

Serum Progesterone an Indicator of Viable Pregnancy in First Trimester

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ABSTRACT

Aim: To investigate the role of serum progesterone as indicator of viable pregnancy.

Methodology: Study was conducted on pregnant women of 8 to 13 weeks of gestation presenting in obstetric department. Status of pregnancy was confirmed on ultrasonography. 53 women having abortion were included in group I, while 28 women with healthy ongoing pregnancy were included in group II. Serum progesterone levels were estimated by ELISA. Median serum progesterone levels were compared between the two groups and receiver operative characteristics (ROC) curve was plotted to find out optimum cut off value of progesterone to assess the viability of a pregnancy.

Results: Median serum progesterone levels of abortion group 3.00 ng/ml (1.71-4.73) were significantly lower than women with viable pregnancy 11.64ng/ml (8.33-18.44). Serum progesterone level of 6.7 ng/ml is 100% sensitive and 85% specific for viable pregnancy

Conclusion: Serum progesterone level can be used to identify viable pregnancy.

Keywords: Progesterone, pregnancy, abortion, first trimester, early pregnancy failure.

INTRODUCTION

Progesterone is a 21 carbon steroid. It helps in maintaining the pregnancy and prevents abortion. It prepares the uterus for implantation. Uterine growth is also promoted by progesterone. It is a suppresser of myometrial contractility¹.

Progesterone plays a cardinal role in pregnancy by preparing female body for conception. It causes the proliferation and differentiation of stromal cells. It also helps in decidualization, resulting in endometrial remodelling. Progesterone has secretory influence on uterine glands. there is influx of uterine specific natural killer cells and also leads to vascular remodelling. It also takes part in preparing the breasts for lactation by promoting the lobuloalveolar growth of breasts^{2,3,4}.

Optimum progesterone levels are required for continuation of pregnancy. Decreased progesterone levels may lead to abortion. Progesterone may be used as a biomarker for viable pregnancy. Many studies have been done to find out the diagnostic value of serum progesterone levels in early pregnancy failure.^{5,6,7,8,9,10} The present study was conducted to investigate the role of serum progesterone as an indicator to discriminate between viable pregnancy and abortion.

SUBJECTS AND METHODS

It was a descriptive, cross-sectional study. Study population was pregnant women presenting in obstetric department of a tertiary care hospital of Lahore, Pakistan. Women included in the study were 18-35 years of age, presenting in obstetric department during first trimester for routine checkup or with complaint of early pregnancy failure and with no history of progesterone intake, having no

systemic illness. Informed consent was taken. Detailed history and examination was done. The viability of the fetus was confirmed by ultrasonography. 53 women having abortion were labeled as Group I, 28 women with viable pregnancy and no complication were included in Group II. Venous blood samples were taken by using aseptic measures. Serum progesterone was measured by immunoenzymometric assay with an automated EIA analyser with the kit (Biocheck progesterone enzyme immunoassay test kit BC-1113).

The data was entered and analysed using SPSS, version 20. Data was explored for normality by using the Shapiro-Wilk test. Median with IQR (interquartile range) was calculated. Man Whitney-U was applied. Receiver operative characteristic (ROC) curve was plotted for progesterone. Sensitivity and specificity levels were calculated for various cut off values of progesterone for viable pregnancy along with the positive likelihood ratio (PLR)

RESULTS

Table 1 shows the median serum progesterone levels of group I and II. Median serum progesterone levels of group I were significantly lower than group II (p<0.01). ROC curve was plotted against various values of progesterone (Figure 1). Area under the curve AUC was 0.94+/- 0.025 (p- value <0.01) with 95% confidence interval of 0.89 -0.99. At 6.7ng/ml cut off value, serum progesterone is 100% sensitive and 85% specific for viable pregnancy with a PLR of 6.6 and NLR of 0.00. Different cut off values for progesterone are given in table II.

Received on 24-12-2018

Accepted on 26-02-2019

Table I: Comparison of serum progesterone in group I and II

Parameter	Group I (n= 53)	Group II (n= 28)	p-value
Progesterone ng/ml	3.00(1.71-4.73)	11.64(8.33-18.44)	<0.01*

Values are expressed as Median (IQR)

*p < 0.05 is considered statistically significant

Comparison of parameters in groups by Mann Whitney-U test

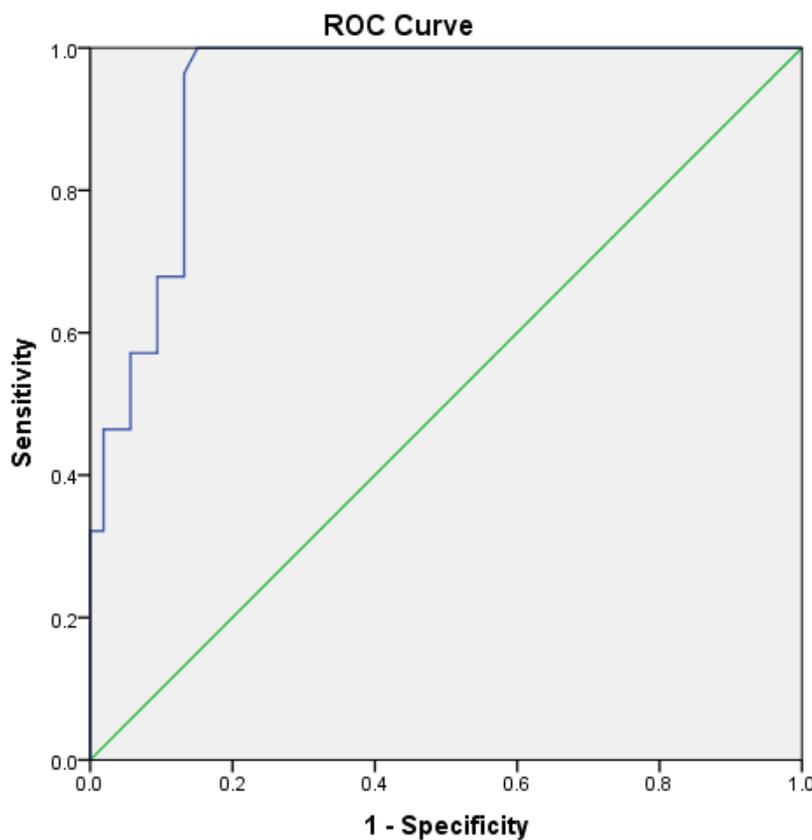
Table II: Cut off values of progesterone

Cut off value (ng/ml)	Sensitivity (%)	Specificity (%)	PLR	NLR
6.7	100	85	6.62	0.00
6.9	96	87	7.3	0.04
8.6	71	87	5.4	0.33
9.9	68	91	7.22	0.25
10.7	61	91	6.45	0.15

PLR =Positive likelihood ratio,

NLR =Negative likelihood ratio

Fig. I: ROC curve of progesterone levels as indicator of viable pregnancies



DISCUSSION

The present study evaluated serum progesterone levels in first trimester pregnant women having spontaneous abortions and women with viable pregnancy. Women having abortions had significantly low serum progesterone levels. This study also provides various cut off values of progesterone to indicate a viable pregnancy during first trimester.

Many studies have been done to find out the optimum value for a healthy on going pregnancy. Aksoy et al. found the cut-off value of serum progesterone for distinguishing between a healthy pregnancy from abortion was

12.3ng/ml.⁵ In the present study almost all the subjects in the abortion group had serum progesterone below this level. Only one women's serum progesterone was above this level.

Abdelazim et al. reported a cut off serum progesterone level of 20ng/ml to be 95.1 % sensitive 98.9 % specific for diagnosis of viable and non-viable pregnancy. They also found serum progesterone level of 10ng/ml to be 79.3% sensitive and 93.3% specific in diagnosing viability of pregnancy.¹¹ Similarly in a recent study cut off value of progesterone for prediction of pregnancy continuation in threatened abortion was 10.05 ng/ml with 93% sensitivity and 90.5 % specificity.¹² While in

the present study 9.92 ng/ml cut off value is 68% sensitive and 91% specific for viable pregnancy. Some studies provide higher cut off levels. In one study the cut off level was 32.7ng/ml with 90 % sensitivity and 92 % specificity¹³.

According to the Royal College of Obstetricians and Gynaecologists, serum progesterone level less than 6ng/ml are highly predictive of failing pregnancy during early pregnancy¹⁴. According to a meta-analysis of 26 cohort studies serum progesterone concentration, less than 3.2 to 6ng/ml rules out viable pregnancy¹⁵. Below this range of progesterone in first trimester, 99.9% of the women had non-viable pregnancies. In our study all the subjects having viable pregnancy had serum progesterone levels above this range. The minimum value was 6.7ng/ml in the viable pregnancy group and is 100% sensitive and 85% specific for viable pregnancy with a PLR of 6.6 and NLR of 0.00. Hence progesterone is a highly sensitive and specific biomarker to predict the viability of pregnancy.

CONCLUSION

The present study concludes that serum progesterone levels are significantly low in women having abortion and hence can be used as a screening tool for viable pregnancy. A serum progesterone level of 6.7ng/ml or above is 100% sensitive and 85% specific in determining the viability of pregnancy during first trimester.

Funding: This study was funded by Center for Research in Endocrinology and Reproductive Sciences (CRERS)

Conflict of interest: The authors declare no conflict of interest

REFERENCES

1. Aruna M, Nagaraja T, Andral S, Tarakeswari S, Sirisha PVS, Reddy AG, et al. Role of progesterone receptor polymorphism in the recurrent spontaneous abortions: Indian case. *PLoS ONE* 2010; 5: e8712.
2. Graham JD and Clarke CL. Physiological action of progesterone in target tissues. *Endocr Rev.* 1997; 18(4): 502-19.
3. Bulun SE and Adashi EY. The physiology and pathology of the female reproductive axis. In: Larsen PR, Kronberg HM, Melmed S and Polonsky KS eds. *Williams textbook of endocrinology*. 10th ed. Pennsylvania:Saunders. 2003: pp. 587-664.
5. Szekeres-Bartho J, Wilczynski JR, Basta P, Kalinka J. Role of progesterone and progestin therapy in threatened abortion and preterm labour. *Front Biosci.* 2008; 13: 1981-90.
6. Aksoy S, Celikkanat H, Senoz S, Gokmen O. The prognostic value of serum estradiol, progesterone, testosterone and free testosterone levels in detecting early abortions. *Europ J Obstet Gynecol and Rep Bio* 1996; 67:5-8
7. Phipps MG, Hogan JW, Peipert JF, Lambert-Masserlian GM, Canick JA and Seifer DB. Progesterone, Inhibin, and hCG multiple marker strategy to differentiate viable from nonviable pregnancies. *Obstet Gynecol.* 2000;95(2):227-31
8. Pillai RN, Konje JC, Tincello DG and Potdar N. Role of serum biomarkers in the prediction of outcomes in women with threatened miscarriage: a systematic review and diagnostic accuracy meta-analysis. 2016; 22(2):228-39
9. Lek SM, Ku CW, Allen Jr JC, Malhotra R, Tan NS, Ostbye T and Tan TC. Validation of serum progesterone < 35nmol/L as a predictor of miscarriage among women with threatened miscarriage. *BMC Pregnancy Childbirth.* 2017; 17(78):1-7
10. Ku CW, Allen JC, Jr., Malhotra R, Chong HC, Tan NS, Ostbye T, et al. How can we better predict the risk of spontaneous miscarriage among women experiencing threatened miscarriage? *Gynecol Endocrinol.* 2015;31(8):1-5
11. Whittaker PG, Schreiber CA and Sammel MD. Gestational hormone trajectories and early pregnancy failure: a reassessment. *Reprod Biol Endocrinol* 2018; 16(95):1-6
12. Abdelazim IA, Elezz AA, and Elsherbiny M. Relation between single serum progesterone assay and viability of first trimester pregnancy. *Springerplus* 2012;1:80-4.
13. Dave A, Patil R, Bansal P, Malhotra A. Role of serum progesterone in threatened miscarriage. *Int J Reprod Contracept Obstet Gynecol* 2018;7:4272-78.
14. Hanita O and Hanisah AH. Potential use of single measurement of serum progesterone in detecting early pregnancy failure. *Malaysian J Pathol* 2012; 34(1): 41-46
15. Memtsa M, Jurkovic D, Jauniaux ERM, on behalf of the Royal College of Obstetricians and Gynaecologists. Diagnostic Biomarkers for Predicting Adverse Early Pregnancy Outcomes. *Scientific Impact Paper No. 58. BJOG* 2018;126:e108-13
16. Verhaegen J, Gallos ID, Mello NMV, Abdel-Aziz M, Takwoingi Y, Deeks JJ et al. Accuracy of single progesterone test to predict early pregnancy outcome in women with pain or bleeding: meta-analysis of cohort studies. *BMJ* 2012; 345:e6077-86.