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HCG and CA-125 Levels In Pregnancy And Abortion Patients.

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Abstract

Spontaneous abortion is one of most common complication of pregnancy. The diagnosis of Pregnancy and spontaneous abortion currently depends on a combination of ultrasonography and other hormonal methods (serum human chorionic gonadotropin (HCG) and another parameter used as a predictive marker for a spontaneous abortion or subsequent outcome of pregnancy is Cancer Antigen-125 (CA-125). The study was included of 30 pregnant women in first trimester ended with abortion confirmed by ultrasound and some of them dilatation and curettage done for them. The women were recruited from SLIMS hospital, Pondicherry. Gestational ages were calculated according to the last menstrual period confirmed by ultrasound. The control group comprised 30 pregnant women who had normal pregnancy in first trimester and who had continued their pregnancy confirmed by antenatal care and follow–up in SLIMS. High levels of βhCG indicate poor prognosis and frequent assays during therapy level correlated to the clinical response. During pregnancy, disruption of the epithelial basement membrane of the fetus membrane or disruption of the decidua could theoretically leads to a rise in the maternal serum CA-125 level; this increase may be a predictor of subsequent spontaneous abortion of the fetus. The value of CA125 in recurrent abortions is still unclear and cannot be recommended on routine basis.

Keywords: human chorionic gonadotropin, Cancer Antigen-125,Pregnancy,Abortion, First trimester

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INTRODUCTION

The rate of fetal loss in clinically evident gestations has been reported to be approximately 10-15%. The rate will be obviously higher if we consider the preclinical losses diagnosed by β- HCG levels starting 3 weeks following the last menstrual period [1]. Accordingly, the expected probability for a woman to have three consecutive abortions should be in the range of 0.3% to 0.4%. The actual frequency of habitual abortion, however, is significantly higher, being in the range of 0.4% to 0.8%. This difference suggests that not only random causes but also some specific factors must be involved in this type of reproductive failure [2]. Beta-HCG and Progesterone titers are widely used to assess the risk of miscarriage at the early stages of pregnancy [3-5]. Serum levels of CA125 turned out to be a valuable parameter not only as a marker of ovarian carcinoma but also in other fields of Obstetrics and Gynecology [6].

Indeed, abnormal levels of hCG have previously been associated with adverse pregnancy outcomes such as fetal loss, preeclampsia, preterm delivery and fetal growth restriction [5–10]. In order to study such clinical associations, it is essential to establish correct gestational age-dependent reference ranges (RRs) which can be difficult because hCG itself has been proposed as a marker of gestational age [11]. hCG has been shown to be and to determine confounding and mediating factors such as differences between different measurement methodologies, pregnancy dating methodologies and differences in population characteristics based on this the study is to evaluate the relation between serum HCG, and CA125 as biochemical markers at different gestational ages in the first trimester for predicting pregnancy loss.

During pregnancy, CA-125 was presented in tissues derived from embryonic coelomic epithelium [8] and through out gestation, significant quantities seen in the deciduas and chorion which is the main source of it [9]. CA-125 had been found in high concentration in human amniotic fluid and the amnion was a major source of it [10]. During pregnancy, disruption of the epithelial basement membrane of the fetus membrane or disruption of the decidua could theoretically leads to a rise in the maternal serum CA-125 level; this increase may be a predictor of subsequent spontaneous abortion of the fetus [11]. A study was initiated to investigate a rise in the serum CA-125 level might predict spontaneous abortion or ongoing pregnancy in pregnant women in first trimester and compare it with normal pregnant women.

MATERIAL AND METHODS

The study was included of 30 pregnant women in first trimester ended with abortion confirmed by ultrasound and some of them dilatation and curettage done for them. The women were recruited from SLIMS hospital, Pondicherry. Gestational ages were calculated according to the last menstrual period confirmed by ultrasound. The control group comprised 30 pregnant women who had normal pregnancy in first trimester and who had continued their pregnancy confirmed by antenatal care and follow–up in SLIMS. Maternal blood samples were taken in the first trimester and the serum was separated and measurement of hCG and CA-125 were done in the Central laboratory by using Enzyme Linked Immuno Sorbent Assay (ELISA).

Statistical Analysis

Data was expressed as mean ± SEM. Statistical analysis was done using SPSS 11.5 version.

RESULTS

Table 1. hCG and CA-125 levels in the serum of pregnant women and abortion women expressed as mean ± standard error mean (M±SEM).

Test	Group-I Normal pregnancy (n=30)	Group-II End with abortion(n=30)	P value
HCG(mIU/ml)	12.8±34.9	39.2±48.8	P< 0.001
CA 125(IU/ml	28.01±4.3	39.6±15.3	Non significant

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DISCUSSION

The ultrasound, serum β-HCG and progesterone titers are widely used to assess the risk of miscarriage at the early stages of pregnancy [12]. They are not considered as satisfactorily sensitive tests during the first three months of pregnancy, therefore their value is limited. Evaluation of serum levels of CA-125 antigens has been considered as a useful marker in diagnosis and monitoring of some ovarian carcinoma [13] but there are previous studies suggesting its predictive value when estimating the risk of miscarriage at early stages of pregnancy [14]. Women with threaten abortion revealed higher values of serum CA-125 antigen than those in the control group and those patients who had presented the highest values of the antigen later miscarried [15]. This high level is likely due to tropho-decidual origin of this marker and invasion of deciduas by chorionic villi. This decidual disruption is associated with vaginal bleeding [16-17].

In the present study, the serum CA125 in the control group showed no significant differences between different gestational age groups . On the other hand, in the present study, serum B-hCG showed highly statistically significant differences ($P < 0.01$) between the control(pregnant) mean value and that of the second (abort)group. Our results suggest that the association between gestational age, hCG and fetal growth can cause less reliable ultrasound derived pregnancy dating, in particular in women with high or low levels of hCG.

Our results showed no significant difference between groups I who end with abortion and group II that had ongoing pregnancy in spite of its higher values 39.6±15.3. Our results were in agreement with Vavilis et al 2001[19] who found that there was no statistically significant difference in CA-125 levels of patients who aborted compared with those women that continued pregnancies. Poliklinik et al 2000[20] was in agreement with our results who reported that CA-125 could not serve as an accurate predictor of pregnancy outcome due to the wide overlap of the ranges.

Serum B-hCG showed a sensitivity of 100%, a specificity of 50%, a PPV of 50% and a NPV of 100% with relatively equal values in different age groups. This matches well with other investigators who found that the best predictor of ongoing pregnancy was βHCG concentration [5]. However, there are also contradictory reports which showed that it may be useful. Some reports demonstrated the prognostic significance of the maternal serum CA-125 measurement in the threatened abortion because it determined the extent of decidual destruction which is directly related to the outcome of pregnancy and its usefulness in predicting early abortion [20, 21]. In general, however, if the hCG levels are dropping in the first trimester, this probably a sign of impending miscarriage. On the other hand, slow-rising hCG levels that do not double every two or three days in early pregnancy can be a sign of problems but can also result in a normal pregnancy.

One report showed the distribution of CA-125 during pregnancy was highest in first trimester than second and third trimester [5, 9, and 11]. This may be due to the secretion of CA-125 and placenta protein 14 (PP14) by the glandular epithelium of the endometrium [5,23]. Serum concentration of these parameters may increase during the first trimester of pregnancy as the concentration of progesterone rise to a maximum in the first trimester [24].This observation suggest that CA-125 is synthesized by normal endometrium in non pregnant female and by deciduas in pregnant women [25].

An aborting pregnancy, if the abortion has occurred, should have a beta-human chorionic gonadotropin decrease of at least 48% within approximately 24 hours. This decline, however, does not guarantee that the abortion is complete. A patient with a serum beta-human chorionic gonadotropin level that has not declined by a minimum of approximately 50% over 24 hours is unlikely to have a complete abortion.

An observation that suggest CA-125 correlates less well with endometrial development in women suffering from recurrent miscarriage [26]. One report demonstrated that concentration of CA-125 in the pregnant women who subsequently aborted were higher than those who did not, thus suggesting that serum CA-125 are not so important in maintaining successful pregnancy [27]. CA-125 may be useful in the assessment of endometrial development in recurrent miscarriage patients and this suggested the importance in preparing the endometrium for embryo implantation [28]. High level of serum CA-125 with high lactate dehydrogenase indicates more extensive trophoblastic tissue damage [29].

In a normal intrauterine pregnancy, the hCG concentration rises in a curvilinear fashion until 41 days of gestation and the mean doubling time for the hormone is 1.4-2.1 days. An hCG concentration that rises, but by less than 50%, suggests a failing or ectopic pregnancy, as does a plateau in hCG level. According to the results of this study, significant differences between serum ß-HCG levels in case and control group were noticed ($p<0.00$). The specificity and sensitivity of single hCG measurement in the detection of ectopic pregnancy at the cut-off level of 104 mIU/ml were 100% and 85% respectively. Although approximately 85% of women with ectopic pregnancy have serum hCG levels lower than those seen in normal pregnancy at a similar age; however, a single quantitative hCG assay cannot be used for the diagnosis of ectopic pregnancy because the actual dates of ovulation and conception are not known for most women. The corpus luteum of women also secretes estradiol (E2) in response to hCG and again could function as a luteal marker of pregnancy dynamics.

In the present study, it is necessary to mention that sample size is a limiting factor (20 participants in each group). But it should always be kept in mind that it is not possible to identify the cause of the recurrent early pregnancy loss in approximately half of the cases and this could be the limiting factor for any biochemical marker [10]. Some found that single serum CA-125 level determinations is valuable in women with imminent abortion presenting with abdominal pain, vaginal bleeding or both [30,31]. Our results are in disagreement. In our opinion this may possibly be attributed to the method of CA-125 measurement. In above reports used radioimmunoassay while we used enzyme immune sorbent assay method.

In conclusion, the value of CA125 in recurrent abortions is still unclear and cannot be recommended on routine basis. On the other hand β-HCG is highly sensitive as a single serum measurement for the prediction of pregnancy outcome.

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