The Relation Between Single Serum Progesterone Level And Viability In Threatened Miscarriage In First Trimester

Dr. Janak Raj Soni [1], Dr . Anuradha Soni [2] , Dr. Suman Mendiratta[3],Dr.Suwaram Saini[4]

[1,2] Resident,[4]Associate professor,[3]Senior professor and unit head , Department of obest. & gynec. SMS Medical College and Hospital , Jaipur

*Corresponding Author:
Dr. Janak Raj Soni
Department of obest. & gynec. SMS Medical College and Hospital , Jaipur

Abstract

Background ; Every woman with an early pregnancy vaginal bleeding and pain should be evaluated.[1] Threatened abortion is very common in the first trimester; about 25-30% of all pregnancies have some bleeding during the pregnnacy.[2,3] 12% to 20% of all clinically recognized pregnancies end up as abortions.

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 serial ultrasound for viability, and their outcome was recorded.

Result A total of 100 patients with early pregnancy threatened miscarriage were enrolled for this study. Of the patients studied, 59 (59%) had a viable pregnancy and 41 (41%) had non-viable pregnancies. The mean serum progesterone was
higher in the viable pregnancy, 18.18 ± 6.09 ng/ml, compared to non-viable group, 6.21 ± 2.86 ng/ml. The area under curve was calculated, and a cut-off value of 9.9 ng/ml was obtained. 59% of viable pregnancies had serum progesterone more than or equal to 9.9 ng/ml which was statistically significant.

Conclusion A single value of progesterone is useful in predicting the viability of the ongoing threatened pregnancy. After analysis of the results, cut off value of serum progesterone as determined by my study came out to be 9.9 ng/ml with 94.9% sensitivity & 92.7% specificity.

Keywords: Progesterone · Viability

Introduction

Every woman with an early pregnancy vaginal bleeding and pain should be evaluated.[1] Threatened abortion is very common in the first trimester; about 25-30% of all pregnancies have some bleeding during the pregnnacy.[2,3]12% to 20% of all clinically recognized pregnancies end up as abortions.[4,5]

Serial quantitative serum beta-hCG and progesterone levels and trans-vaginal sonography are used to ascertain if there is an intrauterine live fetus.[6]

Insufficient progesterone secretion by the corpus luteum or placenta has been associated with an increased incidence of abortion. It has been suggested

196

that abnormal levels of one or more hormones might help to predict on abortion.[7]

a highly sensitive and specific biomarker is required to determine the pregnancy viability for early intervention. Although there is some evidence that measuring serial serum βhCG is helpful in the diagnosis of an ectopic pregnancy, most studies have concluded that it cannot discriminate between viable and non-viable intrauterine pregnancies. This is not surprising, bearing in mind the wide range of hCG levels recorded in normal pregnancy and the long half-life following pregnancy demise. In addition, miscarriages may occur at any time during the first trimester, which further contributes to the variability of hCG measurements.[8]

A number of studies have been published recently which show that serum progesterone levels can be used to assess pregnancy viability. However, the studies differ significantly in their design, study populations and inclusion criteria. Most importantly, a number of studies included patients who conceived following stimulation of ovulation or those receiving luteal support, both of which may affect serum progesterone levels. There have been only a few studies that assess the value of progesterone in very early gestations.[9]

Prompt diagnosis of early pregnancy failure is a difficult dilemma. There is no single test currently available which immediately differentiates continuing from non-continuing intrauterine or tubal pregnancy.[10]

Aim & objective:-

1. To detect the relation between serum progesterone and viability of the pregnancy during the first trimester.

Material and methods

Place of Study: Department of Obstetric and Gynecology, SMS Medical College, Jaipur

Study Type: prospective type of study.

Study Period: feb 2020 to july2021.

Sample Size: 100 pregnant women were taken who were admitted.

Inclusion criteria

Women who had early pregnancy and admitted in the obstetrics ward.

Exclusion criteria

Multiple pregnancies, inevitable miscarriage, ectopic pregnancy, molar pregnancy and pregnancy achieved by artificial reproductive techniques

Methodology

All pregnant women were taken who admitted in the Department of Obstetrics and Gynecology with the complaints of bleeding p/v or pain abdomen during the first trimester were selected for the study. The relevant parameters were recorded in a pre-structured questionnaire which includes identification data, demographic characteristics, socioeconomic data, parity, gestational age that to be calculated from 1st day of last menstrual period and history of any previous early miscarriages. In this study randomly 100 early pregnant women were taken after applying inclusion and exclusion criteria. Women included in the study were certain of dates, had conceived spontaneously with no history of infertility and had a positive pregnancy test.

Results

100 women were hospitalized due to pain abdomen and vaginal bleeding during first trimester of their pregnancy

were taken as study participants.

Table no. 1:-Relation between serum progesterone levels and viability of pregnancy

Pregnancy outcome	Number	Serum progesterone
Viable pregnancy	59	7.9-34.9
Non viable pregnancy	41	1.5-14.8

In the end of the first trimester pregnancy were divided in the two group one for viable pregnancy and another for non viable pregnancy group. The mean of serum progesterone is significantly high in viable pregnancy group18.18 ng/ml(7.9-34.9 ng/ml) while in non viable group average is 6.56 ng/ml (1.5-14.8 ng/ml) This association came out to be statistically significant (p-value < 0.001).

Table no.2:- Relation between serum progesterone levels and maternal age

Maternal Age (in yrs)	Aborted		Continued		Total	
	No.	**%**	**No.**	**%**	**No.**	**%**
<20	3	7.32	5	8.47	8	8.00
21 - 25	16	39.02	26	44.07	42	42.00
26 - 30	19	46.34	22	37.28	41	41.00
>30	3	7.32	6	10.17	9	9.00
Total	**41**	**100.00**	**59**	**100.00**	**100**	**100.00**

This table shows distribution of cases according to maternal age. 41 cases were in the age group of 26 to 30 years, out of these cases, 19 aborted while 22 continued their pregnancy. Only 9 cases had age more than 30 years, out of which 3 aborted while 6 continued. Highest rate of abortions was seen in the age group of 26-30 years. However, this association was statistically insignificant (Chi-square = 0.889 with 3 degrees of freedom, p-value=1.000).

Table – 3

Socio-economic Status of Cases Under Study

Socio-economic Status	Aborted		Continued		Total	
	No.	**%**	**No.**	**%**	**No.**	**%**
Low	17	41.46	26	44.07	43	43.00
Middle	15	36.59	26	44.07	41	41.00
High	9	21.95	7	11.86	16	16.00
Total	**41**	**100.00**	**59**	**100.00**	**100**	**100.00**

This table shows distribution of cases according to socio-economic status. Highest number of cases (43) had low socio-economic status. 41 belonged to middle class while only 16 had high socio-economic status.

However, this association was not statistically significant. (Chi-square = 1.907 with 2 degrees of freedom; p-value = 0.385)

ROC curve in my study had AUC=0.975 with Standard error = 0.013. After statistical analysis, a cut-off value of serum progesterone for predicting viability in threatened abortion came out to be 9.9 ng/ml with sensitivity of 94.9% and specificity of 92.7%.
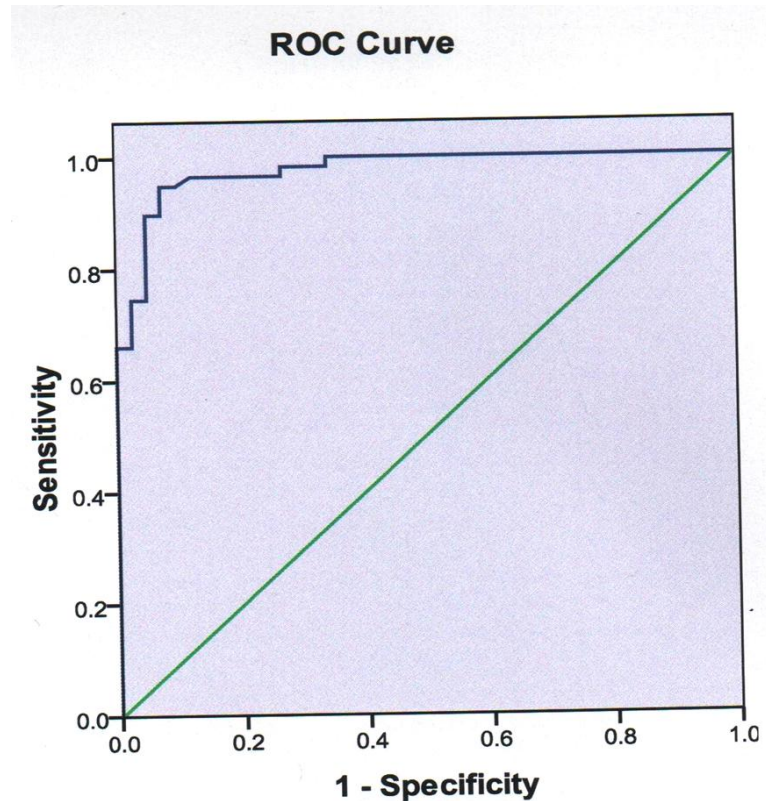
Diagonal segments are produced by ties.

Area Under the Curve				
Test Result Variable(s) : Progesterone				
Area	**Std. Error[a]**	**Asymptotic Sig.[b]**	**Aymptotic 95% Confidence Interval**	
			Lower Bound	**Upper Bound**
.975	.013	.000	.949	1.000
The test result variable(s) : Progesterone has at least one tie between the positive actual state group and the negative actual state group. Statistically may be biased.				
a. Under the nonparametric assumption				
b. Null hypothesis : true area = 0.5				

Discussion

Bleeding in early pregnancy is very common in the first trimester of pregnancy. Less than half proceed to complete miscarriage. Eighty percentage of all miscarriages occur in the first trimester of pregnancy.

The progesterone hormone which is secreted by the granulose cells of the ovary is required for the maintenance of pregnancy. It induces secretary changes in the lining of the uterus and is essential for a successful implantation of the embryo. When fertilization occurs, the progesterone secreted by the corpus luteum has the important function of maintaining the early pregnancy till the placenta takes over its function at 7–9th week of gestation. Moreover, progesterone also modulates the immune response of the mother to prevent rejection of the embryo and enhances uterine quiescence and suppresses uterine contractions. Hence, measurement

of serum progesterone levels in early pregnancy has been regarded as one of the most powerful predictors of pregnancy outcome in natural conception. We have evaluated the correlation of single value serum progesterone in predicting the viability of threatened miscarriage and its risk factors.

In our study, the age of presentation of patients ranged from 18 to 35 yrs with a mean age of 25.62 yrs. This was comparable with study of Khosho et al. [11] in which the mean age was 27.2 yrs. However, this was in contrast to studies done by Hanita et al. (30 yrs) [12] and Abdelazaim et al. [13] (32.7 ± 5.1 yrs). This may be due to delaying of conception in these patients. Relationship of gestation age with serum progesterone has been evaluated by few studies. Studies done by Hanita [12] and Khosho et al. [11] have found no correlation between gestational age and progesterone level. They observed that serum progesterone changes very little during early pregnancy.

As suggested by recent studies measurement of serum progesterone in early pregnancy is most single powerful pregnancy outcome in natural conceptions.This designed prospective study fordetecting relationship between serum progesterone and viable pregnancy during first trimester.

100 pregnant women in first trimester were hospitalized either for vaginal bleeding or abdominal pain for this prospective study. The mean age of

studied population was 22years , the mean gestational age at progesterone assay was8weeks 3days±2weeks. By the first trimester end , pregnant women were classified into viable 59 pregnant group and of 41 non-viable group . The mean serum progesterone was significantly high in viable pregnancy group 18.18 ng/ml as in comparison to non-viable pregnancy group 6.56 ng/ml.These viable group patients were having high level serum b-hcg, these patients were having no history of any previous miscarriages. Yolk sac was seen in ultra sonography in about one fourth patients. Among the studied population, relationship between serum progesterone and the maternal age or gestational age or past history of early miscarriage was stastically insignificant.

95 pregnant women were of 13 weeks or less , recruited as study group. The control was of 14 pregnant women by Hanita and colleagues for determining role of serum progesterone as marker of early pregnancy failure after single assay. It was found a significant lower serum progesterone with non-viable pregnancy(10.7ng/ml) in comparison to viable pregnancy(45.9ng/ml).

In a prospective comparative study by Al-Sebai et al for assessing role of single maternal serum progesterone for immediately diagnosing early pregnancy failure and for fetal viability as long term prognosis. 489 women presented with singleton pregnancy , vaginal bleeding with abdominal pain at 18weeks. The levels of progesterone was significantly lower in non continuing and tubal pregnancy compared to threatened continuing groups with cut off value at 45mmol/l for differentiating viable and non-viable pregnancies with 87.6% sensitivity and87.5%specificity.

Lek et al. [14] suggested 35 nmol/L as a cut-off value for serum progesterone to predict spontaneous miscarriage in patients with early threatened pregnancy. Hanita et al. [12] evaluated serum progesterone as a marker for early pregnancy failure. They said that at a cut-off value of 32.7 ng/ ml, progesterone had 90% sensitivity with 75% negative predictive value and 92% specificity with 97% positive predictive value to diagnose early pregnancy failure. They also observed that the discriminatory efficacy of a single progesterone determination was not increased by serial estimation of progesterone level [12]. Hence, repeated value is usually not done.

The difference in the cut-off value may due to the difference in the studied population and methods used to estimate serum progesterone levels.

Conclusion

A single value of progesterone helps to guide us regarding the viability of the ongoing threatened pregnancy. It prevents unnecessary inconvenience to patients and identifies the one requiring increased surveillance. It is a sensitive and specific test that reliably guides the prognosis of pregnancy. Our study found that serum progesterone cut-off value of 9.9 ng/ml is a reasonably good predictor of a viable early threatened pregnancy.

Funding No financial aid provided for the study.

Compliance with Ethical Standards

Ethical Approval All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Permission was obtained from the scientific and ethical committee of the institution for the study.

Informed Consent Informed consent was obtained from all patients for being included in the study.

References

1. Cunningham G, Lenovo KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield LS. Abortion; Williams Obstetrics, 24th ed. USA : McGraw-Hill Education; 2014:350.

2. Moscrop A. 'Miscarriage or abortion?' Understanding the medical language of pregnancy loss in Britain : a historical perspective. Med Humanit. 2013 Dec;39(2):98-104.

3. Everett C. Incidence and outcome of bleeding before the 20th week of pregnancy : prospective study from general practice. BMJ. 1997;315:32-34.

4. Hemminki E. Treatment of miscarriage : current practice and rationale. Obstet Gynecol. 1998;91:247-53.

5. Blohm F, Friden B, Milsom I. A prospective longitudinal population-based study of clinical miscarriage in an urban Swedish population. BJOG. 2008;115:176-183.

6. Cunningham G, Kenneth J Lenovo, Steven L Bloom, Catherine Y Spong, Jodi S Dashe, Barbara L Hoffman, Brian M Casey, Leanne S Sheffield. Abortion; Williams Obstetrics, 24th ed. USA: McGraw-Hill Education; 2014:P.355.

7. Suror A, Edwar Z, Mahasin M. The value of early pregnancy single serum progesterone measurement in relation to the first trimester viability. Thi-Qar medical Journal (TQMJ). 2011;5(2):133-141.

8. Elson J, Salim R, Tailor A, Banerjee S, Zosmer N, Jurkovic D. Prediction of early pregnancy viability in the absence of an ultrasonically detectable embryo. Ultrasound Obstet Gynecol. 2003;21:57-61.

9. Abdulla ZA. The value of serum progesterone measurement in early pregnancy. Al J Bahrain Medical Bulletin. 2000;22(1).

10. Donald I. Abortion In: Practical Obstetric Problem. 7th edn. New Delhi; BI Publications Pvt. Ltd., 2004:P.14.

11. Khosho EZ, Aiub MM, Adnan S. The value of early pregnancy single serum progesterone measurement in relation to first trimester viability. Thi-Qar Med J. 2011;5(2):133–41.

12. Hanita O, Hanisah AH. Potential use of single measurement of serum progesterone in detecting early pregnancy failure. Malays J Pathol. 2012;34:41–6.

13. Abdelazim IA, Elezz AA, Elsherbiny M. Relation between single serum progesterone assay and viability of the first trimester pregnancy. Springerplus. 2012;1(1):80.

14. Lek SM, Ku CW, Allen JC Jr, et al. Validation of serum progesterone < 35 nmol/L as a predictor of miscarriage among women with threatened miscarriage. BMC Pregnancy Childbirth. 2017;17(1):78.