IMAGING

Screening for fetal spina bifida by ultrasound examination in the first trimester of pregnancy using fetal biparietal diameter

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OBJECTIVE: Prenatal screening for aneuploidies is best achieved in the first trimester when there is no reliable screening test for spina bifida. Early ultrasound features may be too complex for routine screening. We assessed screening potential of simple and reproducible fetal biometric measurements at 11-14 weeks of gestation.

STUDY DESIGN: A total of 34,951 unselected consecutive pregnancies included 18 with spina bifida. Another 28 cases were referred for assessment. Biometric measurements were expressed in multiples of the median for crown-rump length.

RESULTS: Biparietal diameter (BPD) was smaller in spina bifida ($P <$ .0001). In all, 22 of 44 (50%) cases with spina bifida aperta had a BPD $<$5th centile. BPD was independent of maternal adiposity and smoking status.

CONCLUSION: Simple and reproducible BPD at 11-14 weeks of gestation could detect half the cases of open fetal spina bifida by identifying 5% of pregnancies for expert scanning in first- and second-trimester examinations of the fetal spine and cranium.

Key words: biometry, biparietal diameter, myelomeningocele, prenatal diagnosis, ultrasound

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Since the introduction of routine antenatal screening, folic acid supplementation, and staple food fortification, the rate of neural tube defects at birth in developed countries has fallen substantially.[1] Screening is carried out in the second trimester of pregnancy either at 15-19 weeks, with maternal serum α-fetoprotein (AFP) alone or in a multimarker aneuploidy screening test,[2] or at the routine 18-24 weeks' anatomical scan, by direct examination of fetal structures or by "lemon" and "banana" cranial features of spina bifida.[3,4]

Increasingly, aneuploidy screening is now being carried out in the first trimester using maternal serum markers and ultrasound nuchal translucency (NT) at 11-14 weeks. At the time of the NT scan, acrania can readily be detected, and several studies have suggested that spina bifida could also be detected.[5-7] However, these studies were either in high-risk fetuses or carried out by highly skilled operators performing early detailed ultrasound examinations. Attempts at translating this expertise into a routine screening test remain unconvincing.[8,9]

We have also described anatomical features of the fetal brain visible by ultrasound at 11-14 weeks in cases with neural tube defects, but these observations failed to develop into a screening test.[10] In addition to these features, we noted that the head measurements of affected fetuses were small, but did not suggest this as a marker. In the current study, we considered whether such simple cephalic biometric measurements could be used as a screening tool for spina bifida.

Materials and Methods

We retrospectively reviewed all first-trimester biometrics performed routinely during the 11-14 weeks' ultrasound NT scan from April 2001 through July 2011 by 10 operators, all certified by the Fetal Medicine Foundation for first-trimester screening by ultrasound.

A total of 34,951 examinations were performed in 26,956 women, in which both crown-rump length (CRL) and biparietal diameter (BPD) had been recorded. Of these, head circumference (HC) was recorded in 34,389 and abdominal circumference (AC) in 34,273. The BPD and HC were measured on a transverse view of the fetal head in a plane showing both thalami and the third ventricle.[11] In this population, there were 18 fetuses with spina bifida, 10 with anencephaly, and 1 with encephalocele; therefore, a total of 29 neural

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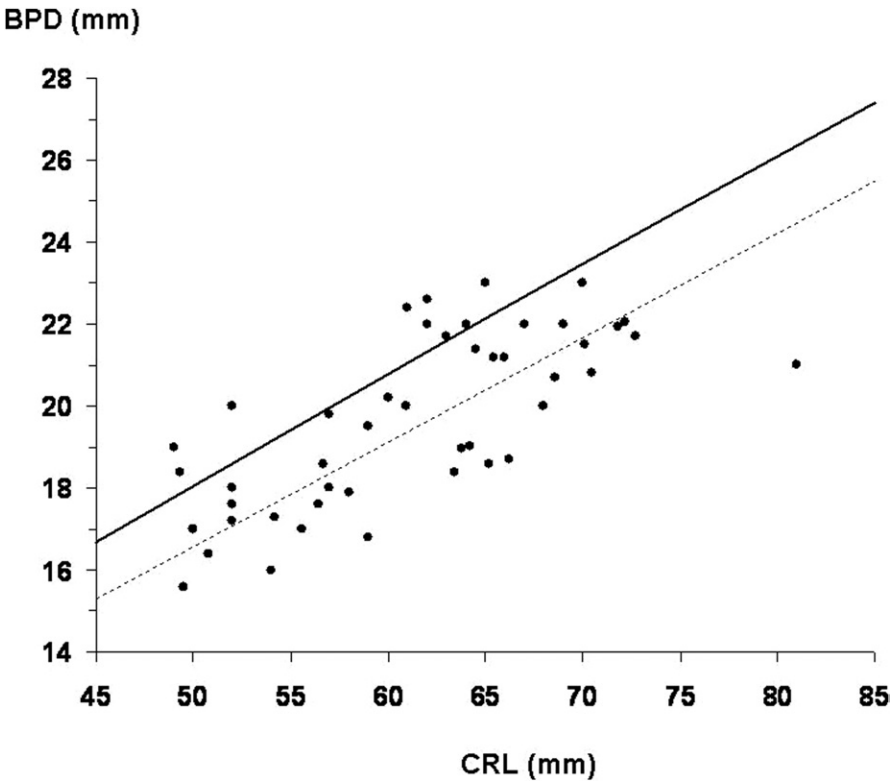
See Journal Club, page 340

FIGURE
BPD measurements in the cases of spina bifida



Biparietal diameter (BPD) and crown-rump length (CRL) measurements for 46 spina bifida cases together with published normal median curve ($3.622+0.3024*CRL-0.000269*CRL^2$)[11] and curve, broken line, corresponding to 5th centile in controls ($3.322+0.2773*CRL-0.000247*CRL^2$).

Bernard. Screening for spina bifida at 11-14 weeks. Am J Obstet Gynecol 2012.

tube defects. Three cases of spina bifida were diagnosed during the examination and an additional 15 cases missed at 11-14 weeks were diagnosed at 20-24 weeks of gestation. We refer to these 18 cases as group 1 of fetuses with spina bifida and the remainder as controls.

In addition, of 106 cases of fetal spina bifida referred to our fetal medicine unit in the second or third trimester of pregnancy during the same period, 28 had had well-documented biometrics at 11-14 weeks performed at the referring institution. We refer to these 28 cases as group 2 of fetuses with spina bifida.

In all 46 cases (groups 1 and 2) and 34,933 controls, the BPD, HC, and AC measurements were expressed as multiples of the median (MoM) for CRL. Following standard practice in antenatal screening, the marker level–the biometric measure–was divided by the expected value for unaffected pregnancies with the same CRL, based on a regression equation. We used our own published equations, derived from 880 unaffected singleton fetuses.[11] Information on body mass index (BMI) and whether or not the woman was a smoker was obtained from the clinical records of cases and controls. To determine if BMI was a covariable of BPD, the correlation coefficient of BMI and MoM was calculated, after excluding outliers >3 SD from the mean. Similarly, the median MoM was computed in smokers and nonsmokers. These were the only potential confounders that we could readily investigate as information on them was routinely collected in the aneuploidy screening database.

All cases were documented following delivery or termination of pregnancy for the upper level of the defect (thoracic, lumbar, or sacral), the presence of Arnold-Chiari malformation, and that of ventriculomegaly as measured (>10 mm) at the level of the atrium and malposition of the feet. Information was also available on mode of conception, gender, and pregnancy outcome.

The distribution of MoMs was compared in cases and controls on the basis of the median value and the proportions >5th centile in controls, the detection rate, and false-positive rate. The area under the receiver operating characteristic curve, the likelihood ratio of a positive result, and likelihood ratio of a negative result were also computed.

RESULTS

The Figure shows the individual BPD measurements for the 46 cases in relation to the published curve. There were 37 (80%) with values below the normal median, and the extent of reduction was not related to the CRL. The median BPD value in the cases was 0.929 MoM compared with the control median of 1.005 MoM, a highly statistically significant reduction ($P < .0001$, Wilcoxon rank sum test). There were 22 (48%) cases <5th centile for controls (0.917 MoM), including 8/18 (44%) in group 1 and 14/28 (50%) in group 2 ($P = .77$, Fisher exact test).

HC was also measured in 25 cases, with a median reduced to a similar extent to BPD (0.925 MoM compared with 0.991 MoM in controls; $P < .0001$) and 11 (44%) were <5th centile. AC was available in 20 cases and the median was slightly increased (1.032 MoM compared with 0.989 MoM in the controls; $P < .001$).

Two of the cases presented with spina bifida occulta and had normal BPD values of 0.95 and 1.03 MoM; among the remainder (spina bifida aperta), the proportion with BPD <5th centile was 50% (22/44). The area under the receiver operating characteristic curve for spina bifida aperta was 0.72, the likelihood ratio of a positive result was 10.9, and the likelihood ratio of a negative result was 0.48. The proportion of cases with a small BPD did not differ markedly with the fetal characteristics (Table). Furthermore, the 2 cases with spina bifida occulta had multiple associated anomalies.