

Fetal kidney length as a useful adjunct parameter for better determination of gestational age

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ABSTRACT

الأهداف: لتحديد صلاحية طول كلية الجنين ومؤشر السائل الامينوسي في تقدير موعد المخاض.

الطريقة: أجريت هذه الدراسة الاستباقية على 180 امرأة حامل تابعن العيادات الخارجية في قسم التوليد وأمراض النساء، مستشفى جامعة غازي عنتاب في تركيا خلال الفترة ما بين يناير 2014م إلى 2015 م. قُدر العمر الحملية عبر قياس الموجات فوق الصوتية المبكرة للجنين وآخر موعد حيض. وجرى قياس المشعرات الروتينية لتقييم العمر الحملية، وطول كلية الجنين، ومشعر السائل، درسنا العلاقة بين كل من طول كلية الجنين و مشعر السائل الامينوسي مع العمر الحملية.

النتائج: كان متوسط العمر الحملية للعينة المعتمدة على آخر موعد حيض (31.98±4.29) (من أسبوع 24 حتى أسبوع 39)، وكان متوسط الطول الكلي (35.66±6.61) 19 إلى 49 ملم) وكان هناك ارتباط هام بين العمر الكلي الحملية وطول على الجنين ($r=0.947, p=0.001$) ولكن كان هناك ارتباط سلبي معتدل بين العمر الحملية ومشعر السائل الامينوسي. وساهم إضافة الطول الكلي إلى باقي القياسات الحيوية الروتينية في تحسين فعالية النموذج المستخدم في تقدير العمر الحملية ($R^2=0.965$ to $R^2=0.987$).

الخاتمة: يمكن التنبؤ بعمر الحمل بشكل أفضل بإضافة طول الجنين إلى المعايير الروتينية.

Objectives: To determine the validity of fetal kidney length and amniotic fluid index (AFI) in labor dating.

Methods: This prospective study included 180 pregnant women followed up in the outpatient clinic at the Department of Obstetrics and Gynecology, Gaziantep University, Turkey, between January 2014 and January 2015. The gestational age (GA) was estimated by early fetal ultrasound measures and last menstrual period. Routine fetal biometric parameters, fetal kidney length, and amniotic fluid index were

measured. We studied the correlation between fetal kidney length, amniotic fluid index, and gestational age.

Result: The mean gestational age depending on last menstrual period and early ultrasound was 31.98±4.29 (24-39 weeks). The mean kidney length was 35.66±6.61 (19-49 mm). There was a significant correlation between gestational age and fetal kidney length ($r=0.947, p=0.001$). However, there was a moderate negative correlation between GA and AFI. Adding fetal kidney length to the routine biometrics improved the effectiveness of the model used to estimate GA ($R^2=0.965$ to $R^2=0.987$).

Conclusion: Gestational age can be better predicted by adding fetal kidney length to other routine parameters.

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Precise assessment of the gestational age (GA) is essential in prenatal medicine to predict fetal health and labor dating. Errors in determining the exact GA may interfere with critical management decisions, such as in preterm labor as well as growth disorders that is considered the leading cause of neonatal morbidity and mortality.¹ Last menstrual period (LMP) has been a reliable predictor in estimating GA, but many pregnant women cannot recall the exact date of their LMP. Garg et al² suggests that 30% of women cannot recall the exact date of LMP.² In the first trimester, the

mean gestational sac diameter and crown-rump length (CRL) are reliable measurements for this purpose.³ In the second trimester, biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), femur length (FL), and trans-cerebellar diameter⁴ are feasible useful parameters. We studied the correlation between GA and fetal kidney length (FKL), also the correlation between amniotic fluid index (AFI) and GA depending on the fact that amniotic fluid is secreted abundantly from kidneys after the second trimester.

Methods. Ethical committee approval was obtained from Gaziantep University Ethical Board. The study was carried out according to the principles of the Helsinki Declaration. We obtained the written consent of patients who visited our clinic for routine obstetric follow-up in the Department of Obstetrics and Gynecology, Gaziantep University, Turkey.

This prospective study was carried out between January 2014 and January 2015, and included 180 pregnant women. The mean age of patients was 28.12 ± 5.86 (16-43) years. Inclusion criteria included uncomplicated singleton pregnancies with a live fetus after 24 weeks of pregnancy, and the gestational age was estimated depending on both LMP and the documented early ultrasound measurements. We discarded the patients who did not recall their LMP, and patients with high risk pregnancies such as preeclampsia, fetal growth restriction (FGR), macrosomia, fetal renal abnormalities, oligohydramnios, and polyhydramnios. Fetal kidney length measurements of both kidneys were made from the upper pole toward the lower pole in the longitudinal section of the fetus in the sagittal plane, then the mean value for both was recorded. Generally, fetal kidney identification before 17 weeks may be very difficult for a routine sonographer, so we selected our cases beyond 24 weeks when fetal kidney evaluation is clear. In addition to the gender of the fetal routine obstetric parameters, BPD, HC, AC, and FL were recorded. Amniotic fluid index was calculated by dividing the uterus into 4 equal quadrants using linea nigra and umbilicus. Each of the deepest pockets (free from umbilical cord and fetal parts) was measured in vertical dimension from each quadrant in centimeters, and AFI is the sum of all 4 quadrants.⁵

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Pearson correlation coefficient was used to detect linear relationship between numerical variables. Univariate and multiple linear regression analyses were performed to estimate Beta coefficients. R^2 was calculated to show the effectiveness of a model. All analyses were performed using the Statistical Package for Social Sciences Version 22.0 for windows (Armonk, NY: IBM Corp), and $p < 0.05$ was accepted as significant.

Results. Mean gestational age depending on LMP and early ultrasound was 31.98 ± 4.29 (24-39) weeks. The mean fetal biometry parameters including BPD of the study population was 31.97 ± 4.35 weeks, FL was 31.76 ± 4.36 weeks, HC was 31.98 ± 4.32 weeks, and AC was 31.62 ± 4.75 weeks. The mean FKL measurement of patients was 35.66 ± 6.61 mm (range 19-49 mm). The mean AFI measurement of patients was 12.62 ± 3.40 . Pearson correlation coefficients for correlation between GA with routine fetal biometric parameters, mean kidney length, and AFI are presented in Table 1.

There was a very strong positive correlation between GA and BPD ($r=0.975$, $p=0.001$), HC ($r=0.974$, $p=0.001$), FL ($r=0.967$, $p=0.001$), and AC ($r=0.852$, $p=0.001$). Also, there was a very strong positive correlation between GA and FKL ($r=0.947$, $p=0.001$) (Figure 1), but a moderate negative correlation between GA and AFI ($r=-0.499$, $p=0.001$). Regression model for FKL (Model 1), FKL and AFI (Model 2), routine fetal biometric parameters (Model 3) are presented in Tables 2-4. Regression model for routine fetal biometric parameters, FKL, and AFI altogether (Model 4) is presented in Table 5.

Discussion. Determining an accurate GA has a substantial effect in prenatal medicine and early termination of pregnancy become urgent upon the immediate maturity of fetus in high risk pregnancy such as severe preeclampsia, severe fetal growth restriction, chronic hypertension, total placenta previa, Rh alloimmunization, and so forth. GA estimation is also crucial in implementing certain tests (amniocentesis, chorionic villus sampling) and when applying certain forms of fetal therapy.⁶ There are variety of methods to calculate GA; in the first trimester LMP and diameter or GS volume are adopted. As pregnancy progresses, other parameters such as BPD, FL, AC, and HC can be utilized. These parameters might be inaccurate in late pregnancy, especially when a pregnant woman cannot recall her LMP. Furthermore, there is a substantial evidence that the standard derivation for these indices are widen as pregnancy progresses,⁶ and this will be even worse if the head is too low or an obvious plane

Table 1 - Pearson correlation coefficients for relation between gestational age (GA) with routine fetal biometric parameters, mean kidney length, and AFI among 180 pregnant women.

| Variables | GA | AFI | BPD | HC | AC | FL | FKL |
|-----------|---------|---------|---------|---------|---------|---------|----------|
| GA | 1 | -0.499* | 0.975* | 0.974* | 0.852* | 0.967* | 0.947* |
| AFI | -0.499* | 1 | -0.480* | -0.484* | -0.404* | -0.520* | -0.0416* |
| BPD | 0.975* | -0.480* | 1 | 0.977* | 0.859* | 0.963* | 0.935* |
| HC | 0.974* | -0.484* | 0.977* | 1 | 0.844* | 0.971* | 0.944* |
| AC | 0.852* | -0.404* | 0.0859* | 0.844* | 1 | 0.845* | 0.811* |
| FL | 0.967* | -0.520* | 0.963* | 0.971* | 0.845* | 1 | 0.925* |

*correlation is significant at the $p=0.001$ level (2-tailed). AFI - amniotic fluid index, BPD - biparietal diameter, HC - head circumference, AC - abdominal circumference, FL - femur length

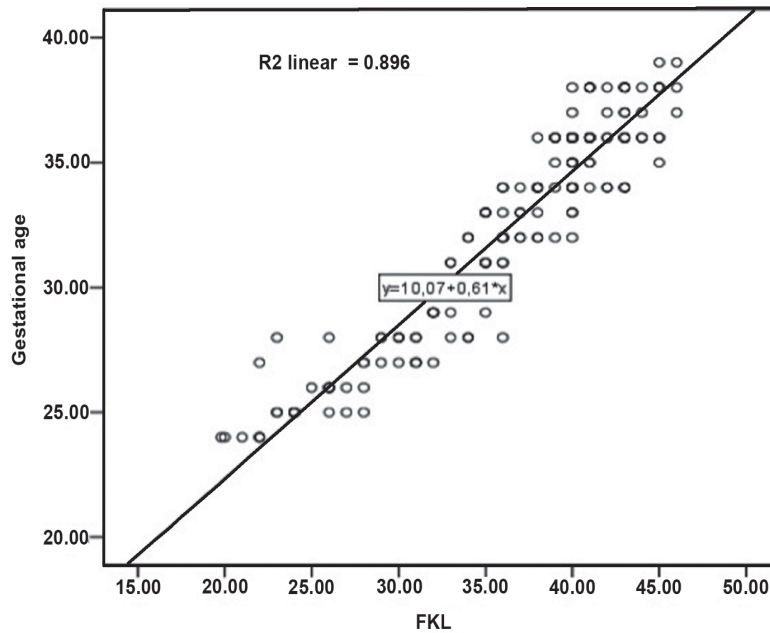


Figure 1 - Correlation between GA and FKL among 180 pregnant women. X - fetal kidney length in mm, Y - gestational age in weeks, GA - gestational age, FKL - fetal kidney length

Table 2 - Regression model for fetal kidney length (FKL) to predict gestational age ($R^2=0.896$, coefficients^a).

| Model 1 | Unstandardized Coefficients | | Standardized coefficients | P-value |
|------------|-----------------------------|------------|---------------------------|---------|
| | B | Std. Error | Beta | |
| (Constant) | 10.065 | 0.568 | | 0.001 |
| FKL | 0.615 | 0.016 | 0.947 | 0.001 |

cannot be obtained, which together will mislead the measurement of BPD and HC. Therefore, many researches have been conducted to determine a precise estimation of GA using ultrasonic measurements throughout the second and the third trimester. In

addition, Ozat et al⁷ suggest that fetal sacral length can be used in dating labor due to the significant correlation between GA and sacral length they found. Sherer et al⁸ conducted a study on 602 pregnant women and used fetal hard palate width as an indicator of GA between 15 and 41 weeks gestation and epitomized that hard palate indices were correlated with GA, BPD, AC, and FL, but the assessment of these measurements needs advanced ultrasonic skills. Therefore, we need other parameters that can give an accurate GA and can be measured easily. There is a similar study that was carried out by Toosi et al.⁹ The results supported that FKL is an accurate parameter in late pregnancy. Moreover, Konje and Abrams¹⁰ investigated FKL between 24 and 38 weeks pregnant women and found that FKL has more

Table 3 - Regression model for fetal kidney length (FKL) and amniotic fluid index (AFI) to predict gestational age (R²=0.954, coefficients^a).

| Model 2 | Unstandardized Coefficients | | Standardized Coefficients | T | Sig. |
|------------|-----------------------------|------------|---------------------------|--------|-------|
| | B | Std. Error | Beta | | |
| (Constant) | 13.318 | 0.826 | | 16.126 | 0.001 |
| AFI | -0.161 | 0.031 | -0.128 | -5.142 | 0.001 |
| FKL | 0.580 | 0.016 | 0.894 | 36.040 | 0.001 |

^adependent variable: gestational age

Table 4 - Regression model for fetal biometric parameters (R²=0.965, Coefficients^a).

| Model 3 | Unstandardized Coefficients | | Standardized Coefficients | T | P-value |
|------------|-----------------------------|------------|---------------------------|-------|---------|
| | B | Std. Error | Beta | | |
| (Constant) | 0.707 | 0.455 | | 1.553 | 0.122 |
| FL | 0.244 | 0.061 | 0.248 | 3.972 | 0.000 |
| BPD | 0.399 | 0.070 | 0.406 | 5.722 | 0.000 |
| HC | 0.308 | 0.077 | 0.311 | 3.992 | 0.000 |
| AC | 0.028 | 0.025 | 0.031 | 1.119 | 0.265 |

^adependent variable: gestational age. FL - femur length, BPD - biparietal diameter, HC - head circumference, AC - abdominal circumference

Table 5 - Regression model for fetal biometric parameters, AFI and FKL (R²=0.987)

| Model 4 | Unstandardized Coefficients | | Standardized Coefficients | T | Sig. |
|------------|-----------------------------|------------|---------------------------|--------|-------|
| | B | Std. Error | Beta | | |
| (Constant) | 3.019 | 0.756 | | 3.995 | 0.001 |
| BPD | 0.353 | 0.067 | 0.358 | 5.287 | 0.001 |
| HC | 0.195 | 0.077 | 0.197 | 2.530 | 0.012 |
| AC | 0.028 | 0.024 | 0.032 | 1.197 | 0.233 |
| FL | 0.203 | 0.060 | 0.207 | 3.382 | 0.001 |
| FKL | 0.128 | 0.027 | 0.197 | 4.719 | 0.001 |
| AFI | -0.037 | 0.020 | -0.030 | -1.864 | 0.064 |

AFI - amniotic fluid index, BPD - biparietal diameter, HC - head circumference, AC - abdominal circumference, FL - femur length

accurate predictive value than the other fetal biometric parameters such as BPD, FL, HC, and AC. Another study in India conducted by Kansaria et al¹¹ proved that utilizing FKL improved dating labor.

Fetal kidney growth is constant, increases ≈1.7 mm fortnightly throughout pregnancy and unchanged by growth disorders,¹² which makes using it more reliable than other parameters in complicated pregnancies. Additionally, Kaul et al⁶ advocated that the single

most accurate parameter for estimating GA is the fetal kidney length.⁶ Witzani et al¹² suggest that renal length measures obtained by MRI are close to those obtained by ultrasound. Ahmadi et al¹³ suggest that fetal kidney size can be used in dating labor, especially when accurate LMP is not available. These findings are consistent with our study in Turkish population, that there is a strong correlation between FKL and GA,

which can use as an eligible parameter in dating labor. There was a very strong positive correlation between GA and FKL ($r= 0.947$, $p=0.001$), but a moderate negative correlation between GA and AFI ($r= -0.499$, $p=0.001$). Interestingly, there was a marked inter-individual variability in FKL between the fetuses of the same GA. A similar variability in FKL has been shown in a previous study concerning renal maturation of preterm infants.¹⁴ In our study, the variability was marked especially at the 27th and 28th weeks, and this variability may be the focus of further large-scaled studies. Regression model for FKL to predict GA is ($R^2=0.896$), whereas regression model for AFI alone to predict GA has a poorer performance ($R^2=0.249$). Applying both of FKL and AFI can enhance our prediction of GA compared with applying FKL alone ($R^2=0.954$), and is close to the regression model for routine fetal biometric parameter ($R^2=0.965$).

Finally, the regression model for routine fetal biometric parameters, AFI and FKL altogether had the best performance to predict GA ($R^2=0.987$). Adding AFI to the other parameters did not change the model ($p=0.064$).

Ultimately, fetal kidney length is a feasible measurement with high predictive value that can be used as an adjunct parameter. Fetal kidney length together with routine fetal biometric parameters can predict a meticulous date of GA in fetuses who are susceptible to growth disorders or when the routine parameters are not present such as achondroplasia, phocomelia, amelia, fetal hepatosplenomegaly, cranial agenesis, or anencephaly.

The limitation of our study is the disability to determine the standardized values for mean fetal kidney length per each week of GA due to the small sample size.

In conclusion, our study concluded that FKL can be measured readily, and adding it to other routine parameters gives a better prediction of GA. However, this is not true for AFI because there was only a moderate negative correlation between GA and AFI.

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