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Araştırma / *Research Article*

Birth Before 37th Gestational Week and Cervicovaginal Prolactin

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Otuz Yedinci Gebelik Haftasından Önce Doğum ve Servikovajinal Prolaktin

ABSTRACT

Introduction: *Aim of the study was to determine whether the presence of prolactin in cervicovaginal washings is associated with preterm birth.*
Methods: *We measured the cervicovaginal prolactin levels in 80 consecutive pregnant women aged 24-34 weeks and compared the levels of prolactin of women who had given preterm delivery (<37 weeks) to those with term delivery.*
Results: *Seventy-three pregnant women were analyzed. Of them, 19 delivered preterm (26%) and 54 delivered at term (74%). Cervicovaginal prolactin levels were significantly higher in the preterm group when compared with those of the term delivery group (0.12 ng/mL vs 0.07 ng/mL; p<0.001). The optimal cut-off value of prolactin was 0.088 ng/mL. Sensitivity and specificity were 73.7% and 81.4%, respectively for this cut-off value.*
Conclusion: *According to the study, high prolactin levels in vaginal secretion of pregnant women may be a sign for preterm delivery. However, this is not a sensitive test that can routinely be used for the prediction of preterm delivery.*

Keywords: *preterm delivery, pregnancy, prolactin, vaginal secretion*

ÖZ

Amaç: *Çalışmanın amacı, servikovajinal yıkama sıvılarında prolaktinin varlığının erken doğumu ile ilişkili olup olmadığını belirlemekti.*
Yöntemler: *Yirmi dört-otuz dört haftalık 80 ardışık gebe kadının servikovaginal prolaktin düzeylerini ölçtük ve preterm doğum yapan (<37 hafta) gebelerin prolaktin seviyelerini term doğum yapanlarla karşılaştırdık.*
Bulgular: *Yetmiş üç gebe kadın analiz edildi. Bunlardan 19'u preterm (%26) ve 54'ü (%74) term idi. Servikovajinal prolaktin düzeyi, preterm grupta, term doğum grubu ile karşılaştırıldığında anlamlı olarak daha yüksekti (0.12 ng/mL'ye karşı 0.07 ng/mL; p<0.001). Prolaktinin optimal kesme değeri 0.088 ng/mL idi. Duyarlılık ve özgüllük bu değer için %73.7 ve %81.4 idi.*
Sonuç: *Çalışmaya göre, gebe kadınların vajinal sekresyonunda yüksek prolaktin düzeyleri preterm doğum için bir işaret olabilir. Ancak, bu, preterm doğumun tahmini için rutin olarak kullanılabilecek hassas bir test değildir.*

Anahtar kelimeler: *erken doğum, gebelik, prolaktin, vajinal sekresyon*

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INTRODUCTION

PPreterm delivery is defined as delivery before the completion of the 37th gestational week and it is one of the main causes of perinatal morbidity and mortality [1]. Nearly 70% of the neonatal deaths are due to preterm delivery [2]. Preterm birth rate differs according to geographical regions, and its incidence has been reported up to 15% [3-5]. Some publications report an increase in the incidence of preterm labor in recent years [6]. The risk of mortality and serious acute morbidities such as respiratory distress syndrome, necrotizing enterocolitis, and intraventricular hemorrhage are related with preterm birth. Many biochemical markers are being investigated for predicting premature birth. Fetal fibronectin,

α-fetoprotein, C-reactive protein (CRP), multiple members of the interleukin family (interleukin-6, interleukin 8, and interleukin 10), matrix metalloproteinases, pregnancy-associated plasma protein A, relaxin, lactate dehydrogenase, thyroid-stimulating hormone, adrenocorticotropic hormone, vascular endothelial growth factor (VEGF), ferritin, prolactin, ceruloplasmin, alkaline phosphatase (ALP), glucose, placental protein 13, corticotropin releasing hormone, tumor necrosis factor-α (TNF-α), tumor necrosis factor-β (TNF-β), estriol and human chorionic gonadotropin (hCG) are some of these [7]. However, there is no strong consensus that these chemical molecules are predictors of preterm birth [8].

In this study, we investigated the relationship between prolactin levels in the cervicovaginal secretion and preterm labor.

MATERIAL and METHODS

This study was carried out with 24-34-week-old pregnant women who applied to Taksim Education and Research Hospital maternity polyclinic for routine antenatal follow-up between November 1, 2008 and March 31, 2009. Patients with vaginal bleeding, membranous rupture, pregnancies with >3 cm of cervical dilatation, mandatory birth due to fetal or maternal reasons were excluded. The history of pregnancies was taken, the last menstrual period (LMP) was recorded and the week of pregnancy was calculated. Gestational weeks were calculated according to the first trimester ultrasonographic examination of pregnant women who do not know their LMPs. The first trimester ultrasonogram was used to determine the gestational week if there was a significant difference (more than 7 days) between the SAT and the first trimester ultrasonography. The pregnants that did not undergo ultrasonographic examination during the first trimester and did not know their LMPs were not included to the study.

Collection of materials

Pregnant women were examined at the gynecological position. Speculum was used to evaluate the vagina and cervix. A 3 cc irrigation fluid (saline) previously received with a sterile syringe was squeezed to the cervix, and vaginal fornix. The irrigation fluid accumulating in the speculum was removed by aspiration with the syringe and the speculum was removed. The irrigation fluid, collected from posterior fornix, was centrifuged for 10 minutes at 2000 rpm. This fluid was maintained in deep freezing (-40 °C) for prolactin measurement.

Those who gave birth at ≥ 37. gestational weeks were considered term pregnants, and those who gave birth before the 37th gestational week were accepted as preterm pregnants. Of the 73 pregnant women, 19 delivered preterm and 54 of them at term. In the study, the results of these two groups were compared.

Cervicovaginal prolactin was assessed by electrochemiluminescence immunoassay (ECLIA) method (Roche Diagnostics GmbH, Moduler Analytics E170, Germany).

Statistical analysis

Mann-Whitney U test was used in the comparisons between independent groups. The Chi-Square test was used to compare expected and observed values. Statistical analyses were made using SPSS program.

The study was planned as a dissertation. Institutional ethics committee approval and informed consent form from each patient were received (number: 169/16.01.2009).

RESULTS

A total of 80 pregnant women were enrolled. After the study was completed, 5 pregnants were lost to follow-up, 2 pregnant women were excluded from the study due to centrifugation and breakage of glass during storage. As a result, statistical analyses were perfoırmed on 73 pregnant women. Of them, 19 delivered preterm (26%) and 54 delivered at term

Table 1. Data of groups preterm and term.

Characteristics	Preterm (n=19)	Term (n=54)	P value
Prolactin, (ng/mL) median (95%CI)	0.12 (0.08-0.39)	0.07 (0.06-0.08)	< 0.001
Gestational age during examination, median (95%CI)	32 (30-33)	32 (28-33)	0.477
Age of birth			
(days) mean±sd	242±11	275±7	< 0.001
(weeks) mean (min-max)	34.6 (33.0-36.1)	39.2 (38.3-40.3)	
Birth weight, (gr) mean±sd	2371±292	3302±430	< 0.001

Table 2. Predictive values of prolactin when the cut-off value of prolactin was 0.088 ng/mL.

	Preterm (n=19)	Term (n=54)	Total
Prolactin > 0.088 ng/mL	58.3% (14)	41.7% (10)	24
Prolactin < 0.088 ng/mL	10.2% (5)	89.8% (44)	49
Total	19	54	73

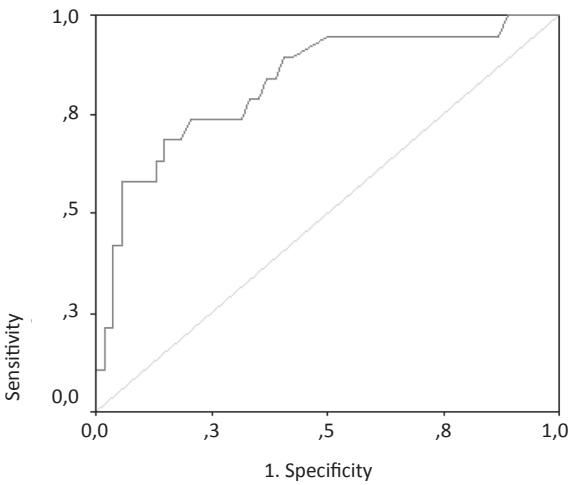

Figure 1. ROC curve of prolactin (The area under the ROC curve is 0.83).

(74%). There was no significant difference between the two groups in terms of median ages of pregnants during the examination (p=0.477). The mean gestational age at birth was determined as 242±11 days for preterm deliveries and 275±7 days for term deliveries. Birth weight was measured as 2371±292 gr at preterm delivery and 3302±430 gr at term delivery with a statistically significant difference (p<0.001) (Table 1).

The cut-off value of prolactin was determined using the ROC curve and the corresponding prolactin values. Cut-off value was determined to be 0.088 ng/mL. Sensitivity, specificity, PPV, NPV and accuracy rates were found as 73.7 %, 81.4%, 58.3%, 89.8% and 79.4%, respectively (Table 2, Figure 1).

DISCUSSION

Prematurity is a major cause of morbidity and mortality. Increases in preterm birth rates have been reported in recent years [9]. Many markers are being investigated for predicting premature birth [2,10].

In this study, we evaluated the importance of cervicovaginal prolactin levels for the prediction of preterm delivery. Prolactin has been shown to be produced by chorionic cytotrophoblast, decidua, amnion and placental syncytiotrophoblast throughout pregnancy. Several studies have shown that high prolactin values detected in cervicovaginal irrigat,on fluids are associated with preterm delivery, but the figures are different in various studies [11-14]. This may be due to the measurement of the cervicovaginal prolactin in different gestational weeks. According to present study, an increase in prolactin level in cervicovaginal fluid may be a predictor of preterm birth. When the cut-off value was taken as 0.088 ng/ml, the preterm delivery rates were 58.3% at higher values and 10.2% at lower values. These were prolactin values detected at the 32th (median) gestational week.

There are few studies in the literature evaluating preterm birth by measuring prolactin level in cervi-

covaginal fluid [7,11,13,14]. In first study on this topic, O'Brien et al. noted (on 80 women) that the cervico-vaginal prolactin level was higher in women with preterm birth and thus, can be used as a biomarker for preterm detection [14]. In a study by Guvenal and colleagues, prolactin test was reported as a low-sensitivity test for the prediction of preterm labor [11]. According to Jodderand et al, cervico-vaginal prolactin seems to be a nonconvincing marker for preterm delivery [15]. Shah et al in their review article noted that the association of prolactin with preterm delivery has not been fully understood yet [7]. However, the relationship between cervicovaginal prolactin level and preterm delivery does not seem to be a strong relation [2]. In our study, 10.2 % of patients had preterm delivery even though prolactin levels were low.

In conclusion, this study showed that the increase in prolactin levels in cervicovaginal secretion correlated with preterm delivery. However, this is not a sensitive test that can routinely be used for the prediction of preterm delivery. This can be used as an adjunct to the prediction of preterm birth.

Conflict of interest: None declared

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