level of the patients were compared between viable and nonviable fetuses.

Results: A total of 97 participants were involved in this study; 57 participants had a viable pregnancy at the end of the first trimester, and 40 participants had un-viable pregnancy that has been terminated either by spontaneous abortion or termination performed for missed abortion. The mean of serum progesterone level in viable pregnancies was (19.358 ng/ml) when compared with the non-viable pregnancies which were (11.082 ng/ml). The differences were statistically significant ($P < 0.001$). The cut-off value (13.68ng/ml) provides the highest sensitivity and specificity.

Conclusion: A single serum progesterone measurement was regarded as a reliable test for the prediction of viable and non-viable pregnancy in women who reported to be experiencing pain and bleeding in the early trimester of pregnancy with or with inconclusive ultrasound.

Keywords: Progesterone; Fetal viability; First trimester.

Introduction

Pain with vaginal bleeding is the most common causes of women seeking medical advice in early pregnancy.¹ These symptoms are a source of anxiety for both the health care providers as well as the pregnant woman due to the fact that these symptoms often lead to miscarriage or ectopic pregnancy in about (15-20%).² Transvaginal ultrasound has been used for detection of fetal viability as a first tool, however situations may differ in cases for the following reasons: when the pregnancy is at an early stage and detecting a fetal

heart may be difficult, another issue may arise if the gestational sac is less than 20mm with no yolk sac or embryo, and finally if the embryo is less than 8mm with negative fetal heart at that time of pregnancy. If uncertain viability is diagnosed, an ultrasound scan may be repeated within 7-10 days. Biochemical tests aids in predicting the viability is BhCG, is sensitive in distinguishing viable from nonviable during pregnancy however for the test to be accurate serial quantitative readings must take place within 48-72 hours as well as the increment

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is expected to double, although a rise of 50-60% still regarded as normal.³⁻⁵ The level of serum progesterone has been studied and validated by researchers in which a conclusion has been drawn to indicate that progesterone level that is more than 25 ng \ml detects fetal viability with 97.5% sensitivity while levels less than 5ng \ml detect nonviable pregnancy with 100% sensitivity.⁶ In recent studies, it has been found that to be a powerful predictor for fetal viability in natural pregnancies. However, the usefulness is still questionable due to the different cutoff levels.^{7,8} A study demonstrates that serum progesterone cut off level 10 ng\dl had 79.3% sensitive to predict nonviable pregnancy and had 93.3% specificity to predict viable pregnancy, and cut off level 20 ng\ml was 95.1% sensitive to predict nonviable pregnancy and was 98.9% specific to predict viable pregnancy during the first trimester.⁹ This research is regarded to be the first to be conducted at the Maternity Teaching Hospital to estimate the use of single serum progesterone level measurement to predict fetal viability in women who experience discomfort, pain, and vaginal bleeding or inconclusive ultrasound diagnosis during the first visit in the first trimester of pregnancy.

Methods

A prospective observational study carried out at Maternity teaching hospital in Erbil city Kurdistan region during the period of the 1st April 2016 till 30th July 2016. 97 pregnant patients attend the hospital experiencing discomfort, pain, and vaginal bleeding or inconclusive ultrasound during the first trimester of their pregnancy. Patients background information was inquired directly in the form of a questionnaire. The questionnaire included the following the questions such as the age of the patient, parity, last menstrual period of the patient, expected date of delivery, gestational age, any present symptom and or recent ultrasound and past obstetrical history. All women included became

pregnant spontaneously, a history of infertility and assisted conception were excluded. Trans-vaginal Ultrasound examination was performed on the patients. Those with ectopic pregnancy, multiple pregnancies, and the hydatiform mole was excluded. Those with viable fetus were followed up at 12-13 weeks to observe the viability. Those with inconclusive ultrasound or unviable pregnancy were followed up with another ultrasound scan after two weeks. If the results were viable, the patient is advised to be followed up on for 12-13 weeks. If the results are unviable, termination of pregnancy was performed for the patient (diagnosed as a case of missed abortion). Upon verbal consent from a patient, 2 ml blood is withdrawn from the patient for serum progesterone measurement, serum separated by centrifugation and the assay done by an enzyme immunoassay competition method with the final fluorescent detection done by the same laboratory. The results were analyzed in ng\ml. Finally, the association between serum progesterone is measured at the first prenatal care visit and pregnancy outcome is analyzed to demonstrate predictability and the significant cut –off level is calculated. The study proposal was approved by the Research Ethics Committee of Hawler Medical University. Informed verbal consent was taken from each participant of the study.

Statistical methods and data analysis:

Data were analyzed using the statistical package for the social sciences (version 19). Frequencies and percentages were calculated. McNemar test was used when the results of progesterone level were compared with ultrasound findings as shown in Table 1.

Table 1: Illustrations of using McNemar test for comparing the results of progesterone level with ultrasound findings.

		Ultrasound findings		P (By McNemar)
		Viable	Non-viable	
Progesterone findings	Positive	TP	FP	
	Negative	FN	TN	
Total		TP+FN	FP+TN	

TP=True positive; TN=True negative; FP=False positive; FN=False negative. Sensitivity = $TP / (TP+FN)*100$ and Specificity = $TN / (FP+TN)*100$. Student's t-test for two independent samples was used to compare the mean of progesterone of women with viable fetuses with the mean progesterone of women with non-viable fetuses. Youdin's index was used to estimate the cut-off point of progesterone. At this point, the maximum sensitivity and specificity levels are obtained to detect fetal viability. Values equal to or more than this cut-off point were considered as a positive test result (i.e., predicting a viable fetus). A *P* value ≤ 0.05 was considered statistically significant.

Results

Ninety seven women participated in the

study. Their mean age \pm SD were between 28 ± 5.7 years, ranging from 17 to 42 years. The median was 27 years. Table 2 illustrates that more than half (56.7%) of the participants fall in the age group of 25-34 years, and 45.4% were nulliparous. The gestational age of one-third of the sample was seven or more weeks. The results of ultrasound examinations are presented in Table 3. More than half (58.8%) of the participant's fetuses were viable in the 13th week of gestation. Table 4 indicates that the mean progesterone level was significantly higher among women with viable fetuses (19.358 ng/ml) than the mean progesterone level (11.082 ng/ml) among women with non-viable fetuses (*P* < 0.001).

Table 2: Distribution of sample by age, parity, and gestational age.

	Categories	No.	%
Age	< 25	29	29.9
	25-34	55	56.7
	≥ 35	13	13.4
Parity	Nulliparous	44	45.4
	1-3	50	51.5
	4-6	3	3.1
Gestational age	5-5.9	24	24.7
	6-6.9	41	42.3
	≥ 7	32	33.0
Total		97	100.0

Table 3: Results of ultrasound by weeks of gestation.

Ultrasound results	N	Viable		Non-viable		Inconclusive	
		No.	%	No.	%	No.	%
1 st week	97	53	54.6	39	40.2	5	5.2
2 nd week	97	57	58.8	40	41.2	0	0
13 weeks	97	57	58.8	40	41.2	0	0

Table 4: Mean progesterone by fetal viability on 13th-week gestation.

US 13 weeks	N	Mean progesterone	SD	<i>P</i> value
Viable	57	19.358	8.618	< 0.001
Non-viable	40	11.082	5.223	

Table 5 shows the correlation analysis between age and gestational age; it was found that ($r = 0.293$, $P = 0.004$), this indicates that there is a weak correlation between age and gestational age. Furthermore, the findings revealed that there is no significant correlation between progesterone levels with gestational age (GA), and age. Figure 1 illustrates that the progesterone level of 13.68 gives the

highest sensitivity and specificity. Table 6 demonstrates the level of progesterone, which had a relatively high sensitivity (78.9%), specificity (82.5%), predictive value positive (86.5%), predictive value negative (73.3%), and agreement (80.4%). No significant difference was detected between progesterone results and ultrasound findings ($P = 0.359$).

Table 5: Correlation analysis.

Variable 1	Variable 2	r	P	N
Age	GA	0.293	0.004	97
Age	Progesterone	0.143	0.163	97
GA	Progesterone	0.078	0.45	97

Table 6: Progesterone accuracy in predicting fetal viability.

Progesterone	Ultrasound finding		Total	P (McNemar)
	Viable	Non viable		
Positive	45	7	52	0.359
Negative	12	33	45	
Total	57	40	97	

Sensitivity	Specificity	Predictive value Pos.	Predictive value Neg.	Agreement
78.9%	82.5%	86.5%	73.3%	80.4%

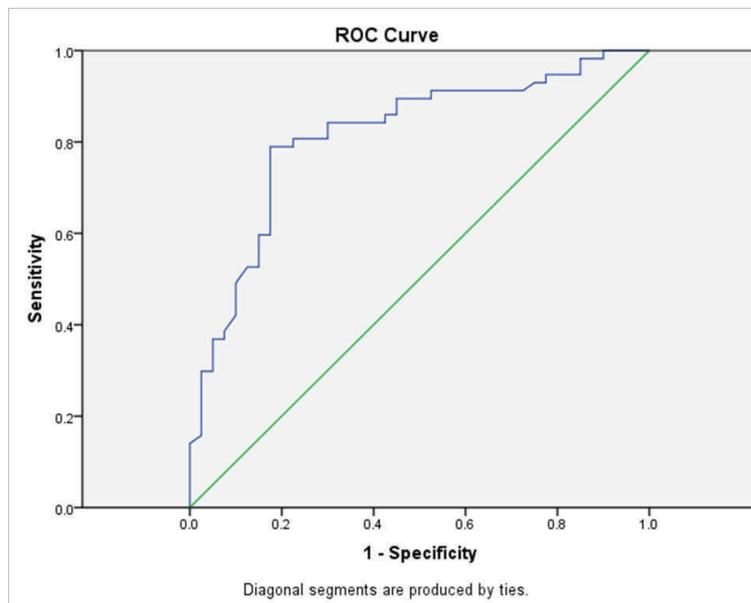


Figure 1: ROC curve, between progesterone levels and fetus viability.

Area under curve (AUC) = 0.814 (95% CI = 0.726 – 0.902), $P < 0.001$

Discussion

The measurement of serum progesterone is suggested to be a valuable test for the prediction of fetal viability during the first trimester of pregnancy in many studies.^{1,7,10}

The study aimed to estimate this relation, the reason for utilizing this test is cost-effectiveness, and the level will not change significantly during pregnancy.^{11,12}

Ninety-seven women participated in this study who attends the hospital early in their pregnancy for pain and bleeding. Participants' average age was 28 ± 5.7 years, the gestational age of one in third was seven or more weeks, according to first ultrasound finding classified into viable pregnancy 53 (54.6%), non-viable pregnancy 39 (40.2%) and inconclusive ultrasound 5 (5.2); the pregnant women are followed by ultrasound at 13 weeks for viability 57 (58.8%) were viable, and 40 (41.2%) were non-viable. A comparison between the two groups done for the mean serum progesterone level and it has been found that its significantly higher in viable pregnancy group (19.358 ng/ml) than nonviable pregnancy group (11.082 ng/ml) with ($P < 0.001$). Similar results have been found by Hahline et al.; in which they found that (99%) of the continuing pregnancies with viable fetus had progesterone level above 30 nmol/L (9.4 ng/ml) and 81% of non-continuing pregnancy had progesterone level less than 30 nmol/L (9.4 ng/ml).¹³ Abdalazim et al. also concluded that the mean serum progesterone was significantly higher in pregnancies with the viable fetus (46.5 ± 7.4 ng/ml) when compared to non-viable pregnancies at the end of the first trimester (9.9 ± 4.8 ng/ml), ($P < 0.05$).¹¹ Daily and colleagues also found significantly higher level for viable fetuses (22.1 ng/ml) than non-viable one (10.1 ng/ml) and they postulated that this test alone is a powerful predictor of the first trimester (especially first 8 weeks) pregnancy outcome (Daily et al. 1994).¹⁴ Similar results have been found in a study done in which the level of progesterone was (20.48 ng/ml) and

(7.78ng/ml) in viable and non-viable pregnancies respectively and also she conducted that this test is a valuable predictor of early pregnancy outcome.¹⁵

The relation between variables have been analyzed in this study, and it has been found that there is no significant effect of the gestational age and patients' age on serum progesterone ($P < 0.001$). In this study the level of serum progesterone was < 10 ng/ml in 10.52% of viable pregnancies when compared with 52.5% of non-viable pregnancy, and serum cutoff level 13.68 ng/ml had higher sensitivity for diagnosing viable from non-viable pregnancy with a sensitivity of (78.9%), specificity (82.5%), positive predictive value (86.5%), and negative predictive value (73.3%). Previous studies found similar results, for instance; a study was carried out by AL-Sebai et al., they found a cut-off level (14.13 ng/ml) differentiate between viable and nonviable pregnancies with 87.6% sensitivity and 87.5% specificity.¹⁶ Furthermore, another study carried out by Abdalazim et al. and included 260 pregnant women with vaginal bleeding and pain found that 6.7% of viable pregnancies had serum progesterone less than 10 ng/ml in comparison to nonviable pregnancies in only 20.7% the level was more than 10ng/ml and the difference were statistically significant. The cut-off level in this study was 10 ng/ml with a sensitivity of 79.3% and specificity of 93.3%.¹¹

Conclusion

This study shows that single serum progesterone level measurement is a reliable biochemical test and can differentiate between viable and non-viable pregnancies.

Competing interests

The author declares no competing interests.

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