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Ultrasonographic assessment of gestational age with the distal femoral and proximal tibialepiphyseal ossification centers in the third trimester

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Abstract

Background: Pregnant women are frequently unsure of their last menstrual period. When this is combined with late booking for antenatal care, gestational age determination becomes a real challenge. Study was conducted to ascertain the predictive values of the distal femoral and proximal tibial epiphyseal ossification centre measurements in estimating pregnancy in the third trimester.

Methods: An observational cohort study using women with singleton pregnancies (30–40 wks) attending antenatal clinic in Jos University Teaching Hospital. The distal femoral and proximal tibial epiphyseal ossification centers were identified and measured by ultrasonography. Monogram of foetal bone development was employed also considering the diameters of the two centers.

Results: Gestational age correlated well with the diameters of the distal femoral and the proximal tibial epiphyseal ossification centers. The presence of the distal femoral and proximal tibial epiphyseal ossification centre had a positive predictive values of 94.3% (n, 106) and 98.7% (n, 136) respectively.

Conclusion: Ultrasonographic measurement of the diameters of the distal femoral and proximal tibial epiphyseal ossification centers may be useful in the estimation of gestational age during the third trimester.

Keywords: Distal femoral epiphyses, Ossification centers, proximal tibial epiphysis, Gestational age, last menstrual period

1. Introduction

Accurate gestational age estimation is one of the most important assessments that an obstetrician makes in pregnancy, given that all of the various management strategies are dependent on knowing the gestational age of the foetus [1]. The lack of accurate GA estimation, particularly in geographical regions at greatest risk of these conditions, means that preterm delivery and small-for-gestational-age rates are mere approximations in many parts of the world [2]. Pregnant women are frequently unsure of the date of their last menstrual period and when this is combined with late booking for antenatal care, determination of gestational age becomes a real challenge even with ultrasonography. Traditional biometry, ancillary biometric and non-biometric measurements can help narrow the biologic variability between foetuses [1, 3]. Reliable estimation of gestational age (GA) is essential as it allows appropriate scheduling of a woman's antenatal care, informs obstetric management decisions and facilitates the correct interpretation of foetus growth assessment [4]. Non-traditional ultrasonographic measurements in late gestation may assist in determining appropriate gestational age and foetal lung maturity and they may be especially important in clinical situations such as oligohydramnios, in which compression of the foetal head and abdomen can lead to difficulty in obtaining an accurate biparietal diameter and abdominal circumference [5, 6]. Non-traditional foetal ultrasound measurements include; distal femoral and proximal tibial epiphyseal ossification centres, the transverse cerebella diameter, foetal foot length, ratios of biometric and non biometric measurements, amniotic fluid volume, and placental grading. These and other miscellaneous markers are essential in evaluating foetuses in order to predict with certainty, the probability of extra-uterine survival and to reduce admission into the special baby care unit due to iatrogenic prematurity [7]. The foetal distal femoral and proximal tibial epiphyseal ossification centres have a characteristic predictable pattern of development that can be identified and assessed sonographically in the third trimester [5, 7, 8]. Both ossification centres are in the same plane and are therefore easily detected sonographically.

The distal femoral epiphysis is identified by visualizing the distal femur and locating the echogenic epiphysis. The proximal tibial epiphysis is also an echogenic structure adjacent to the tibial head. Measurements are obtained in an axial plane from outer to outer margins along the medial lateral surfaces of the epiphysis [7, 9]. Both centres increase in size and are more echodense in appearance with progressive gestational age. Although many different anthropometric measurements of the foetus have been used to date pregnancy, none was very precise when taken for the first time during the third trimester of pregnancy because of significant variability in foetal size. An additional parameter that may help define critical moments of foetal development would therefore be a useful addition to the range of tools available for that purpose, and several authors have already demonstrated the usefulness of the epiphyseal ossification centres [5].

We therefore, sought to sonographically evaluate the distal femoral and proximal tibial epiphyseal ossification centres and to correlate the weekly increase in their diameters with gestational age with a view to using the results obtained to construct a nomogram of sizes of epiphyseal ossification centres with gestational age among our obstetric population.

Methodology

This was a prospective observational cohort and hospital-based study conducted at the antenatal clinic of the Department of Obstetrics and Gynaecology, Jos University Teaching Hospital (JUTH) which is a tertiary health institution located at its permanent site at Lamingo Jos, the Plateau State capital.

Inclusion criteria

Women with singleton pregnancies with established gestational age of at least 30 weeks based on their last normal menstrual period and first trimester ultrasound dating with no obstetric complications and consented were recruited.

Exclusion criteria

This included women with multiple pregnancies, those who were not sure of their last menstrual dates and had no early scan, pregnancies less than 30 weeks of gestation at recruitment and pregnancies associated with medical or obstetric complications. Pregnant women from the antenatal clinic who met the inclusive criteria were recruited consecutively after an informed consent was obtained from each participant in the ultrasound room as they came for their routine ultrasound scan. Ultrasound scan is one of the routine basic investigations done in the antenatal clinic as pregnant women register for antenatal care in JUTH. They were recruited as from 30 weeks of gestation based on last menstrual period or first trimester ultrasound scan dating. Weekly ultrasound scan was done and the gestational ages at which the distal femoral and the proximal tibial epiphyseal ossification centers appeared were recorded. The incremental diameters of these epiphyses in millimeters along the longitudinal femoral plane were also recorded on weekly bases until delivery of each pregnancy. 167 women with singleton pregnancies between 30 – 40 weeks of gestation were enrolled for the study out of which 149 (10.8%) participated were lost to follow up, 2 women had major degree placenta praevia and were electively delivered by Caesarean section at 38 weeks and one pregnancy had a foetus with hydrocephalus.

The data was computed in a preformed table until 149 pregnant women were recruited using the Cochran formula, according to Shripad *et al.*, 2015 [10].

The sample size was calculated using the formula:

$$n = Z^2Pq/d^2$$

$$10.5\% = 0.105$$

$$\frac{3.8416 \times 0.105 \times 0.895}{0.0025}$$

$$0.3610$$

$$0.0021$$

$$n = 144.4$$

Therefore 149 women were sampled considering 10% error.

Statistical analysis

The data was entered and analyzed by the computer software SPSS version 20.

Ethical Approval

This was obtained from the Ethical Committee of the Jos University Teaching Hospital, Jos, Nigeria

Results

During the study, 167 Women with singleton pregnancies between 30–40 weeks of gestation were enrolled, out of which 149 participated from the beginning to the end i.e. 18 enrollees (10.8%) were lost to follow up and these were ignored in the data analysis. Two pregnant women in the study population had major degree placenta praevia and were electively delivered by Caesarean section at 38 weeks. One pregnancy had a foetus with hydrocephalus and she also had elective Caesarean section.

The distal femoral epiphyses (DFE) appeared in 15 of the foetuses (10.1%) as early as the 30th week. The proportion of foetuses in which the DFE was detectable by ultrasonography increased dramatically to 71.1% at 32 weeks of gestation reaching 98.7% at 35 weeks, and 100% at 37 weeks of gestation (Table 1). The proximal tibial epiphyses (PTE) appeared for the first time in 9 (6.4%) of foetuses at 33 weeks and in 31 (20.8%) of foetuses at 34 weeks' gestation. By 35 weeks' gestation, the PTE was detectable in only approximately one third of foetuses, but at 37 weeks it was observed in more than 91.3% of cases, increasing to 93.3% at 38 weeks and 100% at 40 weeks' gestation (Table 1). Each of the 2 epiphyseal ossification centres was most useful as an Indicator of a different gestational age (Table 1)

Table 1: Sonographic Visibility of the Two Epiphyseal Ossification Centers by Gestational Age

Gestational age (weeks)	Number	Distal Femoral Epiphysis (DFE), N (%)	Proximal Tibial Epiphysis (PTE), N (%)
30	149	15(10.1)	0(0.0)
31	149	52(34.9)	0(0.0)
32	149	106 (71.1)	0(0.0)
33	149	145 (97.3)	9 (6.4)
34	149	146 (97.9)	31(20.8)
35	149	147 (98.7)	50 (33.6)
36	149	147 (98.7)	80 (53.7)
37	149	149 (100.0)	136 (91.3)
38	149	146 (100.0)	139 (93.3)
39	149	149 (100.0)	149 (100.0)
40	149	149 (100.0)	149(100.0)

The presence of the DFE had a positive predictive value of 94.3% for indicating a pregnancy of at least 32 weeks (106 of 149 foetuses had this EOC present) as depicted in Table 2

Table 2: Diagnostic Accuracy Values of Distal Femoral Epiphysis as an indicator of gestational age at their time of greatest accuracy

DFE*(mm)	Gestational age (weeks)	Sensitivity	Specificity	+PV	-PV	Accuracy
1.1	30	8.73	88.9	86.7	10.5	17.4
1.2	31	30.2	61.1	86.5	9.6	33.5
1.4	32	67.1	66.7	94.3	19.7	67.1
1.6	33	93.3	66.7	95.9	54.6	90.4
1.9	34	96.0	72.2	96.6	68.4	93.4
2.3	35	51.0	100	100	19.8	56.3
2.8	36	97.3	83.3	98.0	79.0	95.8
3.2	37	98.7	88.9	98.7	88.9	97.6
3.6	38	98.0	100	100	85.7	98.2
4.0	39	98.7	88.9	98.7	88.9	97.6
4.5	40	99.2	100	100	89.7	98.2

*DFE: Distal Femoral Epiphysis, +PV: Positive predictive value, -PV: Negative predictive value

Ultrasonographic detection of the PTE had a positive predictive value of 98.7% for indicating a foetuses of at least 37 weeks of gestation (136 of 149 foetuses had this EOC present).

Table 3: Diagnostic Values of Proximal Tibial Epiphysis as an indicator of gestational age at their time of greatest accuracy

PTE* (mm)	Weeks	Sensitivity	Specificity	+PV	-PV	Accuracy
1.14	33	6.04	100	100	11.4	16.2
1.29	34	18.8	83.3	90.3	11.03	25.8
1.60	35	32.2	88.9	96	13.7	38.3
1.85	36	51.7	83.3	96.3	17.2	55.1
2.05	37	98.9	83.3	98.0	83.3	96.4
2.51	38	98.0	83.3	98.0	83.3	96.5
3.05	39	98.0	83.3	98.0	83.3	96.4
3.62	40	98.0	83.3	98.0	83.3	96.4

*PTE: Proximal Tibial Epiphysis, +PV: Positive predictive value, -PV: Negative predictive value

The correlation between the distal femoral epiphysis diameters in millimetres and the gestational age in weeks were determined on nomogram and regression curve shown in Figure 1. There is an almost perfect correlation at different points (10th, 50th and 90th percentiles) of the DFE diameters and gestational age. The correlation between diameter of distal femoral epiphysis and gestational age was positive and strong, almost perfect at 50th Percentile ($r = 0.978, P < 0.05$). It tends even more towards perfection at 90th percentile ($r = 0.998, P < 0.05$).

in millimetres and the gestational age in weeks were also determined on a nomogram and regression curve on figure 2. There is an almost perfect correlation at different points (10th, 50th and 90th percentiles) of the PTE diameters and gestational age. The diameters of the proximal tibial epiphysis and gestational age were found to have strong positive correlation at 50th Percentile ($r = 0.996, P < 0.05$). Just like the outcome observed with the DFE, the PTE tended perfect correlation at 90th percentile ($r = 0.998, P < 0.05$).

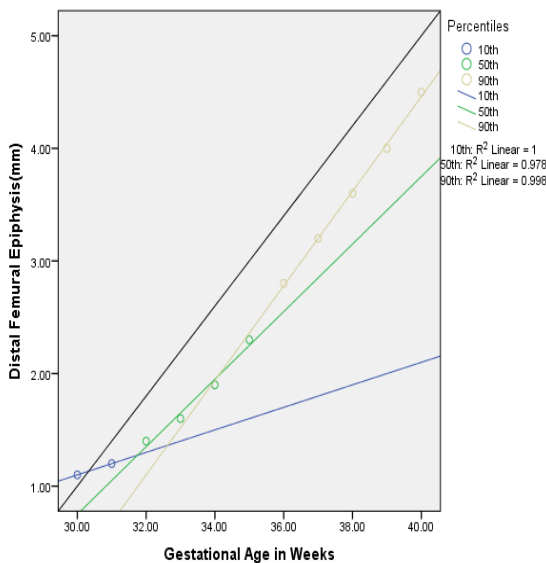


Fig 1: Distribution of the 10th, 50th and 90th percentiles of the diameters of Distal Femoral Epiphysis

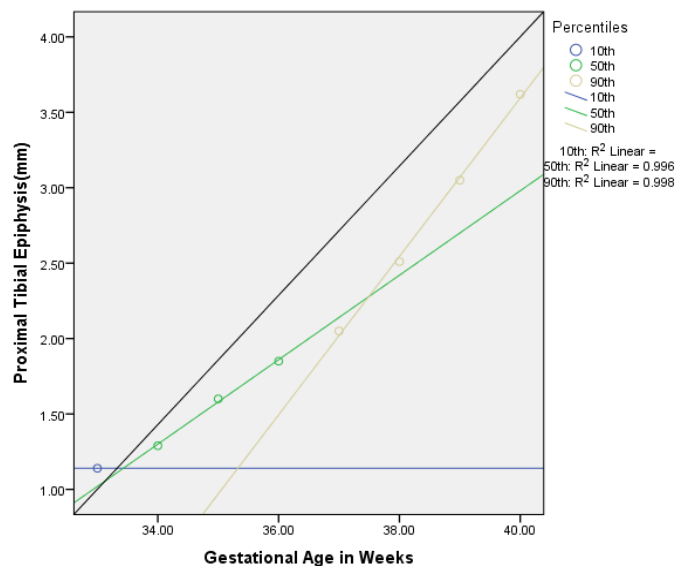


Fig 2: Distribution of the 10th, 50th and 90th percentiles of the diameters of Proximal Tibial Epiphysis

*The points represent real values while the lines represent the linear regression adjustments
The correlation between the proximal tibial epiphysis diameters

*The points represent real values while the lines represent the linear regression adjustments
Figure 3 shows a combined plot of the DFE and the PTE with

their respective correlation coefficients (monogram). As observed on the curve, the distal femoral epiphysis showed a linear growth while the proximal tibial epiphysis showed an exponential growth over weeks of gestational as the pregnancies approached term.

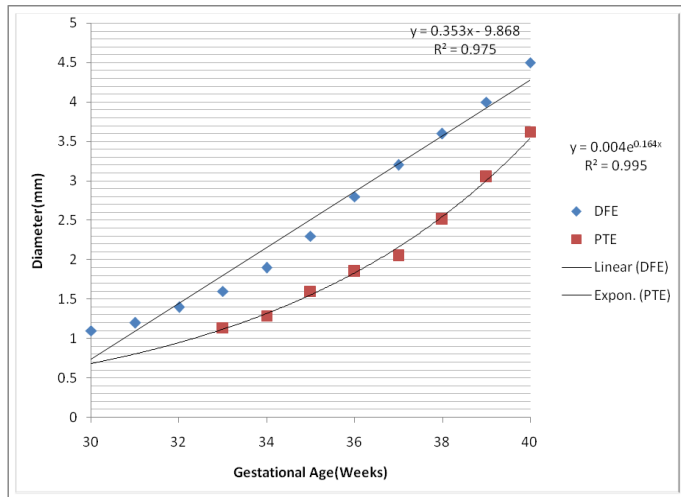


Fig 3: Relationship between Gestational age and Diameter of the DFE and PTE

Discussion

Findings from this study showed strong correlation between the DFE diameter in millimetres and gestational age in weeks as pregnancies approach term and at the correlation coefficient value at 90th percentile the PTE was the exact value with the DFE.

Results further indicate that the epiphyseal ossification centre of each of the two bones studied varied greatly, as is seen in the case of other anthropometric indicators, but their presence or absence can be useful in drawing some specific and critical assumptions with regard to gestational age. If none of the two epiphyseal ossification centres is detected at ultrasonographic examination, there is a very good chance that the foetus has not yet reached 34 weeks' gestation ($P < 0.05$). If only the distal femoral EOC is observed, and particularly if it is less than 3 mm in diameter, the foetus has very probably not yet reached 37 weeks' gestation ($P < 0.05$). On the other hand, if the 2 EOCs are visible, the foetus has certainly completed at least 37 weeks' gestational age. The curve of epiphyseal ossification centre development, constructed using the individual diameters of the 2 epiphyseal ossification centres, makes it possible to evaluate whether there is any delay in bone maturation, as may occur in cases of hypothyroidism, skeletal dysplasia, some forms of trisomia, and even in small-for-gestational-age fetuses^{[11], [12]}. It can be speculated that if the diameters fall below the 10th percentile of the curve, delayed bone maturation may be suspected. The diameters can also be useful as a marker of 37 weeks gestation. Our study showed that foetuses of at least 37 weeks old increased at 84% (3mm), 94% (4mm) and 100% (5mm) respectively. This is however in tandem with a study by^[13], where fetal distal femoral epiphysis DFE was detectable by ultrasonography increased dramatically to 56% at 33 weeks' reaching 94% at 36 weeks and 100% at 37 weeks gestation. It is also closely related with^[14] that asserted that, Gestational age correlated well with the diameters of the distal femoral and the proximal tibial epiphyseal ossification centers but even better with the sum of the three ossification centers. Positive predictive values of the fetus having gestational age of at least 37 weeks

when the sum of the three centers was 7, 11, and 13 mm were 82%, 94%, and 100%, respectively.

This study does not propose substituting other anthropometric measurements, such as biparietal diameter, abdominal and cephalic circumference, or femur length, for the diameters of the 2 EOCs but would like to draw attention to the possibilities offered by this simple marker of foetal development. Mahony *et al.*,^[15] showed that a sum of the DFE and PTE of 11 mm was a good indicator of foetal lung maturity, according to the result of L/S ratio and phosphatidyl glycerol in amniotic fluid. This research therefore used the epiphyseal ossification centres of the foetuses of different women for each observation during the third trimester of pregnancy, specifically preventing any woman from contributing more than one value to the study. In addition, only normal pregnancies were included. The purpose of this method was to maximize the chances of observing a broad range of normalcy instead of observing a smaller number of women several times during the same period. It is possible to postulate that the identification and measurements of the epiphyseal ossification centres may be less influenced by foetal growth restriction or excessive growth than other anthropometric measurements, whereas, a deficit in calcium metabolism may occasionally delay the appearance of the 2 epiphyseal ossification centres.

The limitation of this study was that only pregnancies of 30 weeks and beyond were included and other biochemical factors that serve as markers of foetal maturity were not considered. However, the gains of the study were that multiple ultrasound scans were done reducing the margin of error and the normogram that was constructed from this data may be used to determine gestational age in the third trimester which may assist the obstetricians in making decision on timing of delivery particularly in situations when a dilemma of whether or not to continue with conservative management of a complicated pregnancy is being contemplated.

Conclusion

Accurate gestational age dating in third trimester of pregnancy is possible using diameters of epiphyseal ossification centres as biometric markers, as the diameter of the DFE and the PTE were found to have strong positive correlation with the gestational age in weeks during the third trimester and therefore, may be used to date pregnancies during that period.

However, there is clearly ample space for further research into the possible usefulness of the ultrasonographic visualization of the epiphyseal ossification centres as markers of foetal development and gestational age, not only during normal pregnancy but also in the presence of a number of conditions known to affect foetal growth and development.

Conflict of Interest

The authors declare no conflict of interest

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