

## The value of Serum Progesterone Measurement in Early Pregnancy

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**Objective:** To assess the use of single serum progesterone measurement in early pregnancy and its relation to the pregnancy outcome.

**Setting:** Coombe Women's Hospital, Dublin.

**Design:** Retrospective analysis of pregnancy outcome of the women who had serum progesterone measurement in early pregnancy.

**Results:** The study group included 55 pregnancies. Forty two pregnancies had continued beyond 28 weeks gestation, 12 ended with spontaneous abortion and one was ectopic pregnancy. Serum progesterone level was  $20.48 \pm 6.066$  in continuing pregnancy,  $7.78 \pm 2.06$  in spontaneous abortion group and 3.9 ng / L in the ectopic pregnancy. The difference in the serum progesterone level was highly significant (P value < 0.0001).

**Conclusion:** Serum progesterone measurement is a reliable biochemical test in establishing the diagnosis of early pregnancy failure.

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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<sup>1</sup>. In spite of the introduction of transvaginal sonography and serum measurement of human chorionic gonadotrophin (HCG), clinicians still do encounter cases where it is difficult to reach an immediate definitive diagnosis of ectopic pregnancy.

Several biochemical markers have been used to study the pregnancy outcome. Kunz and Keller<sup>2</sup> established that oestradiol and progesterone were as reliable as HCG and human placental lactogen in predicting the outcome of threatened abortion. Hubinont et al<sup>3</sup> in a study of 46 women with ectopic pregnancy found that HCG, oestradiol, progesterone and 17 hydroxy progesterone levels were significantly lower than in normal pregnancies.

The value of serum progesterone estimation in early pregnancy has been studied by many investigators<sup>1,4-15</sup>, and it was established that serum progesterone was of a great help in differentiating between viable and non viable pregnancy. The diagnosis of ectopic pregnancy was made within a short time and thus helped to reduce the likelihood of rupture<sup>5</sup>.

The aim of this study was to assess the use of single serum progesterone in early pregnancy and its relation to the pregnancy outcome.

### **METHODS**

A retrospective study was carried out using the records of the women who had serum progesterone measurement in early pregnancy between January 1995 and January 1996 inclusive. The venesection was performed either with the screening blood tests at the first antenatal booking or during hospitalization with vaginal bleeding or abdominal pain. The age,

parity, early pregnancy loss and gestational age at the time of venesection were recorded. The serum progesterone was expressed in nano mole / litre (nmol/l), and this was converted to nano gram/ litre (ng/ml) for the purpose of comparing our results with the previous studies (1nmol/l = 0.314 ng/ml). The presence or absence of vaginal bleeding and abdominal pain had been noted. The result of pregnancy ultrasound was evaluated and documented. The pregnancy outcome was grouped as to whether the pregnancy had continued beyond 28 weeks of gestation or ended with miscarriage or ectopic pregnancy . The relationship between serum progesterone level and the pregnancy outcome was analysed using data disk programme. The mean, the range and the standard deviation were calculated. P value of less than 0.05 was considered as statistically significant.

## RESULTS

The study group included 55 pregnancies in 54 women who had serum progesterone measurement in early pregnancy between January 1995 and January 1996 inclusive. The mean age of the woman was 32 years and the parity ranged between 0 to 3. Early pregnancy loss ranged between 0-2 (mean  $\pm$  standard deviation (SD):  $0.42 \pm 0.6$ ). The gestational age at the time of venesection ranged from 6-15 weeks gestation ( $9.1 \pm 2.2$  mean  $\pm$  SD), Table 1.

Table 1. **Data on 54 Women in the Study**

	<i>Mean</i>	<i>SD</i>	<i>Range</i>
Age (years)	32	4.5	24-40
Parity	0.6	0.75	0-3
Gestation at progesterone Assay (weeks)	9.1	2.2	6-15

Fifty two women had an ultrasound scan. Thirty four (65.40/o) revealed a viable fetus while anembryonic pregnancy or missed abortion was diagnosed in 11 (21.2%). One ultrasound examination was suggestive of ectopic pregnancy which turned out to be an intrauterine pregnancy with a functional ovarian cyst. The ultrasound examination was inconclusive in 6 patients (Table 2). Fifteen patients had complained of vaginal bleeding (27.3%), 2 women had abdominal pain and the remaining 38 (69.1%) were asymptomatic. Forty two (76.4%) women had a continuing pregnancy, 12 (21.8%) had miscarriage and 1 (1.8%) had an ectopic pregnancy. The pregnancies which continued had a serum progesterone level varying between 7.1 and 34.2ng/ml (mean  $\pm$  SD =  $20.48 \pm 6.06$ ) and 95% confidence interval (95% CI) was 18.59-22.37ng/ml. The range of serum progesterone in pregnancies which ended with miscarriage was 3.2-12.2 ng/ml (mean  $\pm$  SD =  $7.78 \pm 2.96$  and 95% CI 5.66-9.90), (Table 3). The serum progesterone level was 3.9ng/ml in the lady with ectopic pregnancy. When the pregnancy outcome was compared using ANOVA, the difference of serum progesterone level was highly significant (P value < 0.0001). In the 42 women with a continuing pregnancy only 2 had values below 10ng/ml.

Table 2. **The Result of Ultrasound Examination in 52 Women**

	No.	%
Viable fetus	34	65.4
Missed abortion	11	21.2
Suspected ectopic pregnancy	1	1.9
Inconclusive	6	11.5
Total	52	100

**Table 3. Pregnancy outcome-and progesterone level in 55 Pregnancies**

<i>Outcome (No)</i>	<i>Range (ng/ml)</i>	<i>Mean(SD)</i>	<i>95% CI</i>
Continuing pregnancy (42)	7.1-34.2	20.48(6.06)	18.6-22.4
Miscarriage (12)	3.2-12.2	7.78(2.96)	5.7-9.9
Ectopic pregnancy (1)	3.9		

Multivariate analysis showed that age and previous pregnancy losses did not affect the outcome. There was no correlation between gestational age and progesterone level (P 0.7 and the correlation coefficient was 0.04).

**Table 4. Cut off level of serum progesterone value between viable and non viable pregnancies**

<i>Study</i>	<i>Cut off level ng/ml</i>	<i>Sensitivity %</i>	<i>Specificity %</i>
Al Sebai et al <sup>1</sup>	14.1	87.6	87.5
Hubinont et al <sup>11</sup>	15	64.7	88.9
Saver et al <sup>12</sup>	20	98	100
Yeko et al <sup>15</sup>	15	97	100
Buck et al <sup>16</sup>	20	92	89
Hahlin et al <sup>17</sup>	9.4	86	100
Hahlin et al <sup>18</sup>	9.4	87.6	87.5
Present study	10	69.2	95.2

## DISCUSSION

The measurement of serum progesterone is a valuable test in the diagnosis of early pregnancy failure. The assay is inexpensive and the level changes little during pregnancy<sup>14</sup>. The result of this study is in agreement with other studies which have established that a single serum progesterone level can predict the pregnancy outcome<sup>1,12,21</sup>. The difference of serum progesterone level in pregnancies which continued and those which failed was highly significant (P value < 0.0001). The cut off level of serum progesterone value which can differentiate between viable and non viable pregnancies has varied between 10 ng/ml to

20ng/ml<sup>1,11,12,15-18</sup> (Table 4). In this study, 5% of viable pregnancies had a serum progesterone level less than 10ng/ml while 33% of spontaneous miscarriage had a value of > 10ng /ml. (Sensitivity 69.2% for failed pregnancies and specificity of 95.2% for the value of <10ng/ml). However, no viable pregnancy was present with a progesterone level of less than 5ng/ml, this agrees with the results of Stovall et al<sup>19</sup>.

We found no correlation between progesterone level and gestational age confirming that serum progesterone levels change little during early pregnancy. Hahlin et al<sup>17</sup> reported that the discriminatory efficacy of a single progesterone determination was not increased by serial estimation of progesterone levels. Other studies showed that serum progesterone level of more than or equal to 25ng/ml can exclude ectopic pregnancy with 97.5% sensitivity and a value of less or equal to 5ng/ml is 100% sensitive for diagnosis of non viable pregnancy. In pregnancies with progesterone values of above 5 and below 25ng/ml, viability must be established by sonographic examination<sup>13,14,20</sup>.

The use of serum progesterone was found to be of great help in reaching early diagnosis of ectopic pregnancy and this lead to decreased morbidity of ectopic pregnancy and the use of conservative treatment. Hahlin et al<sup>17</sup> in a study of 158 women with clinical suspicion of ectopic pregnancy, HCG less than 4,000m IU/L and inconclusive endovaginal sonography, found that a single progesterone level was of great importance. Stovall et al<sup>13</sup> in a prospective study of the use of serum progesterone in the emergency department found that it was associated with a decreased time in diagnosis of ectopic pregnancy from 48 to 72 hours to less than 24 hours and this also resulted in a significant reduction of ruptured ectopic pregnancy.

## CONCLUSION

**In summary, though this study was retrospective and the numbers were small, a significant difference of serum progesterone level was shown between viable and non viable pregnancy. This study has demonstrated that serum progesterone measurement is a reliable biochemical test in establishing the diagnosis of early pregnancy failure.**

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