**Zika virus: antenatal screening for microcephaly**

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**Objective**  
Most cases of Zika-related microcephaly in Brazil have only been diagnosed postnatally. This could be credited to deficiencies in access, equipment quality and training in prenatal ultrasound. The current unavailability/unreliability of routine serologic tests for Zika virus infection in pregnancy precludes its use as a primary screening method. On the other hand, sonographic measurement of head circumference is widely available, cost-effective, and reproducible even in the lack of top-quality equipment. This study aims to investigate whether this measurement could be used as a screening tool to select a proportion of cases that would benefit from referral for neurosonography in tertiary centers.

**Methods**  
A dataset of 117 head circumference measurements from 53 fetuses with prenatal diagnosis of microcephaly (study group) diagnosed during the Zika-virus outbreak in Brazil in 2015 was plotted on Intergrowth reference ranges and compared to a dataset of 1214 head circumference measurements from 240 normal fetuses (control group). Measurements in both groups from ranged from 18 to 40 weeks and were converted into Z-scores. Medians and proportions of cases with a head circumference below 2 SD were calculated for subgroups of gestational age allowing comparisons between cases and controls. A ROC curve for the detection of cases of microcephaly from 24w to 40weeks was plotted and detection rates (DR), false-positive rates (FPR) and positive likelihood ratios (LR+) for different cutoffs (-1.0 SD, -1.5SD, -2SD, -2.5 SD, -3 SD) were calculated.

**Results**  
The median Z-scores in the study group decreased with gestational age: -1.33 at 18-23+6w, -3.94 at 24-29+6w, -6.38 at 30-35+6w and -4.35 at 36-30w. Most cases of microcephaly presented additional ultrasound findings. The proportion of cases below -2SD was higher than in the controls in every gestational age subgroup, increasing with gestation: 25% (10/40) at 18-23+6w, 96.5% (28/29) at 24-29+6w, 96.8% (30/11) at 30-35+6w and 88.2% (15/17) at 36-30w. The ROC curve analysis in cases ≥ 24 weeks showed a detection rate of 100% for 9.7% false-positive rate (LR+ 10.3) when using a -1 SD cut, 100% DR for 4.4% FPR (LR+ 22.6) for a -1.5 SD cutoff, 95% DR for a 1.6% FPR (LR+ 57.9) for a -2.0 SD, 90% DR for a 0.8% FPR (LR+ 117.3) for a -2.5 SD cutoff and 84% DR for a 0.2% FPR (LR+ 386.6) for a -3.0 SD cutoff.

**Conclusion**

A single head circumference measurement from 24-40 weeks below -2 SD on Intergrowth reference in endemic areas for Zika virus infection would result in effective screening for prenatally diagnosed microcephaly with a 95% detection rate, requiring referral for neurosonography of only 1.6% of pregnancies. It remains to be studied whether this strategy would also be effective to identify postnatally diagnosed cases, which are likely to represent a less severe spectrum than those diagnosed prenatally.