

Widening of the femoral diaphysis-metaphysis angle at 20-24 weeks: a marker for the detection of achondroplasia prior to the onset of skeletal shortening

OBJECTIVE: Achondroplasia is the most common nonlethal skeletal dysplasia and, despite its autosomal dominant inheritance, most cases are sporadic, resulting from a de novo paternal mutation in the fibroblast growth factor receptor-3 gene.¹ We recently demonstrated that the femoral diaphyseal-metaphyseal angle (DMA) can be measured accurately by ultrasound.² We reported that in the third trimester the angle was on average 36% wider in those with achondroplasia than in normal fetuses, measuring >130 degrees in 83% of cases.² When compared with other antenatal ultrasound features, other than shortening of the long bones, such as macrocephaly and frontal bossing, a widened femoral DMA was the most consistent finding.² However, little is known about the DMA in the second trimester in fetuses with achondroplasia. The main challenge in the prenatal diagnosis of this condition is that the fetal biometry and anatomy are usually normal at the second-trimester anomaly scan, and the traditional ultrasound features are usually apparent only from approximately 25 weeks' gestation, which means that the diagnosis is usually late in pregnancy or indeed postnatal. Here we report the identification of a wide femoral DMA at the 20- to 23-week anomaly scan in fetuses with achondroplasia, weeks before the other ultrasound features of this condition become apparent.

STUDY DESIGN: Cases with achondroplasia (n = 4) confirmed in the third trimester or after birth and a group of normal fetuses (n = 164) were included in this case-control study. At 20⁺⁰ to 23⁺⁶ weeks' gestation the femoral angle between the diaphysis and the metaphysis was prospectively measured at a 45-degree insonation angle in the normal group. For the achondroplasia group images of femur length measurements taken at 20⁺⁰ to 23⁺⁶ weeks were retrieved and the femoral angle was retrospectively measured. Regression analysis was used to identify potential confounders that might affect the femoral DMA.

RESULTS: In the normal fetuses there was no significant relationship between the femoral DMA values measured at 20⁺⁰-23⁺⁶ weeks and the gestational age ($P = .175$) or femur length ($P = .664$). The gestational age at the scan was similar in the cases and controls (median, interquartile range [IQR]: 21.9, 20.6-22.0 vs 21.7, 21.4-21.9 weeks, $P = .283$). The median femoral DMA was significantly wider ($P < .001$) in fetuses with achondroplasia (125.0 degrees, IQR 119.8-131.8 degrees) than in the controls (95.0 degrees, IQR 88.0-99.0 degrees) (Figure). A wide femoral DMA at 20⁺⁰-23⁺⁶ weeks, defined as ≥ 120 degrees, was observed in all 4 fetuses with

achondroplasia. The likelihood ratio for achondroplasia was proportional to the femoral angle, increasing from 18.2 when the angle was >108.5 degrees (corresponding to the 95th centile) to 164.0 when the angle was >116.0 degrees.

CONCLUSION: Femoral DMA is wider than normal in fetuses with achondroplasia at 20-23 weeks' gestation. A widened femoral DMA represents a potential routine second-trimester screening marker for achondroplasia. Combined with noninvasive prenatal diagnosis, this could facilitate the routine diagnosis of this condition far earlier than is currently the case, which would have important clinical implications. A large multicenter prospective screening study will be required to ascertain its predictive performance, investigate the prevalence of a wide femoral DMA in the general population and any association with other pathologies. ■

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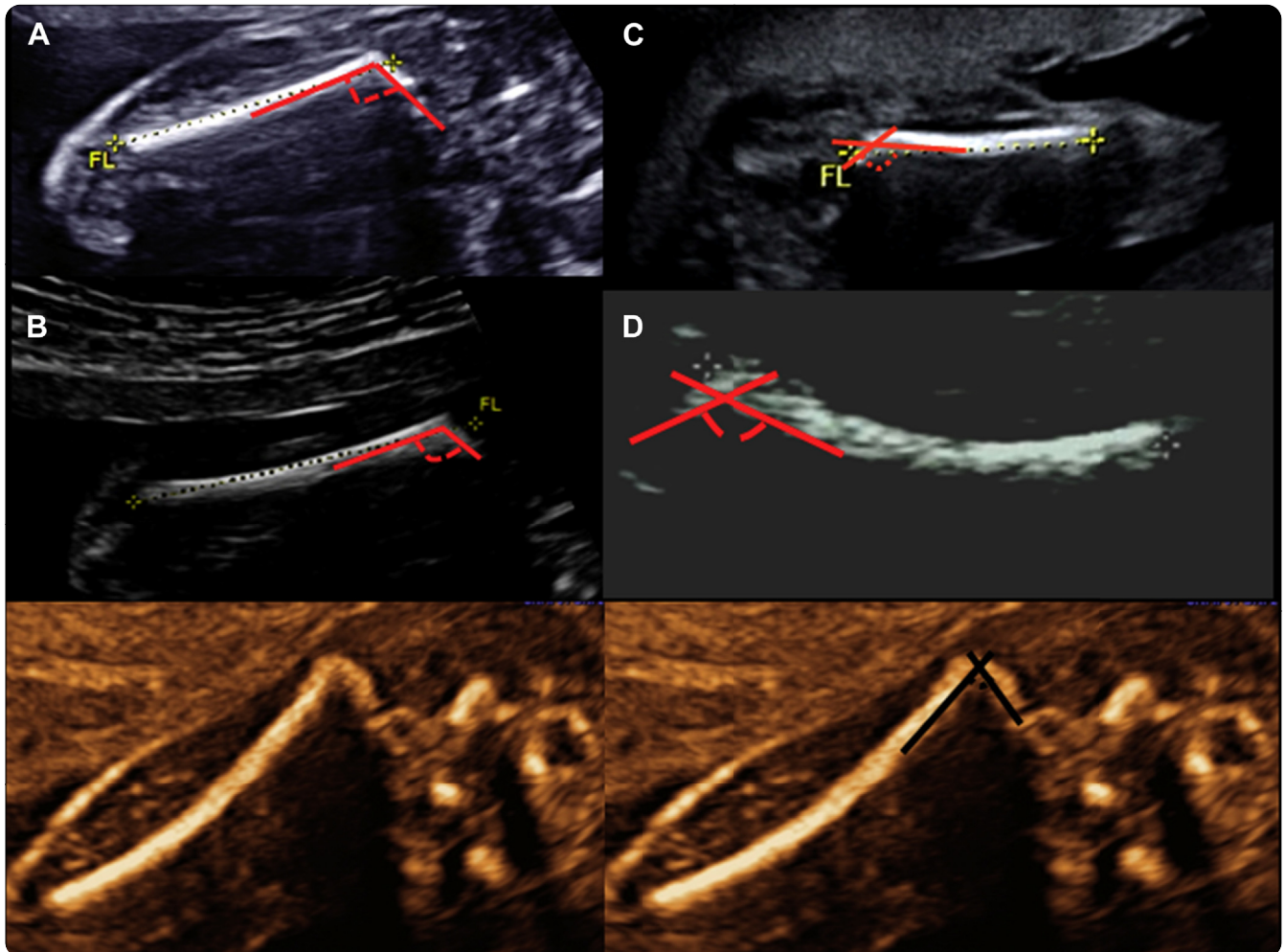
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FIGURE

The femoral angle at 20–24 weeks: in fetuses with achondroplasia



Two-dimensional ultrasound appearance of the femoral proximal diaphysis–metaphysis angle with the femoral angle measured with ultrasound probe positioned at 45 degrees to diaphyseal axis in a normal fetus at 20.4 weeks' gestation and in 4 fetuses with achondroplasia at **A**, 22.0, **B**, 21.9, **C**, 22.0, and **D**, 20.1 weeks' gestation.

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Prevalence of unexpected leiomyosarcoma at myomectomy: a descriptive study

OBJECTIVE: Electric morcellation of uterine fibroids at laparoscopy may cause intraperitoneal dissemination of occult leiomyosarcomas, with worsening of the already

poor prognosis.¹ According to the Food and Drug Administration (FDA) this may occur in 1/498 (0.2%) procedures.² Therefore, myoma morcellation is being