



Serum level of Progesterone and beta-human chorionic gonadotropin in early detection of ectopic pregnancy

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Abstract:

Background: The value of serial measurement of serum β subunit of human chorionic gonadotropin (β -HCG) and ultrasonography in the early diagnosis of ectopic pregnancy has well established. **Objective:** The objective of this study was to explore the diagnostic value of raising level of single measurement of progesterone (P) and serum β -HCG in early diagnosis of ectopic pregnancy. **Materials and Methods:** Serum levels of progesterone and β -HCG were measured by Radio Immuno Sorbent Assay (RIA) technique in 100 symptomatic women with ectopic pregnancy and 100 women with normal intrauterine pregnancy in the wards of Rajkiya mahila Chikitsalya, J.L.N. Medical College and Associated Group of Hospitals, Ajmer, after taking approval from ethical committee.. These values were compared by T-test. By determining cut-off levels of these parameters the sensitivity and specificity of them in prediction of ectopic pregnancy was estimated. **Results:** The mean serum levels of progesterone and β -HCG in patients with ectopic pregnancy (5.86 ± 1.18 ng/ml and 511.7 ± 245.5 mIU/ml) were significantly lower than in women with normal intrauterine pregnancy (23.5 ± 7.38 ng/ml, 1903.0 ± 425.5 mIU/ml, respectively) ($p < 0.001$). **Conclusions:** In this study single measurement of serum progesterone level has the greatest sensitivity (99%) and specificity (100%) in the diagnosis of ectopic pregnancy.

Key words: Progesterone, Beta subunit of Human Chorionic Gonadotropin (β -HCG), Ectopic pregnancy, Normal intrauterine pregnancy.

Introduction:

Ectopic pregnancy (EP) has become life and fertility threatening condition which accounts for 9% of all pregnancy related deaths, now can be detected early for the successful and conservative management of women with ectopic pregnancy. Approximately 98% of ectopic pregnancies (EP) occur in the Fallopian tube [20]. The most significant complication of EP is rupture of the Fallopian tube causing massive internal bleeding, infection, and possibly death [3]. EPs are asymptomatic prior to rupture of the Fallopian tube [3,8] and at present the only way to conclusively diagnose EP is transvaginal ultrasound monitoring, preferably with β -human chorionic gonadotropin (β -HCG) and progesterone (P) confirmation [8]. Although symptom-based diagnosis of tubal EP has improved [11,20], the diagnosis of EP is not always simple or straightforward. It has been reported that more than one-third of the women who have died from EP in the UK since 1997 had been mis-

diagnosed [11]. Although several risk factors for tubal EP have been identified [15-18], the underlying mechanisms leading to tubal EP are not fully understood [19,20]. There is currently no accurate method to identify what treatments for tubal dysfunction should be undertaken to prevent EP [19,20]. Because an early and accurate laboratory diagnosis of tubal EP could assist clinical management, various laboratories have directed their research toward biochemical markers of tubal EP [5,9,13,14]. Several peripheral proteins that might be useful for detecting the presence of EP have been evaluated [2,6], but none have been proven entirely useful in the clinic. Progesterone is a C-21 steroid hormone involved in the female menstrual cycle, pregnancy (supports gestation) and embryogenesis of humans and other species. It is sometimes called the hormone of pregnancy (Bowen R 2000) and it has many roles relating to the development of the fetus. Human chorionic gonadotropin (HCG) composed of two dissimilar subunits alpha (α) and beta (β), linked

together with hydrogen and disulphide bonds. It is a peptide hormone produced in pregnancy that is made by the embryo soon after conception and later by the syncytiotrophoblast (part of the placenta). Its role is to prevent the disintegration of the corpus luteum of the ovary and thereby maintain progesterone production that is critical for a pregnancy in humans. Early pregnancy testing , in general, is based on the detection or measurement of HCG.

Materials and Methods:

The subjects included in the study were 100 of ectopic pregnancy and 100 of intrauterine pregnancy (IUP) of different age groups (20-40 years) attending the out patient clinics or admitted in the wards of Rajkiya mahila Chikitsalya, J.L.N. Medical College and Associated Group of Hospitals, Ajmer, after taking approval from ethical committee. Serum levels of progesterone and β -HCG were measured by Radio Immuno Sorbent Assay (RIA) technique in 100 symptomatic women with ectopic pregnancy and 100 women with normal intrauterine pregnancy. SPSS.13/win statistical software was used for analyzing the data. Data were presented as mean \pm standard deviation. A parametric independent sample t-test was used to compare differences between two groups. Level of statistical significance was set at $p < 0.05$. By determining cut-off levels of these parameters the specificity and sensitivity of each in prediction of ectopic pregnancy were estimated.

Results:

Demographic data of IUP and EP is shown in tables.

Table 1: Mean serum progesterone and β -human chorionic gonadotropin values in normal IUP and EP.

S. No.	Parameters	IUP	EP	t-value	p-value	Statistical Significance
1	Serum progesterone (ng/ml)	23.5 \pm 7.38	5.86 \pm 1.18	23.6	<0.001	Highly Significant
2	Serum β -HCG (mIU/ml)	1903.0 \pm 425.5	511.7 \pm 245.5	28.3	<0.001	Highly Significant

Table 2: Sensitivity , Specificity and Cut off values of parameters.

S. No.	Parameters	Sensitivity	Specificity	Cut off value
1	Serum progesterone	99%	100%	< 15ng/ml
2	Serum β -HCG	91%	85%	<1500mIU/ml

Table 3: Correlation of parameters in IUP and EP.

	Normal Intrauterine pregnancy	Ectopic pregnancy	Serum β -HCG
Serum progesterone	r = 0.281 p < 0.001 (HS)	r = 0.007 p > 0.10 (NS)	r

The mean serum levels of progesterone and β -HCG in patients with ectopic pregnancy (5.86 \pm 1.18 ng/ml and 511.7 \pm 245.5mIU/ml) were significantly lower than in women with normal intrauterine pregnancy (23.5 \pm 7.38 ng/ml, 1903.0 \pm 425.5 mIU/ml, respectively) ($p < 0.001$) (Table 1). In this study, by determining the cut-off level of 15 ng/ml for progesterone, the sensitivity of single measurement of serum progesterone level was 99% and specificity was 100%. Serial measurement of β -HCG with 91% sensitivity and 85% specificity at the cut off level of <1500mIU/ml is the great assistance in early diagnosis of ectopic pregnancy (Table 2). In normal IUP and EP subject groups when progesterone was correlated with β -HCG, the Pearson's correlation (r) derived was that, Correlation between Progesterone level and β -HCG concentrations in normal IUP and EP groups, a highly significant and insignificant positive correlation was obtained [$r = 0.281, p < 0.001$ (HS); $r = 0.007 p > 0.10$ (NS)] (Table 3).

Discussion:

The word 'ectopic' means displaced, and an ectopic pregnancy is when a fertilised egg implants itself outside of the womb (uterus), usually in one of the fallopian tubes. It is an extrauterine pregnancy. Almost all ectopic pregnancies occur in the fallopian tube , but other possible sites include: cervical, interstitial (also referred to as cornual; a pregnancy located in the proximal segment of the fallopian tube that is embedded within the muscular wall of the uterus),

hysterotomy scar, intramural, ovarian, or abdominal. In addition, in rare cases, a multiple gestation may be heterotopic (include both a uterine and extrauterine pregnancy). In normal IUP the corpus luteum (CL) is the primary organ producing progesterone upto 7th and 8th week of pregnancy after which the placenta is capable of producing enough progesterone (Csapo and Pulkkinen 1978). This period during which the placenta is assuming the main responsibility of progesterone production from the CL is called luteoplacental shift. During pregnancy following the development of trophoblast, progesterone is synthesized and secreted in increasing amount from placenta. It stimulates the thickening of the uterine lining in anticipation of implantation of a fertilized ovum. its level relatively low during the preovulatory phase of the menstrual cycle, but rises after ovulation and remain elevated during luteal phase. With ectopic implantation the progesterone synthesis by the CL is diminished as the trophoblast is implanted in the fallopian tube i.e. outside the uterine endometrial cavity so the amount of progesterone synthesized is very low. β -HCG is a glycoprotein synthesized by the embryo soon after conception and later by the syncytiotrophoblast, and it maintains the CL during the beining of pregnancy, causing it to secrete the progesterone. β -HCG production from placenta nourishes the egg after it has been fertilized and becomes attached to the uterine wall. Levels can first be detected by blood test about 11 days after conception and by a urine test about 12-14 days after conception. In general the HCG levels will double every 72 hours. The levels will reach its peak in first 8-11 weeks of pregnancy and them will decline and level off for the remainder of the pregnancy. But in EP as the trophoblast is implanted abnormally in fallopian tube the entirely intact HCG is present in serum. In urine samples there is much lesser propotion of HCG degradation products, β -core fragment and free β -subunit. The level can be low due to it implantation site, distruption of trophoblast by hemorrhage, or due to embryonic death. So, very low leves of β -HCG can be used as diagnostic tool for identifying EP. The results of the present study were found similar to Gharabaghi P (2007), Cartwright (2009), Barnhart K (2011), Jurkovic D (2011), Rausch M E (2012) and Barash J H (2014).

Conclusions:

In this study single measurement of serum progesterone level has the greatest sensitivity (99%) and specificity (100%) in the diagnosis of ectopic pregnancy.

Acknowledgment:

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors/editors/publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

Source of funding:

The authors stated that all of this work was funded by self-financing.

Conflicts of interest:

The authors declare that there is no conflict of interests.

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