



PREDICTIVE VALUE OF SINGLE SERUM PROGESTERONE LEVEL FOR VIABILITY IN THREATENED MISCARRIAGE

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2018

ABSTRACT

Background: A reliable and precise biomarker is very useful to determine the viable and nonviable pregnancy outcome to cater for timely diagnosis and intervention. Maternal serum progesterone assay in first trimester of pregnancy is safe, non-invasive and affordable. The aim of our study is to evaluate the value of single serum progesterone level for finding the viability in threatened miscarriage and determine cut-off value for a viable ongoing pregnancy. **Methods:** This was a prospective study in which patients attending the OPD with early pregnancy and bleeding were recruited. Inclusion criteria were period of amenorrhoea less than 12 weeks, complaints of bleeding per vaginum with or without lower abdominal pain and positive urine pregnancy test or serum beta HCG. Multiple pregnancies, inevitable miscarriage, ectopic pregnancy, molar pregnancy and pregnancy achieved by artificial reproductive techniques were excluded from this study. A detailed clinical examination was done, and routine investigations along with serum progesterone were done. Patients were followed up by ultrasound for viability and their outcome was recorded. **Result:** A total of 100 patients with early pregnancy threatened miscarriage were enrolled for this study. Out of 100 patients, 77% had a viable pregnancy and 23% had non-viable pregnancy. Of the patients studied, the mean serum progesterone levels was higher in viable pregnancy compared to non-viable pregnancy. The area under curve was calculated, and a cut-off value of 10.2ng/ml was obtained. **Conclusion:** A single value of progesterone is useful in predicting the viability of ongoing threatened pregnancy. The cut off value of serum progesterone was 10.2ng/ml with sensitivity of 87% and specificity of 92.2% and P-value of <0.001 which is statistically significant.

DOI Number: 10.48047/NQ.2022.20.20.NQ109209

NeuroQuantology2022;20(20): 2018-2024

INTRODUCTION

There is no doubt that obstetricians face a great deal of challenge to deal with the different kinds of pregnancy losses. Predicting outcome in early pregnancy threatened miscarriage is difficult task. A reliable and precise biomarker is very useful to determine the viable and nonviable kind of pregnancies to cater for timely diagnosis and intervention[1]. Recognition of early pregnancy failure can be made either radiologically or clinically, however, these days

ultrasound is best diagnostic as well as prognostic tool in management of early pregnancy loss. But sometimes both radiological evidences and clinical findings are indeterminate. Many biomarkers have been evaluated for this and among them serum progesterone is highly sensitive, specific, accurate, affordable and of great clinical value [3,12]. The aim of our study was to evaluate the predictive value of single serum progesterone level for finding the viability in threatened



miscarriage and to determine cut-off value for a viable ongoing pregnancy.

MATERIALS AND METHODS

A prospective study was conducted in the Postgraduate Department of Obstetrics and Gynaecology, SMGS (Shri Maharaja Gulab Singh) Hospital, Government Medical College, Jammu, over a period of one year after obtaining ethical clearance from Institutional Ethics Committee. This prospective study was conducted in 100 patients attending OPD with early pregnancy and bleeding. The selection of patients was random. **INCLUSION CRITERIA** were; Patients with period of amenorrhoea less than 12 weeks presenting as a case of threatened abortion (i.e. complaints of bleeding per vaginum, with or without lower abdominal pain, closed cervical os and a positive urine pregnancy test) were selected. **EXCLUSION CRITERIA** were; Multiple pregnancies, inevitable miscarriage, missed miscarriage, ectopic pregnancy, molar pregnancy, pregnancy achieved by artificial reproductive techniques, women with previous episodes of per vagina bleeding or those treated with progesterone for previous per vagina bleeding in current pregnancy. Based on selection criteria women were selected for study. After an informed written consent from the patient, a detailed history was taken including previous obstetric history, socioeconomic status and history of travel, trauma, heavy work or intercourse. A detailed clinical examination and routine investigation was done for all patients. Routine investigations include- haemoglobin, blood sugar, bleeding time, clotting time, urine routine and microscopy, serology. Venous blood sample (2ml) was collected and estimation of serum progesterone level at presentation was done using Chemiluminescent Microparticles Immunoassay (CMIA) technology. Women included in the study were examined by ultrasound for viability of the pregnancy. Those with inconclusive sonographic findings were re-examined by ultrasound after two weeks and reclassified into viable and non-viable

pregnancies according to the findings (anembryonic or missed miscarriage). Women included in this study were followed by ultrasound for the viability of the pregnancy until the end of first trimester and the outcome of their pregnancy was recorded.

Statistical Analysis: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean \pm SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar and pie diagrams. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. In order to determine the optimal cut-off of serum progesterone for prediction of pregnancy outcome, receiver operating characteristic (ROC) analysis was performed. A P-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

RESULTS: This was a prospective study carried out on 100 patients attending OPD with early pregnancy (period of gestation less than 12 weeks) and complaints of bleeding per vaginum with or without lower abdominal pain and positive urine pregnancy test were recruited. In this study maximum percentage of patients i.e. 47% were in the age group of 21-25 years with mean age of 25.6 \pm 3.79 years. 49% were primigravida, 32% of patients were second gravida, 10% of patients were gravida three and 9% of patients were more than or equal to gravida four. The mean gestational age at the time of progesterone assay was 8.9 \pm 2.32 weeks. Majority of patients i.e. 54% presented with bleeding per vaginum and 46% presented with bleeding per vaginum and pain in abdomen. Of the risk factor studied 21% of patients had past history of early miscarriage, 7% of patients had history of trauma, 8% of



patients had history of heavy work, 17% of patients had history of travel, 3% patients had diabetes mellitus and 9% patients had history of thyroid disorders. Of the patients studied 77% had a viable pregnancy and 23% had a non-viable pregnancy. The mean maternal serum progesterone was higher in the viable pregnancy, 22.80 ± 9.12 (ng/ml) compared to non-viable group 8.04 ± 5.04 (ng/ml) as shown in table 1, with a P-value of <0.001 which is statistically significant. Relation between maternal age and serum progesterone was

found to be insignificant. Association of various risk factors like past history of early miscarriage, trauma, heavy work, travel, diabetes mellitus, thyroid disorder were found to be insignificant as shown in Table 3.

The serum progesterone cut-off level was ≤ 10.2 in 20 (87.0%) non-viable pregnancies and 6 (7.8%) viable pregnancies. The serum progesterone cut-off level was > 10.2 in 3 (13%) non-viable pregnancies and 71 (92.2%) of viable pregnancies as shown in table 2. The serum progesterone cut-off level was 10.2 ng/ml.

Table 1: Relation between serum progesterone (ng/ml) and viability of pregnancy				
Pregnancy outcome	N	Mean	SD	P-value
Viable Pregnancy	77	22.80	9.12	$<0.001^*$
Non-viable pregnancy	23	8.04	5.04	

***Statistically Significant (P-value<0.05)**

Table 2: Frequency distribution of patients as per pregnancy outcome and serum progesterone cut-off level					
Serum progesterone (ng/ml)	Non-viable		Viable		P-value
	No.	%age	No.	%age	



≤ 10.2	20	87.0	6	7.8	<0.001*
> 10.2	3	13.0	71	92.2	
Total	23	100	77	100	

*Statistically Significant (P-value<0.05)

2021

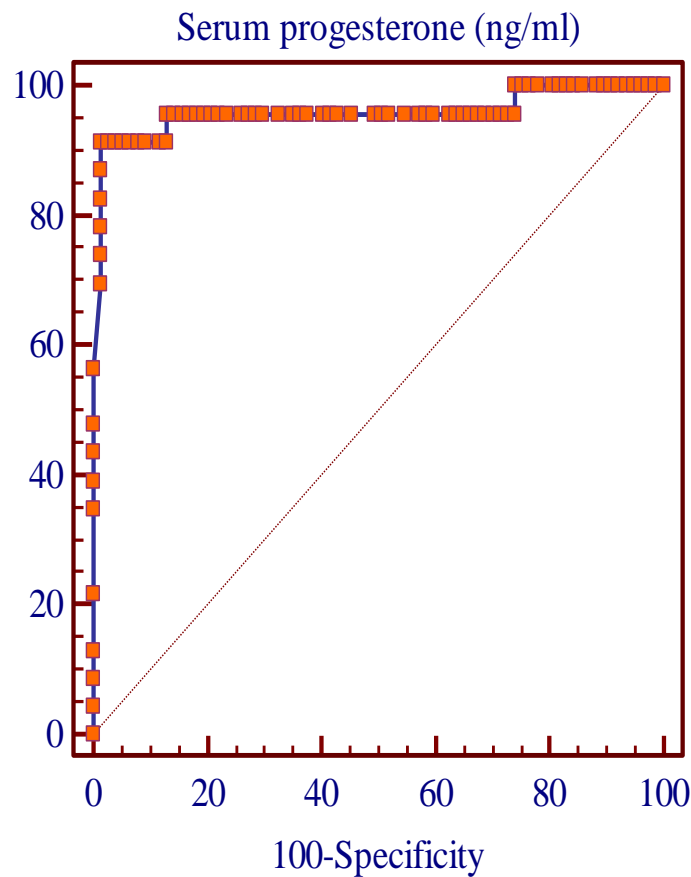
Table 3: Relationship between serum progesterone (ng/ml) and maternal age, gestational age and risk factors and presenting complaints

	N	Mean	SD	P-value
Past h/o early miscarriage	Positive	21	16.17	0.109
	Negative	79	20.27	
H/o trauma	Yes	7	15.44	0.239
	No	93	19.71	
H/o heavy work	Yes	8	18.82	0.869
	No	92	19.46	
H/o travel	Yes	17	17.60	0.435
	No	83	19.78	
H/o diabetes	Yes	3	17.37	0.732
	No	97	19.47	
H/o thyroid disorder	Yes	9	17.87	0.644
	No	91	19.56	
Gestational age	≤ 8 weeks	47	18.09	0.235
	> 8 weeks	53	20.58	
Maternal age	≤25yrs	55	18.72	9.66



	> 25yrs	45	20.47	11.04	0.401
Symptoms	Bleeding	54	20.40	10.50	0.306
	Bleeding and Pain	46	18.25	10.31	

ROC Curve



2022

DISCUSSION

Threatened abortion, a pregnancy complicated by vaginal bleeding through a closed cervical os with or without abdominal pain, is one of the most common complication of pregnancy during the first half of gestation, occurring in 25% of pregnancies[4]. A reliable and precise biomarker is very useful to determine the viable and nonviable kind of pregnancies for timely diagnosis and intervention. Attempts have been made from time to time to find out the diagnostic modality that could predict about the

outcome of pregnancy and immediate diagnosis of pregnancy failure in threatened abortion. Hormone determinations have used for such purpose among which maternal serum progesterone has been found to be a highly specific and sensitive biomarker of early pregnancy failure with good accuracy.

In our study, a total of 100 patients attending the OPD with period of gestation less than 12 weeks and complaints of bleeding per vaginum with or without lower abdominal pain, closed cervical os and positive urine pregnancy test



were recruited. A detailed clinical examination and routine investigation along with serum progesterone were done. Patient were followed up by serial ultrasound for viability and their outcome was recorded. In our study majority of the patients were in the age group of 21-25 years i.e. 47% with mean age of 25.6 ± 3.79 years. Observations made in the study were similar to study done by Kadam VK et al. [6] in which they found majority of patients of threatened abortion 44% belong to age group of 21-25 years and the mean age was 25.62 years. In our study no correlation was found between maternal age and serum progesterone level.

In our study it was found that majority of patients were primigravida which was in contrast to study done by Khanam M et al. [8] where they found that 56% of cases of threatened abortion belonged to multigravida group.

In our study, the relation between gestational age and maternal serum progesterone was evaluated which was statistically insignificant. This observation was comparable to study done by Hanita [5] and Khosho et al. [9] in which no correlation was found between gestational age and serum progesterone.

In our study 54% patients presented with complaint of bleeding per vaginum and 46% patients had both pain in abdomen and bleeding per vaginum. This observation was in accordance with the study done by Newbatt et al. [10] and Kadam VK et al. [6] in which they found that the most common symptom of miscarriage is bleeding during pregnancy.

In our study we also evaluated few risk factors for threatened miscarriage which includes history of previous loss, thyroid disorder and diabetes mellitus. 21% patients had past history of early miscarriage. The most common risk factor was history of previous loss. The relation between maternal serum progesterone and these risk factors were evaluated and was found statistically insignificant. Our results are

consistent with findings of Kadam VK et al. [6] and Arck et al. [2] in which it was found that previous pregnancy loss is associated with increased risk of miscarriage in subsequent pregnancy.

In present study other factors i.e. history of trauma, heavy work, travel were also evaluated. The relation between history of trauma, heavy work, travel and serum progesterone was evaluated, but were not statistically significant. Of the patients studied, 77% had a viable pregnancy and 23% had nonviable pregnancy. The mean serum progesterone levels was higher in viable pregnancy (22.80 ± 9.12 ng/ml) compared to non-viable pregnancy (8.04 ± 5.04 ng/ml). In our study, the cut off value of serum progesterone was 10.2ng/ml with sensitivity of 87% and specificity of 92.2% and P-value of <0.001 which is statistically significant. Dave A et al. [3] stated that the mean serum progesterone of the studied population was significantly high in viable pregnancy (18.09 ± 5.9 ng/ml) compared to non-viable pregnancy group (6.707 ± 3.02 ng/ml). The cut off value of serum progesterone in this study was 10.05 ng/ml. Kadam VK et al. [6] found that the mean serum progesterone was higher in the viable pregnancy compared to non-viable. 83.8% of viable pregnancies had serum progesterone more than or equal to 10.08 ng/ml which was statistically significant. Their study provided a cut off value of serum progesterone of 10.8 ng/ml with an accuracy of 86%. Sakar MN et al. [11] in their study provided a cut off level of 10.7ng/ml, with sensitivity of 92.1% and 44%, respectively for viable pregnancies. Kant RH et al. [7] suggested that mean maternal serum progesterone level in patients of threatened abortion who aborted was 21.5 ± 10.4 ng/ml and patients of threatened abortion who progressed normally to period of viability had maternal serum progesterone level of 41.6 ± 10.8 ng/ml. Their study concluded that serum progesterone was low in patients who aborted and normal in patients who progressed to period of viability.



CONCLUSION

A single value of progesterone is useful in predicting the viability of ongoing threatened pregnancy and to differentiate between viable and non-viable pregnancies.

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