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Cervicovaginal β-HCG Test in Prediction of Spontaneous Preterm Delivery among Normal Pregnant Women

S. Abasalizadeh, F. Abasalizadeh and F. Sahaf
Department of Obstetrics and Gynecology, Alzahra University Hospital,
Tabriz University of Medical Sciences, Tabriz, Iran

Abstract: The chance of predicting a preterm delivery may be the keystone to preventing or at least best management of it. The aim of our study, was to test the possibility of using vaginal β-HCG level measurement to predict the spontaneous preterm delivery. In this prospective study, 150 pregnant women referred for prenatal care to Asadabadi university hospital clinic were studied. At a gestational age of 20-28 weeks, a cotton tip swab was placed into the endocervix and posterior vaginal fornix and sent to laboratory for β-HCG measurement. Data were entered into the computer and analyzed using SPSS 11 and medcalc 8 Statistical software packages. Mean age of participants was 26 years (±25.9). Mean gestational age at time of sampling was 25 weeks. The relative risk of developing a preterm delivery for those having a vaginal β-HCG above 30 mIU mL^{-1} was calculated to be 2.61 (95% CI: 1.25-5.5). The relative risk of developing a preterm delivery for vaginal β-HCG level above 45 mIU mL^{-1} was 4.5 (95% CI: 1.98-10.1). The test for a cutoff value of 45 was quite specific and half sensitive with a negative predictive value of 95.4%. A cervicovaginal β-HCG test with a cutt off value of 45 mIU mL^{-1} can predict the preterm delivery, but a combination screening of cervicovaginal β-HCG test along with clinical risk factor scoring for preterm delivery is suggested to be used in clinical practice.

Key words: Preterm delivery, β-HCG test, sensitivity, specificity

INTRODUCTION

Preterm delivery is encountered before 37th weeks of gestational age in 7-11% of pregnancies and before 34th weeks in 3-4% of pregnancies (Maternal and Child Health Consortium, 1999; Peters *et al*., 1998). Some studies have been done to improve these rates (Crowley, 2000; Makkiabadi, 1993). Nevertheless, the chance of predicting a preterm delivery may be the keystone to preventing or at least best management of it. Several laboratory methods such as fetal fibronectin and cervical alphafetoprotein have been developed for prediction of preterm delivery (Kleytzky *et al*., 1985; Anai *et al*., 1997; Bernstein *et al*., 1998). These methods have their own advantages and limitation but the research is going to be continued on other types of biomedical assays for predicting preterm delivery.

Similar to fibronectin, β-HCG can also be found in vaginal secretions (Kleytzky *et al*., 1985). Some researchers have studied the possibility of using vaginal β-HCG measurement in predicting premature rupture of membranes or preterm delivery in specific groups of pregnant women (Bernstein *et al*., 1998; Young-Han *et al*., 2005; Guvenal *et al*., 2001; Garshasbi *et al*., 2004) but little is known about β-HCG level among general pregnant population which most of whom lack the preterm delivery risk factors.

The aim of our study, was to test the possibility of using vaginal β-HCG level measurement to predict the spontaneous preterm delivery among the pregnant women with or without preterm delivery risk factors.

MATERIALS AND METHODS

Study was conducted in a north western large province of Iran 2005-2006. In this prospective study, 150 pregnant women referred for prenatal care to Asadabadi university hospital clinic were studied. The inclusion criteria were as: Written consent; a gestational age of 20-28 weeks at the time of enrollment; possible estimation of gestational age based on one of the following options 1-A sonography prior to 14th week of gestation 2-Two compatible sonographies between weeks 14-28 3-A sonography prior to 28th week of gestation along with a compatible LMP date. Exclusion criteria were: Fetal anomalies; placenta previa; vaginal bleeding; preeclampsia; fetal distress; premature rupture of membranes; gestational age ambiguity and medical or requested abortion.

Both those women at high risk of preterm delivery and those without risk factors of preterm delivery were included in this study. Similar to methods used before, a cotton tip swab was placed into the endocervix for 30 sec and then to the posterior vaginal fornix for the same

Corresponding Author: Shamsi Abasalizadeh, Alzahra University Hospital, Artesh Jenoubi Ave., Tabriz, Iran

length of time during a single speculum vaginal examination. The swab was then transported to the laboratory inside a clean sterile tube. The samples were examined by a clinical pathologist not later than 48 h. They were kept in refrigerator up to the time of laboratory assay. This method was successfully applied before (Garshasbi *et al*., 2004). Lab Method kit used was Diaplus stat hcg enzyme immunoassay-USA.

Laboratory findings were added to the demographic and medical history and examination data questionnaire. Data were entered into the computer and analyzed using SPSS 11 and medcalc 8 Statistical software packages. Chi-square test was used to compare the proportions and t-test was used to compare means. A multiple logistic regression test was used to check if a positive β-HCG test for selected cutoff values of vaginal β-HCG level was an independent predictor of preterm delivery or not. Roc curves were graphed using medcalc 8 Software.

RESULTS

Mean age of participants was 26 years (±25.9). Mean gestational age at time of sampling was 25 weeks. A history of preterm delivery was observed among 7.4% of participants. Mean diastolic pressure at the time of sampling was 57.2 and mean systolic pressure was 111.5 mmHg.

Sixteen of women were considered as high risk of preterm delivery. Among these 3 had experienced preterm delivery, 7 a history of it among their sisters or mothers, 2 had uterine anomalies, 4 had previous second trimester abortions and one had pre diagnosed uterine leiomyoma. All of these except for one patient had only a single risk factor.

During this study, preterm delivery was noticed in 11 patients (7.4%). Although the β-HCG level was higher among this group compared to term deliveries, but overall mean comparison was not statistically significant. Having a β-HCG above 30 was shown to be associated with higher risk of preterm delivery ($p<0.05$). The relative risk of developing a preterm delivery for those having a vaginal β-HCG above 30 mIU mL^{-1} Was calculated to be 2.61 (95% CI: 1.25-5.5). The relative risk of developing a preterm delivery for vaginal β-HCG level above 45 mIU mL^{-1} was 4.5 (95% CI: 1.98-10.1). Sensitivity, specificity and predictive values of β-HCG test to predict preterm delivery with two cutoff points of 30 and 45 mIU mL^{-1}, are given in Table 1 and ROC curve is given in Fig. 1.

Multiple logistic regression model was used to check the independency of test at the given cutoff values for prediction of preterm delivery. It showed an independent prediction of outcome both for vaginal β-HCG level cut off value on 45 and 30 mIU mL^{-1}.

Table 1: Sensitivity, specificity and predictive values of vaginal β-HCG test to predict preterm delivery

Cutoff value	Sensitivity	Specificity	Negative PV
30	45.5	83	95
43	45.5	91.2	95.4

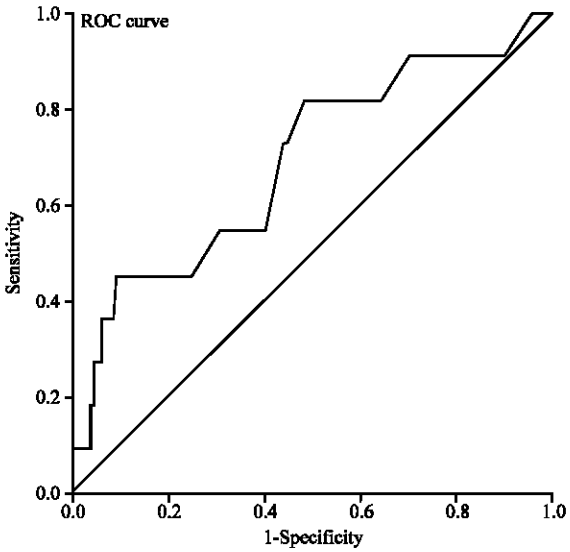

Fig. 1: ROC curve for sensitivity and specificity of vaginal β-HCG in diagnosis of preterm delivery

DISCUSSION

β-HCG is present in amniotic fluid, maternal blood and urine with the range of 2,000-70 000 mIU mL^{-1}. Also, it is secreted by cervical glands. Therefore, it should be present at a certain level in the vaginal fluid. Our study reported lower vaginal β-HCG level in patients who were delivered at term when compared to preterm delivery. We found that cervicovaginal β-HCG above cutoff value of 45 mIU mL^{-1} can predict the preterm delivery in a normal pregnancy.

Several studies have checked the role of cervicovaginal β-HCG in predicting preterm labour of premature rupture of membranes. Two studies were found to study the role of vaginal β-HCG in predicting premature rupture of membranes. In one of them samples were analyzed from 188 normal pregnant women. The median and 95% Confidence Intervals (CIs) of vaginal fluid hCG levels of normal pregnant women were 37.9 (1.9, 725.6), 9.5 (0.8, 95.8) and 6.3 (0.6, 62.2) mIU mL^{-1} during the first, second and third trimesters, respectively. That of women with PROM was 420.6 (216.3, 918.3) mIU mL^{-1}. For the second trimester, sensitivity was 100%, specificity 91.8% and for the third trimester, sensitivity was 100%, specificity 96.5%, using a threshold value of 50 mIU mL^{-1} (Anai *et al*., 1997). The second study although focused on premature rupture of membranes but had also checked

premature delivery. In this study, vaginal β-HCG level in patients who underwent premature delivery was significantly higher than in patients who were delivered at term (Kim *et al*., 2005).

In a study, conducted by Bernstein *et al.* (1998) on 77 pregnant women who were high risk for preterm labor, a single beta-human chorionic gonadotropin value >50 mIU mL^{-1} obtained between 24 and 28 weeks' gestation was associated with a significant increase in the incidence of delivery before 34 weeks' gestation. This cutoff value had sensitivity, specificity and positive and negative predictive values for predicting delivery before 34 weeks' gestation of 50, 87, 33 and 93%, respectively (Bernstein *et al*., 1998).

In another study, by Guvenal *et al.* (2001) conducted on 60 patients, Cervicovaginal β-HCG and prolactin levels were significantly higher in the preterm group when compared with those of the term delivery group. The optimal cut-off value for β-HCG (27.1 mIU mL^{-1}) gave a sensitivity level of 87.5% (47.4-97.9; 95% C.I.) at a specificity of 65.4% (50.9-78.0; 95% C.I.) with positive and negative predictive values of 28 and 97%, respectively. These researchers have concluded that Cervicovaginal β-HCG measurement in patients with preterm labor may be used as a predictive test. Cervicovaginal prolactin is not a sensitive test compared with the β-HCG test (Guvenal *et al*., 2001).

Most of the above mentioned studies suffer small sample size and very wide confidence intervals, while a later study conducted on 540 Iranian pregnant women showed that there was 3.2-fold increase in cervicovaginal β-HCG concentrations among patients with SPB vs. term delivery. A single cervicovaginal β-HCG)77.8 mIUyml, between 20 and 28 weeks' gestation, identified patients with subsequent SPB vs. term delivery with sensitivity of 87.5% (95% CI: 47.4-97.9) and a specificity of 97% (95% CI: 86.5-99.4) with positive and negative predictive values of 88.5 and 98%, respectively. This study has concluded that cervicovaginal β-HCG is a sensitive and specific predictor of patients with subsequent preterm delivery. Although this study has a nice statistical design and analysis providing adequate internal validity but as it is conducted only on patients who had at least one risk factor, it doesn't provide information on general pregnant population. Our study had a larger number of pregnant women without preterm labour risk factors when compared to the previous studies. It showed that although the cervicovaginal β-HCG test has a very high specificity it lacks a nice sensitivity. It has been shown that screening can be performed by the identification and scoring of clinical risk factors for preterm birth Nevertheless, the risk factor scoring method has been proven to have not only a poor detection rate, but also a poor predictive value (Creasy *et al*., 1980; McLean *et al*., 1993). So our recommendation is a combination screening of cervicovaginal β-HCG test along with clinical risk factor scoring for preterm delivery to be used in clinical practice. Further studies, can get focused on statistical modeling of laboratory and clinical risks of preterm delivery.

CONCLUSION

A cervicovaginal β-HCG test with a cutt off value of 45 mIU mL^{-1} can predict the preterm delivery, but a combination screening of cervicovaginal β-HCG test along with clinical risk factor scoring for preterm delivery is suggested to be used in clinical practice.

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