Özgün Araştırma / Original Article

Jinekoloji - Obstetrik ve Neonatoloji Tıp Dergisi
The Journal of Gynecology - Obstetrics and Neonatology

DOI: 10.38136/jgon.1397142

Erken Başlangıçlı Fetal Büyüme Kısıtlamasını (FGR) Öngörmede İlk Trimester CRL (baş popo mesafesi) Ölçümünün NT (ense saydımlığı) Ölçümlerine Oranının Rolü

The role of the ratio of first trimester CRL (crown rump length) measurement to NT(nuchal translucency) measurements in predicting early-onset fetal growth restriction (FGR)

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ÖZ

Amaç: Amacımız, ilk trimester CRL (baş popo mesafesi) ölçümünün NT (ense saydamlığı) ölçümlerine oranının erken başlangıçlı fetal büyüme kısıtlamasını (FBK) öngörmedeki rolünü değerlendirmek ve mevcut literatüre katkıda bulunmaktır.

Yöntemler: Mevcut vaka-kontrol çalışmasında, erken başlangıçlı FBK'lı fetüsler, frekans eşleştirilmiş düşük riskli kontrol grubuyla karşılaştırıldı. Bu çalışma, 2020-2023 yılları arasında Ankara Bilkent Şehir Hastanesi Perinatoloji kliniğinde gerçekleştirildi. Erken başlangıçlı FBK'lı gebe kadınlar (n=39) ve FBK'sı olmayan hamile kadınlar (n=50) arasında anne yaşı, gravida , parite, baş popo mesafesi (CRL) ve ense saydamlığı (NT) ölçümleri karşılaştırıldı.

Bulgular: Çalışmaya katılan FBK'lı gebelerin yaş ortalaması 27,1±0,8, FBK olmayan gebelerin yaş ortalaması 26,3±0,6 olup iki grup arasında istatistiksel olarak anlamlı fark saptanmadı (p=0,4)). Ortalama CRL FBK'lı grupta 54,98±1,08 mm, FBK'sız grupta ise 56,99±1,11 mm idi; iki grup arasında anlamlı fark yoktu (p=0,2). NT değeri FBK grubunda 1,11±0,04 mm, FBK olmayan grupta 1,13±0,02 mm olup iki grup arasında anlamlı fark yoktu (p=0,73). Erken başlangıçlı FBK'lı grupta ortalama CRL/NT oranı 52,00±2,33, FBK'sız grupta ise 51,46±1,48 olup iki grup arasında istatistiksel olarak anlamlı fark yoktu (p=0,83).

Erken gelişen FBK grubu kendi içinde değerlendirildiğinde ortalama tanı yaşı 31,7±0,3 hafta idi. Tanı anındaki EFW ortalama persantil 4,5±0,6 ve AC persantil 2,9±0,4 idi. Ortalama umbilikal arter sistol/diyastol oranı (UA-SD) 2,9±0,16 ve ortalama umbilikal arter pulsatilite indeksi (UA-PI) 1,02±0,05 idi.

Sonuç: Baş popo mesafesi/ense saydamlığı oranı, erken başlangıçlı FBK'yı tahmin etmede klinik olarak yararlı değildir.

ABSTRACT

Objective: Our aim is to evaluate the role of the ratio of first-trimester CRL (crown rump length) measurement to NT (nuchal translucency) measurements in predicting early-onset fetal growth restriction (FGR) and to contribute to the existing literature.

Methods: In the present case-control study, fetuses with early-onset FGR were compared with a gestational age-matched low-risk control group. This study was conducted in the perinatology clinic of Ankara Bilkent City Hospital between 2020 and 2023. Maternal age, gravidity, parity, crown-rump length (CRL), and nuchal translucency (NT) measurements were compared between pregnant women with early onset FGR (n=39) and pregnant women without FGR (n=50).

Results: The mean age of pregnant women with FGR who participated in the study was 27.1±0.8, and the mean age of pregnant women without FGR was 26.3±0.6, and no statistically significant difference was found between the two groups (p=0.4)). Mean CRL was 54.98±1.08 mm in the group with FGR and 56.99±1.11 mm in the group without FGR; there was no significant difference between the two groups (p=0.2). The mean NT value was 1.11 ± 0.04 mm in the FGR group and 1.13 ± 0.02 mm in the without FGR group, there was no significant difference between the two groups (p=0.73). The mean CRL/NT ratio was 52.00±2.33 in the group with early onset FGR and 51.46±1.48 in the group without FGR and there was no statistically significant difference between the two groups (p=0.83).

When the early developing FGR group is evaluated within itself, the mean gestational age at diagnosis was 31.7±0.3 weeks. The mean estimated fetal weight (EFW) percentile at diagnosis was 4.5±0.6 and AC percentile was 2.9±0.4. The mean umbilical artery systole/diastole ratio (UA-SD) was 2.9±0.16 and the mean umbilical artery pulsatility index (UA-PI) was 1.02±0.05.

Conclusion: Crown-rump length to nuchal translucency ratio is not clinically useful to predict early-onset FGR.

Keywords: CRL, NT, crown-rump length, nuchal translucency, fetal growth restriction, FGR

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Başvuru tarihi: 29.11.2023
Kabul tarihi: 25.01.2024

INTRODUCTION

Normal growth of the fetus is a multifactorial process and genetic, placental, and maternal factors affect the process (1). Disruption of this multifactorial cycle prevents the fetus from reaching its genetic growth potential and fetal growth restriction occurs. In FGR, the nutritional resources of the fetus are compromised The fetus responds to this situation by reducing its overall size and maintaining brain growth, accelerating lung development, and increasing erythrocyte production (2). In the fetus, blood is directed to the more vital organs: the heart, brain, adrenal gland, and placenta. Total fat tissue and bone mineralization decrease, leading to a weakened appearance in babies with FGR (3). Nitrogen and protein levels are low due to reduced muscle mass. Liver and muscle glycogen levels are reduced due to low glucose and insulin levels (4). The determining factor in early and late fetal development restriction is the placenta. It plays an important role in the development of early onset FGR, such as placental insufficiency, as a result of abnormal trophoblastic invasion of spiral arterioles in the first and second trimester. It is more common in patients with autoimmune diseases, hypertensive disorders, and patients where placental vessels are affected. While early FGR and preeclampsia are usually seen together, late FGR is not accompanied either. Early onset fetal growth restriction (FGR) is defined as an abdominal circumference (AC) or estimated fetal weight (EFW) below the 3rd percentile or absence of end-diastolic flow in the umbilical artery (UA-AEDF) before 32 weeks of gestation. AC and EFW below the 10th percentile and a concomitant uterine artery pulsatility index (UtA-PI) or umbilical artery pulsatility index (UA-PI) above the 95th percentile are also used to make the diagnosis (5). Although there are different criteria for defining fetal growth restriction, none of them are successful in fully predicting adverse neonatal outcomes (6). Babies with developmental delay are usually born preterm and therefore may lead to morbidity, mortality, and short and long-term sequelae (7). The most commonly associated long-term effects of FGR are neurodevelopmental disorders in childhood and cardiovascular disorders, glucose intolerance and diabetes, and blood lipid profile disorders in adulthood (8, 9).

During the first trimester of pregnancy, Nuchal Translucency (NT) refers to the sonographic observation of subcutaneous fluid accumulation in the posterior part of the fetal neck. NT measurement is a sensitive method used in chromosomal abnormality screening. Cardiac malformations, extracellular matrix disorders, and unusual or delayed development of the lymphatic system may also lead to the thickening of the NT, in addition to chromosomal abnormalities. NT measurements above the 95th percentile are considered abnormal. Increased NT is associated with chromosomal and non-chromosomal abnormalities, but also with miscarriage, fetal structural malformations, and fetal death (10-12).

Prenatal diagnosis of fetal growth restriction is a key place to disseminate new strategies and prevent stillbirths, which can reach up to 30%. This study aims to try to predict early-onset fetal growth restriction as early as the first trimester and to organise prospective strategies and to prevent adverse factors that can be prevented in this multifactorial process.

MATERIALS AND METHOD

This study was designed retrospectively in the perinatology clinic of Ankara Bilkent City Hospital. Pregnant women who were followed up for early onset FGR and pregnant women with similar demographic characteristics and without FGR between 2020 and 2023 were included in the study. The study protocol was approved by the ethics committee with the reference number E2-23-5657 and all participants gave written consent. Crown-rump length (CRL), nuchal translucency (NT) measurements in the first trimester, biparietal diameter (BPD), Head circumference (HC), abdominal circumference (AC) percentage, femur length (FL), Estimated fetal weight (EFW) percentage, umbilical artery pulsatility index (UA-Pİ) percentage, uterine artery pulsatility index (UtA-Pı), percentage were reported.

All ultrasound evaluations were performed by the same perinatologist (A.T.) using Voluson E8 with a 2-9 Mhz abdominal convex probe.The first fetal ultrasound scan was performed at 11-14 weeks of gestation, with further ultrasound scans performed at 2-week intervals until the time of delivery. The Delphi procedure was adopted as a consensus criterion for FGR (5). Early-onset FGR is defined as pregnancies that occur before 32 weeks of gestation and have either an estimated fetal weight (EFW) or abdominal circumference (AC) below the 3rd percentile or loss of end-diastolic flow in the umbilical artery. According to the same consensus, other diagnostic criteria include an AC or EFW below the 10th percentile and an accompanying umbilical artery or uterine artery pulsatility index above the 95th percentile.

The statistical analysis was performed by SPSS 22 (IBM Corp., NY). Kolmogrov-Smirnov test was used to assess whether the

data is normally distributed. Mean and standard deviation values were used for normally distributed continuous variables. Categorical variables were presented as numbers and percentages. A p-value <0.05 is considered as statistically significant.

RESULTS

A total of 89 patients, including 39 pregnant women with early onset FGR and 50 pregnant women without FGR, were included in the study. Demographic characteristics and first-trimester CRL and NT measurements were summarised in Table 1.

Table 1: Demographic characteristics and first-trimester CRL and NT measurements

	With FGR (n=39)	Without FGR (n=50)	p
Age	27.1±0.8	26.3±0.6	0.4
Gravidity	1.92±0.21	1.76±0.14	0.51
Parity	0.51±0.1	0.6±0.12	0.58
CRL (mm)	54.98±1.08	56.99±1.11	0.2
CRL (week)	11.46±0.8	11.56±0.9	0.45
NT (mm)	1.11 ± 0.04	1.13 ±0.02	0.73
NT (mom)	0.79±0.035	0.76±0.022	0.58
CRL (mm) /NT (mm)	52.00±2.33	51.46±1,48	0.83

FGR: Fetal growth restriction, CRL: Crown-rump length, NT: nuchal translucency

The mean age of pregnant women with FGR who participated in the study was 27.1±0.8, and the mean age of pregnant women without FGR was 26.3±0.6, and no statistically significant difference was found between the two groups (p=0.4). The mean gravidity of the FGR group was 1.92±0.21, the mean gravidity of the without FGR group was 1.76±0.14, and no significant difference was detected between the two groups (p=0.51).

Table 2: Ultrasonographic measurements in the group with early-onset FGR

EFW (percentile)	4.5±0,6
AC (percentile)	2.9±0.4
UA-SD	2.9±0,16
UA-PI	1.02±0.05
Gestational age of diagnosis (week)	31.7±0.3

EFW: Estimated fetal weight, AC: Abdominal circumference, UA-SD: Umbilical artery systole/diastole ratio, UA-PI: Umbilical artery pulsatility index

The mean parity was 0.51±0.1 in the group with FGR and 0.6±0.12 in the group without FGR, and there was no significant difference between the two groups (p = 0.58). Mean CRL was 54.98±1.08 mm in the group with FGR and 56.99±1.11 mm in the group without FGR; there was no significant difference between the two groups (p=0.2). CRL measurement time was 11.46±0.8 weeks in the group with FGR, and 11.56±0.9 weeks in the group without FGR, and there was no significant difference between the two groups (p = 0.45). The NT value was 1.11 ± 0.04 mm in the FGR group and 1.13 ± 0.02 mm in the without FGR group, there was no significant difference between the two groups (p=0.73). The mean CRL/NT ratio was 52.00±2.33 in the group with early onset FGR and 51.46±1.48 in the group without FGR and there was no statistically significant difference between the two groups (p=0.83).

When the early developing FGR group is evaluated within itself, the mean age at diagnosis was 31.7±0.3 weeks. Ultrasonographic measurements in the group with early-onset FGR were summarised in Table 2. EFW mean percentile at diagnosis was 4.5±0.6 and ac percentile was 2.9±0.4. The mean umbilical artery systole/diastole ratio (UA-SD) was 2.9±0.16 and the mean umbilical artery pulsatility index (UA-PI) was 1.02±0.05.

DISCUSSION

In the present study, CRL to NT ratio was not found to be clinically useful in the prediction of early-onset FGR.

In a single-center retrospective study, the prediction of first-trimester crown-rump length (CRL), pregnancy-related plasma protein-A (PAPP-A), and nuchal translucency (NT) values for adverse pregnancy outcomes were investigated. A total of 12592 pregnant women were included in the study There were preterm labour in 852 (6.8%) and preeclampsia in 352 (2.8%) patients. Small for gestational age (SGA) occurred in 1824 (14.5%), and miscarriage occurred in 73 (0.6%) patients. Stillbirths occurred in 37 (0.3%), perinatal deaths occurred in 73 (0.6%) and neonatal death occurred in 38 (0.30%) patients. It was concluded that PAPP-A, NT, and CRL are independent prognostic factors for unfavorable pregnancy outcomes, especially the risk of SGA increases with low PAPP-A (13).

In a cohort study including 8012 patients, the relationship between the first trimester (free human chorionic gonadotropin-β [hCG], pregnancy-associated plasma protein A [PAPP-A], NT and adverse pregnancy outcomes was investigated. PAPP-A values below the 1st and 5th percentiles and free β-hCG below the 1st percentile values were associated with an increased risk of developing FGR. PAPP-A values below the 5th percentile and NT values above the 99th percentile were associated with an increased risk of preterm birth before 34 weeks. As a result of the study, it was concluded that extreme values of first-trimester free β-hCG, PAPP-A, and NT were all associated with adverse pregnancy outcomes, and especially PAPP-A levels below the 1 percentile have a particularly high predictive value for FGR (14).

In a prospective study including 6026 patients, the relationship

between unexplained nuchal translucency thickness increase and pregnancy adverse outcomes was investigated. Pregnant women with comorbidities, and fetuses with fetal chromosomal or structural abnormalities were excluded from the study. The NT of 277 fetuses in the study was found to be above the 95th percentile, and the NT of 5749 fetuses was below the 95th percentile. The miscarriage rate was significantly higher in the group with NT above the 95th percentile; 18/277 (6.5%) versus 55/5749 (1.0%). Preeclampsia, premature birth, fetal growth restriction, and low birth weight rates were found to be slightly but significantly higher in the group with NT above the 95th percentile. It was concluded that increased NT measurements above the 95th percentile in the first trimester are associated with a significantly increased risk of miscarriage, fetal growth restriction, preterm birth, low birth weight, and preeclampsia (15).

In a study involving 427 pregnant women, the association with adverse outcomes was investigated in fetuses with normal karyotype and increased NT. The patient groups were divided into 3 groups: nt ≥ 3 mm, ≥ 3.5 mm, and ≥ 4.5 mm, it was concluded that high NT values in fetuses with normal karyotypes do not reliably discriminate between normal and unfavorable outcomes (16). However, in the present study, no significant difference was present between the control and early-onset FGR groups in terms of CRL to NT ratio.

The main strength of the present study was its novelty. However, retrospective design and a relatively low number of cases were the main limitations.

CONCLUSION

In conclusion, CRL to NT ratio is not clinically useful to predict early-onset FGR.

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