Role of Serum Progesterone in the Diagnosis of Ectopic Pregnancy and Missed Abortion

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ABSTRACT:
BACKGROUND: diagnosis of early pregnancy failure (ectopic pregnancy and missed abortion) still challenging even by using of serial B-HCG and ultrasound. Serum progesterone hormone level value is regarded as one of the important diagnostic tools in the diagnosis of many obstetrical and gynecological conditions; one of these is early pregnancy failure.

OBJECTIVE: To assess the role of serum progesterone level in early diagnosis of ectopic pregnancy and missed abortion.

PATIENTS AND METHODS: The study is conducted at Al-Elwiya Maternity Teaching Hospital throughout the period between (April 2010 – July 2011). Ninety women participated in the study, they are at their early weeks of gestation (6-10) weeks. Their ages were between 18-40 years. thirty of them served as a control group (normal intrauterine pregnancy) and sixty pregnant women included in the study group and subcategorized into 2 groups. thirty women with suspected sub-acute or chronic cases of ectopic pregnancy according to ultrasound and β-HCG results and 30 women served as suspected missed abortion. blood samples were taken from the three groups followed by another blood samples after two-day interval to measure of serum progesterone levels. the results were compared among the three groups at first and second readings. p-value, standard deviation and 95% confidence interval calculated and statistically analyzed.

RESULTS: P-value of the serial measurements of serum progesterone levels in two-day interval in the three groups was statistically insignificant. while serum progesterone levels of both ectopic pregnancy and missed abortion were greatly lower than serum progesterone levels of normal intrauterine pregnancy in both first and second readings, with statistically significant deference, P-value is

CONCLUSION: Serum progesterone levels has a useful role in diagnosing ectopic pregnancy and missed abortion.

KEY WORDS: progesterone, ectopic pregnancy, missed abortion

INTRODUCTION: Progesterone is produced during pregnancy. At first, the source is the corpus luteum that has been “rescued” by the presence of human chorionic gonadotropins (HCG) from the conceptus. However, after the 8th week, production of progestin shifts to placenta (1). Progesterone is sometimes called the “hormone of pregnancy”, it decreases contractility of the uterine smooth muscle (2), the progesterone production from corpus luteum is dependent on the slop of hCG increase in early pregnancy. The half-life of progesterone clearance is only 2 h compared to 24-36 h for serum HCG. As a result serum progesterone levels will respond quickly to any decrease in HCG production. The progesterone measurement can therefore be used as a bioassay of early pregnancy viability. Serum progesterone <20 nmol/l reflects fast decreasing HCG levels and can be used to diagnose spontaneously resolving pregnancies with a sensitivity of 94% and specificity of 91%. Progesterone levels > 60 nmol / indicate a normal increase in HCG levels, but those between 20 and
60 are strongly associated with abnormal pregnancies \( ^3 \). In clinical practice serum progesterone measurements are particularly useful in women with a non-diagnostic ultrasound scan. Although the majority of these women have failed intrauterine pregnancies, they are usually followed up with serial HCG measurement because of the fear of missing potentially significant ectopic pregnancies\(^2,4,5\). The routine measurement of serum progesterone can reliably diagnose pregnancies in regression and can reduce by 50-60% the need for follow-up scans and serial HCG measurements in pregnant women with non-diagnostic scan findings \(^6\).

Aims of the study is to assess the role of serum progesterone level in diagnosing early pregnancy failure and to see if serial serum progesterone level can affect the diagnosis and prognosis of both normal intrauterine pregnancy and early pregnancy failure.

**PATIENTS AND METHODS:**
This prospective study was conducted during the period from the 1\(^{st}\) of April 2010 to the 1\(^{st}\) of July 2011 in the out-patient clinic of Al-Elwiya Maternity Teaching Hospital. Verbal consent was taken from the patients prior to blood sample collection. The research was approved by ethical committee of the hospital and the Iraqi Board. Ninety women at their early weeks of gestation (6-10) were included in the study. Thirty women served as control group and sixty designed to be a study group. These women attended to the Al-Elwyah Maternity Hospital to confirm their pregnancy or seeking advice for their problems like abdominal pain or vaginal bleeding. The maternal ages were between (18-40) years. The women were classified into three groups: normal intrauterine pregnancy, suspected ectopic pregnancy and missed abortion.

![Figure 1](image)

Figure 1 shows comparison between means of the first readings of progesterone level of the three groups. We notice that the mean levels of ectopic pregnancy and missed abortion are greatly lower than normal pregnancy.
Figure 1: Comparison of the Mean’s in First Readings.

Figure (2) shows comparison between means of the second readings of the three groups. We notice that the mean levels of progesterone in both ectopic pregnancy and missed abortion are greatly lower than progesterone levels in normal pregnancy.

Figure 2: Comparison of the Mean’s in Second Readings.

Table 1: Shows Progesterone Level of Two–Day Interval in Normal Pregnancy, Ectopic Pregnancy and missed abortion.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Progesterone Level (ng/ml)</th>
<th>P. Value</th>
<th>95%C.I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reading 1</td>
<td>Reading 2</td>
<td></td>
</tr>
<tr>
<td>Normal pregnancy</td>
<td>32.81 (8.68)</td>
<td>36.93 (7.92)</td>
<td>0.059</td>
</tr>
<tr>
<td>Ectopic pregnancy</td>
<td>10.13 (5.4)</td>
<td>8.73 (4.7)</td>
<td>0.286</td>
</tr>
<tr>
<td>Missed Abortion</td>
<td>5.49 (2.37)</td>
<td>4.95 (2.18)</td>
<td>0.365</td>
</tr>
</tbody>
</table>

In normal pregnancy, the mean progesterone level increased from the first reading to the second reading, P-value = 0.59 which is insignificant. And in ectopic the mean progesterone level decreased from the first reading to second reading, p-value < 0.286 which is insignificant. And in missed abortion mean progesterone level decreased from the first readings to the second readings P-value < 0.365 which is insignificant as seen in the table 1. When comparing serum progesterone level between first readings of normal pregnancy and first readings of ectopic pregnancy and first reading of missed abortion, the mean serum...
progesterone level in ectopic pregnancy is much lower than normal intrauterine pregnancy with a P-value < 0.00005 which is highly significant and similarly with missed abortion with a P-value < 0.00007 which is highly significant as seen in table 2. Similarly in the same table we can notice that, comparison of mean serum progesterone level between second readings of normal pregnancy with second readings of ectopic pregnancy and missed abortion. We notice that the level in ectopic is much lower than normal pregnancy with a P-value < 0.00003 and the level in missed abortion is also lower than normal with a P-value < 0.000015, which in both is highly significant.

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In this study, the role of serum progesterone was evaluated by comparing first readings of the three groups (normal pregnancy, ectopic pregnancy and missed abortion) and then the second readings of them compared between progesterone levels in normal pregnancy with those suffering from pregnancy failure which was very significant.

Serial measurement of progesterone value in normal pregnancy got a P-value <0.059 which is statistically insignificant. Also, for ectopic pregnancy P-value was 0.286 and for missed abortion was 0.365 which is again statistically insignificant. Our study agreed with a study done by Thomas, et al (7) who proved that a single measurement of serum progesterone is more sensitive and specific than serial measurement of serum progesterone in screening of ectopic pregnancy and missed abortion with a P-value < 0.05.

Mean progesterone level for normal pregnancy in its first reading was (32.81 ng/ml) (n=30). For ectopic pregnancy the mean of the first reading was (10.13 ng/ml) (n=30). For missed abortion the mean of the first reading was (5.49 ng/ml) (n=30). For the second readings the mean progesterone was (36.93 ng/ml) (n=30) for normal pregnancy, the mean of second readings for ectopic pregnancy was (8.73 ng/ml) and the mean progesterone level for missed abortion in the second readings was (4.95 ng/ml). We notice that progesterone level increased slightly in the normal pregnancy while decreased slightly in ectopic pregnancy and missed abortion but this increase and decrease still statistically insignificant. The progesterone levels in both types of early pregnancy failure were significantly lower than normal pregnancy. Williams RS et al (9) found that the mean progesterone for normal pregnancy was 32.8 +/- 4.25 ng/ml , for ectopic pregnancies was 7.8 +/- 0.79 ng/ml and pregnancies which spontaneously aborted 8.1 +/- 0.91 ng/ml.

When using individual prediction limits progesterone greater than 24 ng/ml can exclude an ectopic pregnancy in 99% of patients. His results agreed greatly with our study results in their first readings. We agree the study done by Al Sebai M. A (10) concluded that a single serum progesterone measurement taken in early pregnancy is valuable in the immediate diagnosis of early pregnancy failure and the long term prognosis of viability.

In our study we reported a high level of progesterone in normal pregnancy (mean 32+/-81) in first readings and (mean 36+/-93) in second readings, these levels very effective in diagnosis normal intrauterine pregnancy even with single measurement. Our results agreed with Aksoy S et al (11) who concluded that serum progesterone levels can be used as a screening test with high sensitivity and specificity to predict a normal pregnancy. Another aspect of the study is that we tried to differentiate between ectopic pregnancy and missed abortion by progesterone level, the mean levels of ectopic pregnancy was (10.13) and for missed abortion was (5.49), these levels are very close that the difference between them cannot be used statistically to differentiate between them. We agree to some extent with a study done by Choe JK et al (12) he showed that single progesterone level is not diagnostic for ectopic pregnancy since mean progesterone levels in ectopic pregnancy were similar to those with spontaneous abortion though significantly lower than those in controls. McCord M L. et al (13) obtained in his study that the diagnostic accuracy for ectopic pregnancy versus normal pregnancy was 88.7 O+/-.0.1%, for spontaneous abortion versus normal pregnancy was 93.8 +/- 0.4%. Diagnostic accuracy for abortion versus ectopic pregnancy was only
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39.4±/ 0.2 %. They concluded that for progesterone level greater than or =17.5 ng/ml, patients thought to be at risk for ectopic pregnancy may be followed reasonably without ultrasound or further invasive procedure.

We have some agreement with a study done by BW MOL et al (14) who concluded that single serum progesterone measurement could not discriminate between ectopic pregnancy and non-ectopic pregnancy. It is concluded that serum progesterone measurement can identify patients at risk for ectopic pregnancy, who need further evaluation, but its discriminative capacity is insufficient to diagnose ectopic pregnancy with certainty. Stovall TG et al (15) showed in his study about preventing ruptured ectopic pregnancy with a single serum progesterone test for ectopic pregnancy, 80.6% had a progesterone level less than 15 ng/ml, only 1.5% of ruptured ectopic pregnancy was associated with progesterone level greater than 25 ng/ml. For normal pregnancy 10.6% had progesterone level less than 15 ng/ml, and 61% had a progesterone level greater than 25 ng/ml. They decrease minimum time for diagnosis from 48-72 hours to less than 24 hours in maximum delay. They concluded that the determination of serum progesterone should be used for ectopic pregnancy or at any time when the diagnosis is in question.

CONCLUSION:

Serum progesterone level has a useful role in diagnosing ectopic pregnancy and missed abortion.

REFERENCES: