

## Sonographic detection of the distal femoral epiphyseal ossification center and its relation to the fetal age and fetal weight

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**Abstract: Background:** Distal Femoral Epiphysis is identified by locating the echogenic epiphyseal structure near the distal end of femur and its measurement is obtained in an axial plane along the medio-lateral surfaces of the epiphyses from the outer to outer margin. Epiphyseal ossification centers appears in late gestational ages, when traditional biometric measurements are not accurate enough. The mean age at DFE appearance is 32 to 33 weeks gestations, and it is not visualized before 28 weeks gestation. In 94% of fetuses the DFE is observed at 34 weeks gestation. So if a DFE is not visualized, the fetus is most likely less than 34 menstrual weeks gestation. **Methods:** 50 Pregnant women planned for sonographic detection of the distal femoral epiphyseal ossification center with the following inclusion/exclusion criteria: Inclusion criteria: 1) Singleton pregnancy. 2) Gestational age 28 weeks (calculated from reliable menstrual dates and/or late first-trimester or early second- trimester ultrasound scan). 3) four twin pregnancies. Exclusion criteria: 1) Diabetic women. 2) pregnant women with malformed fetuses. 3) Any cases showing fetuses with gross congenital anomalies, as hydrocephaly, microcephaly, or any neural canal defect. **Conclusion:** The results of the present study express the belief that the sonographic detection of the ossific center of the distal femoral epiphysis is a valid one in evaluating the fetal growth. The present study suggests the use of the ossific center of the distal femoral epiphysis detected sonographically, as a cross-sectional screening method for identification of intrauterine growth-retardation, together with biparietal diameter, head and abdominal circumferences, and femur length for more detailed evaluation.

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**Keywords:** DFE- Distal Femoral Epiphysis, Fetal age, Fetal weight, Ossification center

### 1. Introduction

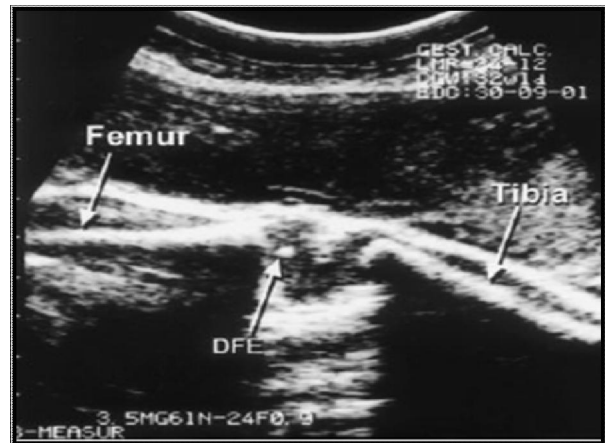
The mean age at DFE appearance is 32 to 33 weeks gestations, and it is not visualized before 28 weeks gestation<sup>(1)</sup>. In 94% of fetuses the DFE is observed at 34 weeks gestation. So if a DFE is not visualized, the fetus is most likely less than 34 menstrual weeks gestation<sup>(2,3)</sup>.

Distal Femoral Epiphysis is identified by locating the echogenic epiphyseal structure near the distal end of femur; and its measurement is obtained in an axial plane along the medio-lateral surfaces of the epiphyses from the outer to outer margins<sup>(4)</sup>.

Epiphyseal ossification centers appears in late gestational ages, when traditional biometric measurements are not accurate enough. So they can be a useful adjunct in determining gestational age in a pregnancy with unknown dates especially in third trimester. Reference charts for gestational age according to DFE have been published and are now used widely in some countries<sup>(4)</sup>.

More recently, Donne and Coworkers sought to verify the predictive value of the epiphysis ossification center measurements in estimating gestational age<sup>(1)</sup>. They confirmed that the presence of the distal femoral

epiphyses had a positive predictive value of 96% for indicating a pregnancy of at least 32 weeks or greater.



**Figure (1):** Longitudinal scan of the fetal knee 32 weeks after last menstrual period. Note the presence of the distal femoral epiphyseal ossification center (DFE)<sup>(5)</sup>.

### **Anatomy of the distal femoral epiphyseal ossification center:**

The embryonic development of the femur begins during week 4 of gestation, with the appearance of the limb bud. Rapid mesenchymal growth follows, and the endochondral ossification occurs during week 8. The femoral shaft is the primary ossification center. Secondary ossification, at the upper end, begins at the gestational age of 6 months. Ossification of the femoral head occurs at the age of 4-5 months. The distal femoral ossification center appears during month 7 of gestation.

### **Ultrasound:**

The distal femoral epiphysis is identified by visualizing the distal femur and locating the echogenic epiphysis.

Measurements are obtained in an axial plane from outer to outer margins along the medial lateral surfaces of the epiphysis<sup>(6)</sup>.

Both centers increase in size and are more echodense in appearance with progressive gestational age.

- < 28 weeks gestation - Not identifiable.
- At 33 weeks gestation - Observed in 72% of fetuses.
- At 34 weeks gestation - Observed in 94% of fetuses.
- Size of 1-2mm = Gestational age > 33 weeks (87% of fetuses).
- Size of 3mm = Gestational age > 37 weeks (85% of fetuses).

## **2. Patients and Methods**

This prospective study has been carried out in Sayed Galal University Maternity Hospital. The study was conducted on 50 pregnant women at Ultrasound scan ward, they planned for sonographic detection of the distal femoral epiphyseal ossification center with the following inclusion/exclusion criteria:

### **Inclusion criteria:**

- 1) Singleton pregnancy.
- 2) Gestational age 28 weeks (calculated from reliable menstrual dates and/or late first-trimester or early second- trimester ultrasound scan).
- 3) four twin pregnancies.

### **Exclusion criteria:**

- 1) Diabetic women.
- 2) pregnant women with malformed fetuses. 3) Any cases showing fetuses with gross congenital anomalies, as hydrocephaly, microcephaly, or any neural canal defect.

### **Procedures:**

**All cases selected for the study were subjected to the following:**

1. Full history, clinical examination (General and local) were done at 28<sup>th</sup> week of gestation.

2. Fasting blood sugar and postprandial were estimated to exclude diabetic pregnant woman.

3. Real time ultrasound scans were carried out with a GE Voluson E6 scanner, equipped with 2-5 MHz GE 4C-D convex probe (scan speed 1, 540 m/sec). Using ultrasound we evaluated the following:

### **Biparietal diameter (BPD) measurement:**

This is measured by sonographic transaxial plane at the widest portion of the skull, with the thalamus position in the midline. A leading edge to leading edge measurement will obtain from the first echo of the closer temporoparietalcalvarial table, to the first echo of the further temporoparietalcalvarial table.

### **Head circumference (HC) measurement:**

When the ultrasound transaxial scan shows the thalami well positioned in the midline. A dotted line will create by a digitizer, outlines the correct perimeter, just outside the hyperechoic calvarium to obtain the circumference measurement.

### **Abdominal circumference (AC) measurement:**

When the ultrasound transaxial scan shows the umbilical portion of the left portal vein, correctly positioned within the liver and equidistant from the lateral wall, a dotted line, created by digitizer, outlines the outer margin of the abdomen giving the abdominal circumference measurement.

### **Femur length (FL) measurement:**

The femur is measured along the long axis of the diaphysis with a straight measurement from end to the other, disregarding the curvature of the medial border of the femoral diaphysis.

### **Distal femoral epiphyseal ossification center detection:**

The distal epiphysis of the femur was identified by visualizing the femur, distinguishing its distal end, and locating the echogenic epiphyseal structure, for the presence or absence of the ossific center.

4. The fetal gestational age was estimated with the help of sonographic estimation of biparietal diameter measurement.

5. The fetal weight was calculated by a sonographic formula which had been reported by Hadlock et al giving the predicting fetal weight in grams.

**Log (Fetal weight in grams) = 1.304 + (0.05281xAC) + (0.1938xFL) - (0.004x ACxFL)**

6. All cases were followed up every week, a general and local examination, ultrasound examination for the detection of the ossific center of the distal femoral epiphysis, and calculation of both the fetal age and weight were carried on.

## **3. Results**

Analysis was performed on the date of 50 pregnant women between 28 to 40 weeks of gestation, 4 of them had twins and 46 were singleton

uncomplicated gestations, with mean maternal age of 27.5±5.1 years (Table 1).

The distal femoral epiphysis (DFE) is not visualized in 28 week's gestations. It appeared in a small proportion of the fetuses (3 of 50, 5%) as early as

the 29<sup>th</sup> week. The proportion of fetuses in which the DFE was detectable by ultrasonography increased dramatically to 56% at 33 weeks reaching 94% at 36 weeks, and 100% at 37 weeks gestation (Table 1).

Table 1. Distribution of gestational age according to DFE diameter.

| DFE (mm) GA (W) | 0  | 1 | 2  | 3 | 4  | 5  | 6  | 7  | 8 | 9 |
|-----------------|----|---|----|---|----|----|----|----|---|---|
| 28 W            | 50 |   |    |   |    |    |    |    |   |   |
| 29 W            | 47 | 2 | 1  |   |    |    |    |    |   |   |
| 30 W            | 42 | 2 | 6  |   |    |    |    |    |   |   |
| 31 W            | 40 | 4 | 6  |   |    |    |    |    |   |   |
| 32 W            | 38 |   | 12 |   |    |    |    |    |   |   |
| 33 W            | 22 |   | 24 | 3 | 1  |    |    |    |   |   |
| 34 W            | 8  |   | 28 | 6 | 4  | 2  | 2  |    |   |   |
| 35 W            | 6  |   | 30 |   | 6  | 6  | 2  |    |   |   |
| 36 W            | 3  |   | 15 | 8 | 10 | 8  | 6  |    |   |   |
| 37 W            |    |   | 8  | 6 | 18 | 10 | 8  |    |   |   |
| 38 W            |    |   | 2  | 4 | 10 | 18 | 8  | 6  | 2 |   |
| 39 W            |    |   |    | 4 | 8  | 16 | 10 | 8  | 4 |   |
| 40 W            |    |   |    |   |    | 10 | 18 | 10 | 6 | 6 |

DFE: distal femoral epiphyseal ossification center, GA: gestational age.

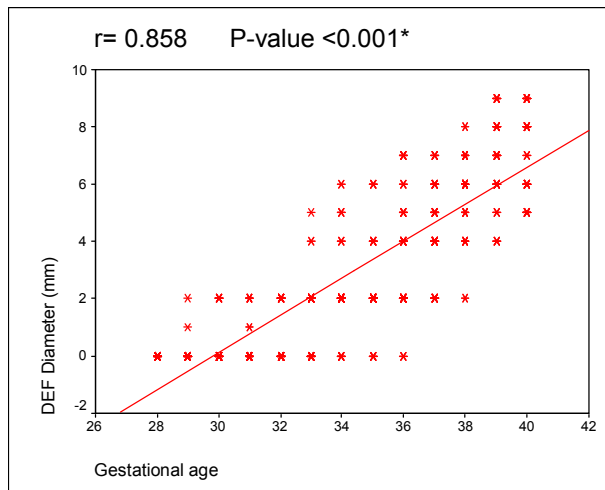


Figure 2. Distribution of gestational age according to DFE diameter.

Reference chart for gestational age according to DFE is summarized in Table 2. Mean DFE diameter in 29<sup>th</sup> week was 0.08±0.35 mm. The diameter increases with increment of gestational age in a way, that fetus with DFE ≥ 3 are almost always ≥ 33 weeks of gestation and fetuses with DFE ≥ 7 are almost always ≥ 36 weeks of gestation. Mean DFE diameter in 33<sup>th</sup> and 37<sup>th</sup> weeks were 1.28±1.32 and 4.53±1.62 mm, respectively.

Table 2. Mean DFE diameter in various gestational ages.

| Gestational age (w) | DEF Diameter Mean ±SD |
|---------------------|-----------------------|
| 28 W                | 0                     |
| 29 W                | 0.08±0.35             |
| 30 W                | 0.30±0.72             |
| 31 W                | 0.35±0.74             |
| 32 W                | 0.55±0.90             |
| 33 W                | 1.28±1.32             |
| 34 W                | 2.28±1.54             |
| 35 W                | 2.45±1.60             |
| 36 W                | 3.68±2.12             |
| 37 W                | 4.53±1.62             |
| 38 W                | 5.68±1.37             |
| 39 W                | 6.90±1.53             |
| 40 W                | 7.08±1.53             |

DFE: distal femoral epiphyseal ossification center, GA: gestational age

According to our chart third trimester's gestational age can be estimated by DFE diameter, table 3 (correlation coefficient=0.8). With DFE diameter of 0, 5 and 9 mm estimated gestational age would be 30.45±1.97, 37.52±2.00 and 39.59±0.51, respectively.

Table 3. Mean gestational age according to DFE diameter.

| DEF Diameter (mm) | Gestational age<br>Mean $\pm$ SD |
|-------------------|----------------------------------|
| 0                 | 30.45 $\pm$ 1.97                 |
| 1                 | 30.33 $\pm$ 1.15                 |
| 2                 | 33.99 $\pm$ 1.90                 |
| 4                 | 36.44 $\pm$ 1.58                 |
| 5                 | 37.52 $\pm$ 2.00                 |
| 6                 | 37.90 $\pm$ 1.64                 |
| 7                 | 37.97 $\pm$ 1.28                 |
| 8                 | 39.37 $\pm$ 0.68                 |
| 9                 | 39.59 $\pm$ 0.51                 |

DFE: distal femoral epiphyseal ossification center, GA: Gestational age.

Epiphyseal measurements are recorded in Table 4 for 46 single normal fetuses and 4 twins of the present investigation.

The distal femoral epiphysis was present in 100% of both normal fetuses and twins; the average diameter of the DFE was 4.7 mm in twins and 5.6 mm in normal fetuses. The measurements of the largest diameter exceeded 4 mm in 31 of 46 normal fetuses and in only 2 of twins fetuses (p equal to 0.005).

Table 4. Distal femoral epiphysis in relation to gestation and weight

| Source of data       | No. of Fetuses | Sex  |        | Gestations |           | Weight    | Distal femoral Epiphysis |                           |                            |
|----------------------|----------------|------|--------|------------|-----------|-----------|--------------------------|---------------------------|----------------------------|
|                      |                | Male | Female | Average    | Range     | Average   | Percent-age present      | Average Greatest diameter | Range of Greatest diameter |
| <b>Present study</b> |                |      |        | <b>wk</b>  | <b>wk</b> | <b>gm</b> |                          | <b>mm</b>                 | <b>mm</b>                  |
| <b>Normal</b>        | 46             | 28   | 22     | 39.48      | 36-40     | 3257      | 100                      | 5.57                      | 2-9                        |
| <b>Twins</b>         | 4              | 3    | 1      | 39         | 36-40     | 2415      | 100                      | 4.75                      | 1-7                        |

#### 4. Discussion

The results of this study indicates that the DFE ossification diameter varies 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.

In 28<sup>th</sup> week of gestation DFE would not be visualized in ultrasound examination, when DFE  $\geq$  3 mm fetus is almost always  $\geq$  33 weeks of gestation and fetus with DFE  $\geq$  7 mm is almost always  $\geq$  36 weeks of gestation.

In an Iranian population study of DFE, *Birang S* <sup>(7)</sup> emphasized the use of DFE as a marker for determining gestational age. A reference chart was also prepared for DFE. He showed the presence of DFE at 29 weeks of gestation in 5% and at 30 weeks of gestation in 15% as compared to ours.

*Donne*. <sup>(1)</sup> in a study on 3 ossification centers in Brazil showed that, Ultrasonographic visualization of the epiphysis ossification centers may be a useful marker of fetal gestational age. DFE appeared in a small proportion of the fetuses (6 of 36, 17%) as early as the 30<sup>th</sup> week compared with 29 week in this study.

DFE was detectable by ultrasonography in 71% at 32 weeks. Where in 72% of our 32 week study DFE was not visible by ultrasound, yet. In his study DFE was detectable in 100% of fetuses at 37 weeks gestation, just as ours.

In line with the results of this study, it has previously shown that the DFE is not visualized before

28 weeks gestation in american population and the mean age at DFE appearance is 32 to 33 weeks gestation 4. If a DFE is not visualized, the fetus is most likely less than 34 menstrual weeks gestation as the DFE is observed in 94% of fetuses at 34 weeks gestations <sup>(2)</sup>.

Moreover, a DFE of 3 mm or more is associated with a gestational age of greater than 37 weeks in 84% of fetuses <sup>(9)</sup>. It is comparable with the mean gestational age 36.71 in this study.

*WU et al.*, <sup>(3)</sup> has also reported that, 29 weeks gestation for first appearance of DFE in Chinese. However the DFE was detectable in 100% of fetuses at the end of 34 week, compared with 37 weeks in this study.

*Gentili et al.*, <sup>(5)</sup> reported that the fetal ossific centers become visible sonographically at different gestational ages; before 24 weeks, they are not detectable; the calcaneal ossification center is detectable at 24 weeks; the talar ossification center from 26 weeks, the distal femoral epiphyseal ossification center from 32 weeks; and the proximal tibial epiphyseal ossification center from 36 weeks <sup>(5)</sup>.

*McLeary et al.*, <sup>(8)</sup> reported a sonographic study of the distal femoral epiphyseal ossification center and observed that there is a good correlation between the ultrasonic appearance of the ossific center of the distal epiphysis, and its radiologic appearance. They also reported that the distal femoral epiphyseal ossification center begins to ossify at 30 weeks of gestation, and that incidence of ossification had increased to 100

percent by 38 weeks of gestation <sup>(8)</sup>.

**Goldstein et al.**, <sup>(9)</sup> confirmed the previous study and reported that the distal femoral epiphyseal ossification center was not identifiable before 28 weeks of gestation, it was observed in 100 percent of fetuses at 36 weeks of gestation of well dated pregnant women with uncomplicated gestation <sup>(9)</sup>.

The measurement of epiphyses ossification centers of long bones as markers of gestational age using radiography was first described 50 years ago. These studies were based on the findings of maternal abdominal x-rays carried out during pregnancy <sup>(10,14,2)</sup> and on x-rays of neonatal extremities <sup>(1)</sup>. However, the fear of exposing the fetus to radiation, the technical problem involved in visualizing the epiphyses ossification centers, and the large variability in the figures obtained led to the discontinuation of this method for determination of gestational age. The advent of ultrasonography, however, solved most of the technical problems encountered with radiography and eliminated the fear of fetal radiation <sup>(1)</sup>.

Ultrasound is able to identify each epiphyses ossification center at much earlier stage, as long as the diameter is at least 1 mm <sup>(2)</sup>.

As the epiphyseal ossification centers appear late in gestation, when traditional biometric measurements are the least accurate, they are a useful adjunct in determining gestational age and evaluating for IUGR in a pregnancy with unknown dates.

**Scott et al.**, <sup>(11)</sup> reported a sonographic study on 30 malnourished fetuses and observed that the DFE was absent in 37 percent (11 of 30) and in none of the normal fetuses.

**Gentili et al.**, <sup>(5)</sup> also reported that in IUGR fetuses there was a delay in the appearance or absence of the distal femoral epiphyseal ossification center in 66.6 percent of cases. The greatest retardation of ossification center growth was observed in cases of symmetrical IUGR.

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