Single Serum Progesterone Measurement in Pregnancy Prognosis

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Abstract

Background:

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

Patients and methods: This cross sectional study was done in Al Basra general hospital and Al Basra maternity and child hospital from June 2013 through January 2014. The study included 64 patient, all have 1st trimester vaginal bleeding and/or abdominal pain. From each patient a 5 cc blood sample was obtained for assessment of progesterone and β-HCG, and then patients were sent to ultrasound examination.

Result: Mean age of women enrolled in the present study was 31.21± 4.23 years and it ranged from 20 to 35 years. Mean gestational age was 8.30 ±2.15 and it ranged from 6 to 12 weeks. Ultrasound examination revealed that 36 patients (56.3%) had viable pregnancy, 18 patients (28.1 %) had failing pregnancy and 10 patients (15.6%) had ectopic pregnancy. Mean serum progesterone in women with viable, failed and ectopic pregnancies was 20.01 ± 1.7 ng/ml, 9.09 ± 8.2 ng/ml and 19.7± 16.3 ng/ml. The sensitivity and specify of single serum progesterone measurement in diagnosis of pregnancy failure in this study were 72.2% and 66.6%, respectively while those of serum β-HCG were 95.4% and 98.1%.

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

Key words: Single serum progesterone, viable, failed pregnancy

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

chorionic gonadotropin (HCG) is a glycoprotein composed of 237amino 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 hormone is produced by the syncytiotrophoblast, a component of fertilized egg [8]. After conception HCG interacts with HCG receptors of blastocyst andpromotes the Maintenance of corpus luteum during the beginning of pregnancy. Due to its highly negative charge, HCG may repel the immune cells of the mothersprotecting the fetus from rejection during the first trimester [9]. It has been suggested that HCG levels are linked to the severity of morningsickness 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 65001U/ [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 abnormalpregnancy. In normal pregnancy doubling time is 1.4 days before 5 weeksgestations 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 hormoneinvolved in the female menstrual cycle, pregnancy (support gestation) and embryogenesis [15]. Like other steroids, progesterone consist of four interconnect cyclic hydrocarbons [16]. At first, the source is the corpus luteum that has been rescued by the presence of HCG from conceptus; however, after 81h week, production of progesterone shift to the placenta which utilizes maternal cholesterol as the initial substrate and most of the produced progesterone enters the maternal circulation [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 begins 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: It converts the endometrium to it's secretory stage to prepare uterus for implantation, decreases the maternal immune response to allow for the acceptance of the pregnancy, decreases contractility of uterine smooth muscles, inhibits lactation during pregnancy [20]. Establishment pregnancy was defined by HCG level more than 10IU/ L further Subdivided into: Chemical pregnancy, where in spite of the B.HCG test being "positive" the pregnancy Fails to progress to the point of ultrasound confirmation;

Ongoing pregnancy, defined as pregnancy beyond 12 weeks of viable gestation; failed pregnancy: embryo not progress to viable fetus [21] . 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 bloods vessels for signs of abnormalities [23]. The gestational sac can sometimes be visualized

most miscarriages also happen by 7 weeks gestation. The rate of miscarriage, especially threatened miscarriage, drops significantly if normal heartbeat is detected [25]. So the aim of the current study was to evaluate single serum progesterone measurement in identifying fate of pregnancy.

Patients and methods

A cross sectional study was 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 tubethen sent for laboratory unit. In the laboratory serum was separated by centrifugation and stored at 2-8 c untilhormonal level measurement. The assay principle combines an enzyme immunoassay competition method with final fluorescent detection at the end of the assay, result were analyzed using ng/ ml unit. Then the patients were sent for ultrasound department to evaluate and document the results. Abdominal ultrasound was done as preferred by patients. Patients with multiple pregnancy, molar pregnancy, recurrent miscarriagefetal abnormalities, cervical pregnancy, luteal support and unsure of as early as 4.5 weeks ofgestational 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,
lastmenstrual period were excluded from these study. The relationship between serum progesterone and B.HCG level and the pregnancy Outcome was analyzed using data program. The mean, the range, standard deviation, specificity and sensitivity were Calculated.

Result:

Table (1) Shows demographic character of women enrolled in the study. According to age group (21.8%) below 20 years, (43.75%) for women between 21-30 years old and (43.37%) for women between 31-40 years old. According to gravidity (31.25%) for women who are primigravida, (37.5%) forwomen who are Para two or Para three and (31.25%) for women who are Para four or more.According to gestational age (31.25%) for those between 6-8 weeks gestation and (68.75%) for those 10 weeks gestation or more. Table (2), 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 (3) Show progesterone level in relation to pregnancy outcome in 1sttrimester. Pregnancies which continued had a serum progesterone level varying between 3.38-52 ng/mL. (mean± SD= 20.006 ± 1.7). While the rang of serum progesterone in Non- Viable Pregnancies was 1.1-30.1 ng/mL. (mean ± SD = 9.09 ± 8.2). Rang of serum progesterone in ectopic pregnancy was 1.9-75.9 ng/ mL. (mean ± SD 19.7 ± 16.3), as shown in table (3).

Table (1): 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 (2): Results of Ultrasound examination.

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

Table (3): Progesterone level in related to pregnancy outcome

character	Mean of progesterone	Range of progesterone	Standardivisondivisio n
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

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 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 11 ng/dl with p-value 0.61 and 0.54 respectively at (95% CI). The sensitivity and specifity of single progesterone in diagnosis of pregnancy failure in our study 72.2%, 66.6% respectively which is very low in comparismwith 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 Ramahietal study which showed that single progesterone measurement was not useful inpredicting pregnancy outcome [30]. Also regarding diagnosis of ectopic pregnancy in related to serum progesterone measurement, the difference was statistically insignificant p-value >0.005 at level of confidence interval 95%. Stoveletal showed that single serum progesterone measurement is helpful indiagnosis of ectopic pregnancy and this is disagreement with our study [31].

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