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Relationship between the amniotic fluid prolactin level at early second trimester and pregnancy outcome

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ABSTRACT

Aim: The aim of this study was to determine whether early second trimester amniotic fluid prolactin level were associated with pregnancy outcome.

Material and Method: This study included 125 women who underwent amniocentesis for variable indications. Healthy subjects with no history of drug use were included in this study. The gestational age was determined by ultrasonic examination before 10 weeks in all cases. Amniotic fluid specimens were taken while performing amniocentesis for other indications. Amniotic fluid was collected by transabdominal amniocentesis. Amniotic fluid prolactin concentrations were utilized to predict pregnancy complication among women who underwent amniocentesis due to the variable indications.

Results: Among all study population, pregnancy was unremarkable in 102 (81.6%) cases, on the other hand, most common fetal abnormality was found to be the fetal hydrops fetalis and the second most commonly encountered fetal anomaly was trisomy, intrauterine growth restriction and intrauterine fetal demise. All study population was divided into two groups as complicated (n=23) and uncomplicated (n=102) pregnancies. Amniotic fluid prolactin concentration did not have any predictive value for complicated pregnancies (AUC=0.479).

Conclusion: Our data showed ; there is no relationship between early second trimester amniotic fluid prolactin level and pregnancy outcome.

Keywords: Decidual prolactin, pregnancy outcome, early second trimester

INTRODUCTION

The biological roles of the decidual protein hormones during pregnancy are unclear, countless studies suggest that the hormones may act locally to affect the function of the placenta, decidua, and fetal development. These decidual hormones are released into the circulation and function to regulate uterus, placenta and fetal membrane activity via autocrine/paracrine factors (1). Prolactin which is one of the decidual hormones ,increase during pregnancy and are involved with many aspects of maternal metabolic adaptation to pregnancy. The metabolic roles of prolactin propose an interesting scenario in which the central nervous system and indirectly whole body development (2).

In a previous study, which was conducted to figure out the possible effect of decidual prolactin on materno-fetal physiology,late second trimester amniotic fluid (AF) prolactin levels were shown to be associated with recurrent polyhydramnios (3).

Additionally, previous data indicated significant relationship between AF prolactin and preterm premature rupture of membrane at third trimester , study revealed that increased AF prolactin resulted in impairment of structural integrity of fetal membranes through electrolytes disturbances (4). Furthermore, fetal and maternal tissues were shown to express prolactin receptors in late pregnancy. Increased expression in the chorion, decidua, and placenta was reported during labor and delivery which supported an autocrine/paracrine role for decidual prolactin in the peripartum (5). There is no study in the literature so, we aimed to assess the relationship between early second trimester AF prolactin level and pregnancy outcome.

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MATERIAL AND METHOD

This prospective cohort study was performed at perinatology clinic of Zeynep Kamil Women and Children's Health Training and Research Hospital between January 2017 and April 2018. This study was approved by Zeynep Kamil Women and Children's Health Training and Research Hospital Clinical Researches Ethics Committee (Date: 18.11.2017, Decision No: 144) and informed consent was obtained from each participant. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Sample and study participants: The study group included 125 women who underwent amniocentesis for variable indications.

Healthy subjects with no history of drug use were included in this study. The gestational age was determined by ultrasonic examination before 10 weeks in all cases. AF specimens were taken while performing amniocentesis for other indications. AF was collected by transabdominal amniocentesis.

AF samples were centrifuged at 400 rpm for 10 minutes. The amniotic supernatant and the serum were separated and stored at 20"C until assayed. Total prolactin in AF samples was measured by the Tandem-E PRL immunoenzymetric assay.

Intrauterine growth retardation was diagnosed in cases with a fetal weight that is below the 10th percentile for gestational age as determined through an ultrasound (6).

Cases were accepted to have spina bifida defect if the spinal cord and its meninges are exposed through a gap in the backbone (7).

Hydrops fetalis was defined as abnormal accumulation of fluid in two or more fetal compartments, including ascites, pleural effusion, pericardial effusion, and skin edema (8).

Pregnancies with high blood pressure (140/90 mmHg) that develops during pregnancy or during the postpartum period that is associated with overt protein in the urine or the new development of decreased blood platelets, with the kidney or liver function tests, fluid in the lungs, or signs of neurological symptoms such as seizures and/or visual disturbances were diagnosed to be complicated with preeclampsia (9).

In all cases, amniocentesis was indicated based on the results of screening tests such as ultrasound or biochemical markers. AF prolactin concentrations were utilized to predict any pregnancy complication among women who underwent amniocentesis due to the variable indications.

Data Analysis: SPSS version 15 (Chicago, USA, 2006) was used for statistical analysis. Student-t test was used to compare continuous variables while categorical variables were compared by Chi-square test. $P<0.05$ was accepted to be statistically significant.

RESULTS

Summary characteristics of some demographic and clinical characteristics of whole study population were shown in **Table 1**. Indications for amniocentesis were shown in **Table 2**, which shows that the most frequent indication as high risk for trisomy detected by first or second trimester screening tests. Fetal sex distributions were shown in **Table 3**. Among all study population, pregnancy was uneventful in 102 (81.6%) cases, on the other hand, most common fetal abnormality was found to be the fetal hydrops fetalis and the second most commonly encountered fetal anomaly was trisomies, intrauterine growth restriction and intrauterine fetal demise (2.4%, **Table 4**). All study population was divided into two groups as complicated (n=23) and uncomplicated (n=102) pregnancies. AF prolactin concentration did not have any predictive value for complicated pregnancies (AUC=0.479, **Figure 1**).

Table 1. Summary characteristics of some demographic and clinical characteristics of whole study population

	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	19	45	33.4	5.9
Gestational age (weeks)	15	22	18.1	1.5
AF prolactin concentration (mcg/L)	28.9	31.412	5972.7	4774.4
Gestational age at delivery (weeks)	17	42	36.5	5.7

Table 2. Indications for amniocentesis

	Frequency	Percent
Cystic Hygroma	1	.8
Double Bouble	3	2.4
High risk for trisomy in first trimester screening test	59	47.2
High risk for trisomy in second trimester screening test	41	32.8
Advanced maternal age	6	4.8
High NT thickness	5	4.0
Maternal anxiety	6	4.8
High risk for trisomy in quadriple test	3	2.4
Fetal Hydocephaly	1	.8
Total	125	100.0

Table 3. Fetal sex distributions

	Frequency	Percent
Undetermined sex	15	12.0
Male	55	44.0
Female	55	44.0
Total	125	100.0

Table 4. Pregnancy outcome distributions		
	Frequency	Percent
Normal fetus	102	81.6
Undetermined	1	0.8
Di-George	1	0.8
Hidrops Fetalis	4	3.2
Hipoplastic left heart	1	0.8
Skelatal Dysplasia	2	1.6
IUGR	3	2.4
Intrauterine Fetal Demise	3	2.4
Preeclampsia	1	0.8
Spina Bifida	2	1.6
Termination for variable reasons	2	1.6
Trisomy 13-18	1	0.8
Trisomy 21	2	1.6
Total	125	100.0

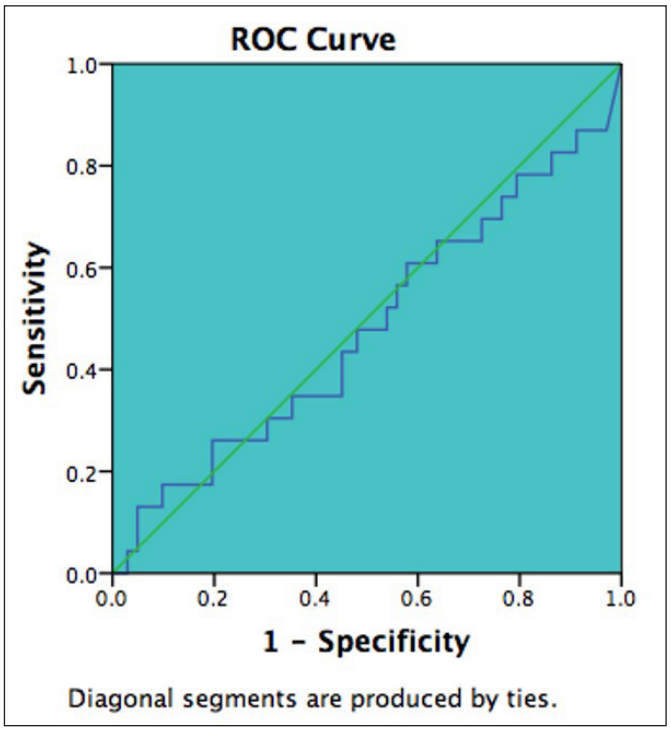

Figure 1. ROC cur of AFprolactin to predict poor pregnancy outcome

DISCUSSION

Measuring prolactin level at different trimester of pregnancies inside decidual cells and amniotic fluid indicated that changes in decidual cells are consistent with the changes of the concentration of amniotic fluid prolactin (10) Prolactin was found to be increased by the fetal pituitary gland and was immunologically determined by 10th week and biologically determined at the 18th week. Fetal plasma prolactin levels were low until 30 weeks of gestation, then a striking increase occured between 30 weeks and term (11)

Tyson et al. suggested that AF decidual prolactin may have an inhibitory influence on prostaglandin (PGE2) synthetic pathways (12). When the amniotic membrane disrupts, this inhibitory function of AF prolactin disappears, additionally increasing surface area of distrupted membrane result in higher production of prostaglandin (PGE2). All this data indicate the critical role of AF prolactin on active labor (13,14). This hypothesis led us to consider that, AF prolactin values in postterm pregnancies may be higher than in term pregnants. No significant differences were shown between the amniotic fluid, maternal serum and cord blood prolactin values in term and post-term pregnancies. Thus, the hypothesis has not been supported by the results of the study by Demir et al.(15).

Amniotic fluid, maternal serum and cord blood prolactin values of normal term pregnancy group in a study by Demir et al. were in agreement with those in the literature (13-16). On the other hand, other regulatory factors such as platelet activating factor and calcium in conjunction with estrogens, progesterone and cortisol were shown to have significant impact on the release of prolactin from the decidua (18). Amniotic transport occurs through intercellular channels between amniotic epithelial cells and can be modulated by AF prolactin levels (19). Based on these information some studies have been conducted to assess relationship between prolactin and some pregnancy complications, one of these studies assess prolactin concentrations in women with preeclampsia. Preeclampsia was shown to be characterized by increased excretion of urinary prolactin. Prolactin concentrations and isoforms were suggested to be appropriate markers for assessing the severity of preeclampsia and the occurrence of adverse outcomes. Therefore, it was suggested that prolactin and /or isoforms may play a role in the pathophysiology of preeclampsia (20). Furthermore, it was suggested that hormonal changes may play a role in AF volume arrangement. Prolactin receptors, on both fetal and maternal tissues increase while the pregnancy progresses. ıt is a deciduous prolactin and it was shown to affect amniotic permeability (2).

In a previous study, prolactin concentrations secreted by decidua were compared among groups of women with different pregnancy complications including induced abortions, and diabetes mellitus, preeclampsia, chronic hypertension, and polyhydramnios and normal term pregnancies. Study revealed lower prolactin levels in amniotic fluid, decidual prolactin content and production were in pregnancies complicated by either hypertension or polyhydramnios (21).

Some physiologic functions of prolactin have been defined, for example prolactin has been found to inhibit the secretion of different proinflammatory chemokines by human fetal membranes (22). Additionally, amniotic prolactin was shown to play a role in the pathogenesis of polyhydramnios due to osmoregulatory effect (23).

Maternal serum prolactin levels in normal pregnancies was not found to differ from serum levels in complicated pregnancies, on the other hand significantly lower levels of prolactin in AF of pregnancies complicated by hypertension or polyhydramnios were determined in a previous study, authors suggested that this difference was probably due to adverse effects of these conditions on the synthesis and release of prolactin by decidua (24). Previously published studies showed that amniotic prolactin concentrations in normal human pregnancy decrease from the second trimester of pregnancy and a plateau of low levels were observed in the late third trimester (25, 26). This data consistently support the possible effect of prolactin on labor.

First report of acute recurrent polyhydramnios with high levels of AF prolactin levels was published by De Santis et al. (2). In that study, AF prolactin levels was within normal limits in cases with acute recurrent polyhydramnios but close up to the upper limits of levels in normal pregnancies (24,25). De Santis et al. put forward hypothesis of acute recurrence of polyhydramnios may be linked to the dysfunctional chorionic receptors for prolactin. Previous study assessed AF prolactin levels three times during the pregnancy, study revealed no change with advancing gestational age (27). No change was determined in this study, however intervals that the samples were obtained too short to detect decreasing concentrations with advancing gestational age.

In normal pregnancies, a significant correlation between the production of AF and the amniotic prolactin level, which was shown to peak at 23-25 gestational weeks and reaches a plateau after 34 gestational weeks (26). Peak levels were obtained at 23-25 weeks of gestation in their study. Consistently, decreasing amniotic prolactin levels in the third trimester of normal pregnancies was shown to be parallel to the decreasing amniotic fluid production (28), study speculated that amniotic prolactin concentration measurements may be utilized to determine whether the AF production in polyhydramnios begins to normalize or not.

Further data indicated that, prolactin may have a role in fetal growth process and maturation of the gut mucosa (29).

Decidual cells synthesize endometrial prolactin and some variations in prolactin gene expression were shown within each area of decidua. Study showed periodic differences in prolactin gene expression in the decidual cells during pregnancy (30).

Plasma and AF prolactin concentrations were compared between preterm and term pregnancies. Study included 20 patients with preterm labor and 20 patients with preterm labor who responded to tocolysis and delivered at term. Prolactin concentrations were generally found to be significantly higher in preterm than at term (31).

Our data showed that, AF prolactin concentration determined between 16 to 20 gestational ages was not a significant predictor for any pregnancy complication.

All these aforementioned studies suggest that there is still contraversies on the physiological function of decidual prolactin during pregnancy and its relationship between the pregnancy complications.

CONCLUSION

No significant relationship was determined between early first trimester prolactin level and any of the pregnancy complication.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by Zeynep Kamil Women and Children's Health Training and Research Hospital Clinical Researches Ethics Committee (Date: 18.11.2017, Decision No: 144)

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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