

Single Serum Progesterone Measurement in Pregnancy Prognosis

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By

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Abstract

Objective: To assess the value of single serum progesterone in diagnosis of viable, ectopic and failing pregnancy.

Study design: Prospective study done in Al Basra general hospital and Al Basra maternity and child hospital from June 2013-2014. 64 patient was included in the study , all have 1st trimester vaginal bleeding and/or abdominal pain .5cc of blood was taken for assessment of progesterone and B.HCG, then patient subjected to ultrasound department

Result: 64 women enrolled in our study , main age group 28 (43.75%) patients from 21-30 years old 44 (68.75%) patients with gestational age from (6-12) weeks gestation. By ultrasound examination found 36 (56.26)% patients with viable pregnancy, 18 (28.12)% patients diagnosed as failing pregnancy and 10 (15.62%) patients diagnosed as ectopic pregnancy.

Pregnancies which continued has a serum progesterone level varing between 3.38-52 ngL/ml (mean \pm SD=20.006 \pm 1.7), while the range of serum progesterone in non viable pregnancies was 1.1-30.1ng /ml (mean \pm SD = 9.09 \pm 8.2). Range of serum progesterone in ectopic 1.9-75.9 ng/ml (mean \pm SD = 19.7 \pm 16.3)

The sensitivity and specifity of single progesterone in diagnosis of pregnancy failure in our study 72.2%, 66,6% respectively in comparism with95.4%sensetivity of B.HCG.

Conclusion: Single serum progesterone is not of significant value in predicting pregnancy outcome..

Introduction:

Vaginal bleeding and abdominal pain are the most common causes of consultation in early pregnancy; 30% of women will experience pain or bleeding in their first trimester ⁽¹⁾. These symptoms lead to anxiety and can be the first sign of a possible miscarriage or an ectopic pregnancy ⁽²⁾.

Most women seeking medical advice have a transvaginal ultrasound scan to confirm a viable pregnancy, miscarriage or ectopic pregnancy. The high incidence of miscarriage and ectopic pregnancies in women with inconclusive ultrasound results warrants further tests to reach diagnoses ⁽³⁾.

Measurement of serum B-hCG can be useful, but often more than one B-hCG measurements is needed to make a diagnosis. Serum progesterone has been proposed as a useful test to distinguish a viable pregnancy ⁽⁴⁾.

Previous studies have revealed that progesterone is the most powerful single indicator of pregnancy outcome ⁽⁵⁾.

✕ • **Pregnancy biomarkers:**

A lot of biomarkers have been used for early diagnoses of pregnancy like Human chorionic gonadotropin (HCG), progesterone, inhibin and pregnancy associated plasma protein-A (PAPP-A)⁽⁶⁾.

Human chorionic gonadotropin (HCG):

Is a glycoprotein composed of 237 amino acid with molecular mass of 25-7 KDa. It is heterodimeric with an alpha subunit identical to that of LH, FSH & TSH & beta subunit that is unique to HCG⁽⁷⁾.

The two subunits create a small hydrophobic core surrounded by high surface area to volume ratio 2.8 times that of sphere, but the vast majority of amino acids are hydrophilic. HCG a hormone produced by the syncytiotrophoblast, a component of fertilized egg⁽⁸⁾.

After conception HCG interacts with HCG receptors of blastocyst and promotes the maintenance of corpus luteum during the beginning of pregnancy. Due to its highly negative charge, HCG may repel the immune cells of the mothers, protecting the fetus from rejection during the first trimester⁽⁹⁾.

It has been suggested that HCG levels are linked to the severity of morning sickness in pregnant women⁽¹⁰⁾.

The ability to quantitate the B.HCG level is useful in the follow up care after miscarriage and in diagnosis and follow up care of ectopic pregnancy⁽¹¹⁾. With the use of transabdominal ultrasound now pregnancy could be seen in most cases when serum HCG exceed 6500IU/⁽¹²⁾.

With transvaginal ultrasound this threshold can be lowered to 1000IU/L⁽¹³⁾. These observations have helped to introduce the concept of "discriminatory zone", which a normal intrauterine pregnancy should be detected on ultrasound scan.

Abnormally slow rise in serum HCG has also been used to diagnose abnormal pregnancy. In normal pregnancy doubling time is 1.4 days before 5 weeks gestations and 2.4 days from them until 7 weeks gestations⁽¹⁴⁾.

Progesterone:

Also known as p4 (pregn-4-ene-3,20-dione) is a c-21 steroid hormone involved in the female menstrual cycle, pregnancy (support gestation) and embryogenesis⁽¹⁵⁾. Like other steroids, progesterone consist of four interconnect cyclic hydrocarbons⁽¹⁶⁾.

In human progesterone produced during pregnancy:

1. At first, the source is the corpus luteum that has been rescued by the presence of HCG from conceptus.
2. However, after 8th week, production of progesterone shift to the placenta .the placenta utilize maternal cholesterol as the initial substrate and most of the produced progesterone enters the maternal circulation .At term the placenta produce 250mg progesterone/ day⁽¹⁷⁾.

In women, progesterone levels are relatively low during the pre-ovulatory face of the menstrual cycle, rise after ovulation, and are elevated during luteal phase. progesterone levels tend to be < 2ng / ml prior to ovulation and >5ng/ml after ovulation. If pregnancy occurs, HCG is released maintaining the corpus luteum allowing it to maintain level of progesterone. At around 12weeks the placenta begin to produce progesterone in place of corpus luteum, this process named the luteal-placental shift.

After luteal- placental shift levels start to rise further and may reach 100-200ng/ml at term ⁽¹⁸⁾. Progesterone is sometimes called "hormone of pregnancy" and it has many roles relating to the development of fetus:

1. Progesterone converts the endometrium to it's secretory stage to prepare uterus for implantation.
2. During implantation and gestation, progesterone appear to decrease the maternal immune response to allow for the acceptance of the pregnancy.
3. Progesterone decrease contractility of uterine smooth muscles.
4. Progesterone inhibits lactation during pregnancy.
5. Drop in pregnancy is possibly one step that facilitate the onset of labour.⁽²⁰⁾.

Pregnancy outcome classification:

Establishment pregnancy was defined by HCG level more than 10IU/ L further Subdivided into:

- A. Chemical pregnancy:** where in spite of the B.HCG test being "positive" the pregnancy Fails to progress to the point of ultrasound confirmation.
- B. Ongoing pregnancy:** defined as pregnancy beyond 12 weeks of viable gestation.
- C. Failed pregnancy:** embryo not progress to viable fetus ⁽²¹⁾.

Ultrasound and early pregnancy:

Traditional obstetric sonograms are done by placing a transducer on the abdomen of the pregnant woman. One variant, a transvaginal sonography, is done with a probe placed in the woman's vagina. Transvaginal scans usually provide clearer pictures during early pregnancy and in obese women ⁽²²⁾.

Also used is Doppler sonography which detects the heartbeat of the fetus. Doppler sonography can be used to evaluate the pulsations in the fetal heart and blood vessels for signs of abnormalities ⁽²³⁾.

The gestational sac can sometimes be visualized as early as 4.5 weeks of gestational age (approximately 2.5 weeks after ovulation) and the yolk sac at about 5 weeks gestation. The embryo can be observed and measured by about 5.5 weeks. The heartbeat may be seen as early as 5 weeks of gestational age. It is usually visible by 7 weeks ⁽²⁴⁾.

Coincidentally, most miscarriages also happen by 7 weeks gestation. The rate of miscarriage, especially threatened miscarriage, drops significantly if normal heartbeat is detected ⁽²⁵⁾.

Methodology:

A prospective study were done in Basra general hospital and Basra maternity and child hospital from June 2013 to June2014. 64 patients with first trimester vaginal bleeding and/ or abdominal pain were seen by the same resident doctor preceded by taking history which include (age, parity, last menstrual period and gestational age at time of the study were confirmed by last menstrual period.

After taking informed consent 5cc of blood was drawn from the patients for measurement of B.HCG and serum progesterone collected in dry tube then sent for laboratory unit.

In the lab. Serum was separated by centrifugation and stored at 2-8 c until hormonal level measurement.

The assay principle combines an enzyme immunoassay competition method with With final fluorescent detection .At the end of the assay, result were analyzed using ng/ ml unit. Then the patients was send for ultrasound department to evaluate and document the results . Abdominal ultrasound was done as preferred by patients.

Ex Patients with multiple pregnancy, molar pregnancy, recurrent miscarriage , fetal abnormalities, cervical pregnancy, luteal support and unsure of last menstrual period were excluded from these study.

The relationship between serum progesterone and B.HCG level and the pregnancy Outcome was analyzed using data programme .

The mean , the range , standard deviation , specifity and sensitivity were Calculated.

Result:

Our study included 64 women in Basra maternity hospital and general Basra hospital between June 2013 to June 2014. All of them admitted to the hospital in the emergency room complaining of vaginal bleeding and/or abdominal pain. All women had serum progesterone and serum HCG measurement and send for ultrasound department to confirm the result.

Table (I): Demographic character of women enrolled in the study

character	variable	No.	Percent
Age Group	< 20	14	21.87
	21-30	28	43.75
	31- 40	22	34.37
Gravidity	Primi	20	31.25
	2-3	24	37.5
	≥ 4	20	31.25
Gestational age at time of Presentation	6-9 Weeks	20	31.25
	≥ 10	44	68.75

Table (1): Show demographic character of women enrolled in the study:

According to age group 14 (21.8%) patient below 20 years, 28 (43.75%) patient for women between 21-30 years old and 22 (43.37%) patient for women between 31-40 years old.

According to gravidity 20 (31.25%) patient for women who are primigravida, 24 (37.5%) patient for women who are Para two or Para three and 20 (31.25%) patient for women who are Para four or more.

According to gestational age 20 (31.25%) patient for those between 6-8 weeks gestation and 44 (68.75%) patient for those 10 weeks gestation or more.

Table (II): Results of Ultrasound examination.

character	No.	Percent
Viable	36	56.26
Failing	18	28.12
Ectopic	10	15.62
Total	64	100

Table (II): By Ultrasound examination 36 (56.26%) patients was found as a viable pregnancy, 18 (28.12%) patients diagnosed as failing pregnancy and 10 (15.62%) patients was diagnosed as ectopic pregnancy.

Table (III): Progesterone level in related to pregnancy outcome.

character	Mean of progesterone	Range of progesterone	Standard division
Viable	20.006	3.38-52	1.7
Non- Viable	9.09	1.1-30.1	8.2
Ectopic	19.7	1.9-75.9	16.3

Table (III) Show progesterone level in relation to pregnancy outcome in 1st trimester. Pregnancies which continued had a serum progesterone level varying between 3.38-52 ng/ mL. (mean \pm SD= 20.006 \pm 1.7).

While the rang of serum progesterone in Non- Viable Pregnancies was 1.1-30.1 ng/mL. (mean \pm SD = 9.09 \pm 8.2).

Rang of serum progesterone in ectopic pregnancy was 1.9-75.9 ng/ mL. (mean \pm SD = 19.7 \pm 16.3).

Discussion

To overcome problems encountered in diagnosis of early pregnancy failure, a lot of studies done to find ideal biomarker which is simple, safe and reliable. In spite of introduction of ultrasound and B.HCG measurement, still a lot of difficulties found to diagnosis early pregnancy failure and ectopic.

In our study we try to concentrate on use of simple measurement of serum progesterone as a biomarker .

In our study 28 (43.75%) patients occurred between 21-30 years of age (reproductive age group), 44 (68.75%) patients more than 10 weeks of gestations at time of presentation. Women included in the study classified according to ultrasound results to 36 (56.26%) patients where viable, 18 (28.12%) patients nonviable, 10 (15.62%) patients ectopic pregnancies.

In our study, single progesterone measurement was found to be not helpful in ^{the} discrimination between viable and non-viable pregnancy at cut off level (11), as only 6% of viable pregnancy showed single serum progesterone level above 11ng/dl, 16% of non-viable below 11ng/ dl with p-value 0.61 and 0.54 respectively at (95% CI).

The sensitivity and specificity of single progesterone in diagnosis of pregnancy failure in our study 72.2%, 66.6% respectively which is very low in comparison with 95.4% sensitivity of B. HCG ⁽²⁶⁾.

This is disagreement with studies done by Al-Sebai ,Zainab Ali and Hanita, Which showed the single Serum progesterone is powerful Biomarker aids in diagnosis of pregnancy failure ^(27,28,29) and agreement with Muataz al Ramahi etal study which showed that single progesterone measurement was not useful in predicting pregnancy outcome.⁽³⁰⁾

Also regarding diagnosis of ectopic pregnancy in related to serum progesterone measurement, the difference was statistically insignificant $p\text{-value} > 0.005$ at level of confidence interval 95%.

Stovel et al showed that single serum progesterone measurement is helpful in diagnosis of ectopic pregnancy and this is disagreement with our study⁽³¹⁾.

Conclusion:

"Single serum progesterone measurement is not of significant value in prediction of pregnancy outcome".

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الخلاصه:

الهدف: دراسه فعاليه هرمون البروجستيرون في تشخيص الحمل داخل وخارج الرحم في الاشهر الاولى من الحمل .

المكان: مستشفى البصره العام

مستشفى الولاده والطفل في البصره

معالجه المعلومات وتحليل البيانات: أجريت هذه الدراسه على ٦٤ امراه حامل في الاشهر الاولى من الحمل (٦-١٢) أسبوع يعانين من نزف أو ألم البطن . تم سحب عينه من الدم وتم إرسالها الى المختبر لغرض قياس نسبه هرمون البروجيستيرون والبيتا أج سي جي (B.HCG) في الدم. ثم أرسلت المريضات الى وحده السونار لغرض تشخيص أستمراريه وموقع الحمل داخل أو خارج الرحم .

النتائج: بعد الحصول على نتائج التحاليل المختبريه وتقارير وحده السونار والأخيره أظهرت أن ٣٦ (٥٦.٢٦%) مريضه لديها مستمر وحي و ١٨ (٢٨.١٢%) مريضه تعاني من فشل الحمل و ١٠ (١٥.١٢%) لديها حمل خارج الرحم بينما أظهرت النتائج المختبريه كون نسبه هرمون البروجيستيرون للحمل المستمر الحي تتراوح من (٣.٣٨- ٥٢) وللحمل المستمر الغير الحي (١.١-٣٠.١) وللحمل خارج الرحم (١.٩- ٧٥.٩) حيث وجد هناك أختلاف كبير في تشخيص أستمراريه الحمل من عدمه $p = ٠,٦١\% \& ٠,٥٤\%$ (value).

الاستنتاج: هرمون البروجيستيرون ليس ذات قيمه في تشخيص أستمراريه الحمل داخل الرحم (حي أو ميت) أو خارجه.