

# Serum Estradiol levels during First Trimester of Pregnancy

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## ABSTRACT

**Aim:** To investigate serum estradiol levels during first trimester.

**Methods:** It was a descriptive, cross-sectional study, conducted on pregnant women between 18 to 35 years of age presenting during first trimester in obstetric unit of a tertiary care hospital in Lahore, Pakistan. Ultrasonography was done to confirm the viability of fetus. 53 women with nonviable pregnancy were included Group 1 and 28 women with viable fetus and no complication were included in Group 2. Those having any systemic illness or history of estrogen intake were excluded. Using aseptic measures, venous blood samples were taken, and serum was separated. Serum estradiol levels were measured by using immunoenzymometric assay (EIA). Median serum Estradiol levels were compared. Receiver operative characteristics (ROC) curve was plotted.

**Results:** Median serum estradiol levels of women with viable pregnancy 150.49 ng/mL (71.01-393.75) were significantly higher than abortion group 9.96ng/mL (2.87-37.7). A cut off value 47.9ng/ml of serum estradiol is 82% sensitive and 81% specific for a viable pregnancy.

**Conclusion:** Optimal serum estradiol levels are necessary for viability of pregnancy.

**Keywords:** Estradiol, pregnancy, abortion, first trimester, early pregnancy failure.

## INTRODUCTION

Estradiol, 18 Carbon steroid, mainly secreted from ovaries so represents ovarian function. During pregnancy estradiol production increases from non pregnant levels of 100-300 micrograms to milligrams per day.<sup>1,2</sup> On reaching the target organs estrogen bind with its receptors (ERs). ER  $\alpha$  and ER  $\beta$  are the two main nuclear estrogen receptors, which on binding produces genomic actions. Transcription is stimulated. Estrogen also have immediate non-genomic effects which are due to cell membrane receptors<sup>3,4,5</sup>.

Estradiol is indispensable for pregnancy. It promotes breast, uterine and vaginal growth. It causes proliferation of uterine endometrium and mammary ducts. Milk production during pregnancy is prohibited by estrogen. It regulates placental angiogenesis by stimulation various angiogenic factors<sup>6</sup>. It keeps in check many proinflammatory pathways. It acts as an immunomodulator during pregnancy. High levels of estradiol during pregnancy suppresses various immune responses and helps in continuation of pregnancy<sup>7,8</sup>. An imbalance between estrogen and progesterone levels may lead to abortion.

The present study was planned to evaluate serum estradiol levels in spontaneous abortion and its role to predict early miscarriage.

## SUBJECTS AND METHODS

It was a cross-sectional, descriptive study. 100 pregnant women between 18 to 35 years of age presenting during 6 to 12 completed weeks of gestation in obstetric unit of a tertiary care hospital in Lahore, Pakistan were interviewed. After informed consent and permission from Ethical Committee, a detailed history was taken along with examination of the subjects. Ultrasonography was done to confirm the viability of the fetus. Group 1 included 53 women with nonviable pregnancy and Group 2 included 28 women with viable pregnancy confirmed on ultrasonography. Those women having any complication or systemic illness or history of estrogen intake were excluded. Using aseptic measures, venous blood samples were taken and serum was separated. Serum estradiol levels were measured by using enzyme immunoassay (EIA) with an automated analyser with commercially available kit (Biocheck estradiol enzyme EIA test kit, BC 1111)<sup>9</sup>.

SPSS version 20 was used for data entry and analysis. Median along with IQR (interquartile range), was calculated. Comparison was done by Man Whitney-U. For various values of estradiol receiver operative characteristic (ROC) curve for was plotted. Area under the curve (AUC) was calculated. Positive and negative likelihood ratios were also calculated. Sensitivities and specificities at different cut off values of estradiol levels were calculated.

## RESULTS

Median serum estradiol levels of group 1 and 2 are shown in table 1. Median serum estradiol levels of group 2 were significantly higher than group 1 (p-value<0.01). ROC curve against various values of estradiol was plotted and is shown in Figure 1. With 95% confidence interval of 0.77 -0.94, AUC was 0.86 +/- 0.043, (p-value<0.01). Cut-off value of 47.9 ng/ml of serum estradiol is 82% sensitive and 81% specific for viable fetus, with a PLR of 4.34 and NLR of 0.22. Different cut-off values for estradiol are given in table II.

Table I: Serum estradiol levels in group 1 and 2

Estradiol ng/ml Median(IQR)	Group 1 n=53	Group 2 n=28	P value
	9.96 (2.87-37.7)	150.49 (71.01-393.75)	<0.01*

\*p-value < 0.05 was considered statistically significant

Mann Whitney-U test was applied for comparison of groups

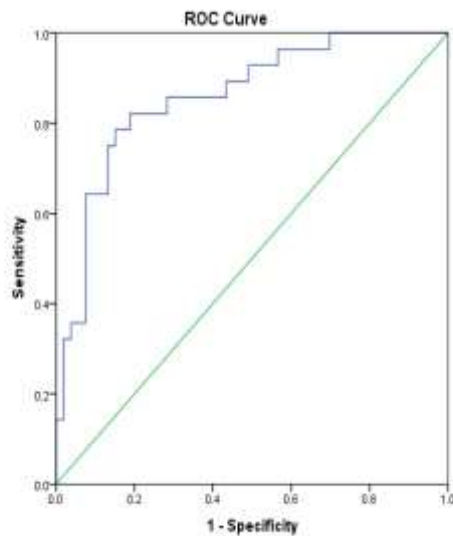
Table II: Sensitivity and specificity of different Cut-off values of estradiol

Cut-off value Estradiol (ng/ml)	Sensitivity (%)	Specificity (%)	Positive likelihood ratio, PLR	Negative likelihood ratio, NLR
9.93	93	50	1.82	0.14
47.9	82	81	4.34	0.22
150.495	50	93	6.67	0.54
217.79	32	98	16.89	0.69

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Figure I: Receiver Operative Curve (ROC) curve of estradiol levels for viable pregnancy



## DISCUSSION

This study reported median serum estradiol levels in first trimester viable pregnancy to be 150.49pg/ml. The present study showed significantly lower levels of serum estradiol levels in women with spontaneous abortion as compared to viable pregnancy during first trimester. 90% of the subjects belonging to abortion group, had serum estradiol level less than 107pg/ml and 75% had levels below 38pg/ml. While in case of viable group 75% of the subjects had levels above 71pg/ml.

Many studies have reported the significance of high serum estradiol levels in viable pregnancy<sup>10,11,12</sup>. Aksoy et al reported a cut-off value of 350pg/ml of serum estradiol during first trimester is 80% sensitive and 70% specific for predicting viable pregnancy.<sup>13</sup> Deng et al reported a cut-off diagnostic value of 576pg/ml with 80% specificity and 83% sensitivity during 7 to 9 weeks identified abortion and for abortion at 5 to 6 weeks the cut off value was 320pg/ml with 80% sensitivity and 57% specificity<sup>14</sup>. Similarly 590.5pg/mL was the cut off value of estradiol with 84.7% specificity during 7<sup>th</sup> week of gestation by Li et al<sup>15</sup>. The serial estradiol levels failed to increase in the abortion group with ongoing gestation. While ongoing pregnancy showed continuous increase in the levels of estradiol in weekly serial samples.<sup>15</sup> In our study we did not collect serial samples.

According to a meta-analysis serum estradiol can be used as a biomarker in threatened pregnancies to predict the outcome, with 45% sensitivity and 87% specificity, positive likelihood ratio of 3.72 and negative likelihood ratio of 0.62<sup>11</sup>.

Low levels of estradiol might have caused disturbance in various mechanisms and lead to spontaneous abortion. These may include endometrial remodeling, placental villous angiogenesis, progesterone expression, inhibition of proinflammatory pathways, and maternal immune tolerance to fetus via increased Regulatory T Cells.<sup>16</sup> Hence by keeping in check estrogen levels prediction of viable pregnancy can be done. Future studies are required to further explore the optimum levels of

estradiol during early pregnancy so that timely interventions may prevent pregnancy loss.

## CONCLUSION

It was concluded that optimum serum estradiol levels are indispensable for ongoing viability of pregnancy. Lower levels may cause pregnancy loss. A cut off value of 47.9 ng/ml of serum estradiol or higher is 82% sensitive, and 81% specific in predicting the viability of fetus during the first trimester of pregnancy.

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