Objective
Zika Virus infection has been implicated in the outbreak of microcephaly in Brazil in 2015. Microcephaly is known to be difficult to diagnose / rule out before the third trimester. This study aims to investigate whether a combination of ultrasounds that would be capable of effectively screen such cases in the second trimester.

Methods
This is a case-control study, comprising 36 fetuses with prenatal diagnosis of microcephaly (study group) diagnosed during the Zika-virus outbreak in Brazil in 2015 and 1961 normal fetuses (control group). A Head circumference measurement was obtained from 18 to 23+6 weeks of gestation and converted into Z-scores, according to Intergrowth reference, in all cases and controls. Head Circumference / Abdominal circumference and Femur Length / Head Circumference ratios were also converted into Z-scores, according to regression of these variables in the control group. In all cases, the presence or absence of additional ultrasound findings was recorded (ventriculomegaly, callosal disgenesis, posterior fossa abnormalities, club foot, arthrogryposis and calcifications). Cases and controls were screened as positive if one of these findings was present or if Head Circumference Measurement was below -2 SD (Intergrowth). Detection and false positive rates were estimated for this model and for a second model including the addition of a HC/AC ratio below -2 SD or a FL/HC ratio above 2 SD as further criteria.

Results
A Head circumference below -2SD was found in 25% (9/36) cases and in 4.5% (88/1961) controls. A HC/AC ratio below -2SD was found in 6.3% (3/36) cases and in 1.4% (28/1961) controls. A FL/HC ratio above 2SD was found in 25% (9/36) cases and in 2.9% (57/1961) controls. Additional ultrasound findings were found in 55% (20/36) cases, the most common being ventriculomegaly (19/36) cases. A model in which all cases with a HC < -2SD or presence of additional ultrasound findings are screened as positive would result in a 63.9% detection rate for a 4.5% false positive rate. The addition of a HC/AC ratio below -2 SD or a FL/HC ratio above 2 SD would increase detection rate to 69.4% at the expense of an increase of the false-positive rate to about 7.9%.

Conclusion
Screening for microcephaly in the second trimester has limited performance if limited to biometric evaluation. The focus should be on the identification of additional ultrasound findings. Head circumference ratios do not appear to contribute significantly for the improvement of screening.