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PRENATAL DIAGNOSIS OF MACROCEPHALY

- Macrocephaly is defined as a head circumference >2 SD?
 3SD? No consensus.
- Imitations in accuracy of US HC measurements and inconsistency between prenatal and postnatal growth curves.
- Most patients are non syndromic and have normal development.
- There is a need for a better tool for the diagnosis of macrocephaly and prognosis.



RESEARCH QUESTION

what is the connection between fetal brain volume, measured using a semi-automated MRI program, to neurodevelopmental scores at childhood?

METHODS

•Study design: Historical cohort study.



Setting:

- Volume of brain structures measured using coronal T2 MR imaging preformed at Sheba Medical Center between 2011-2017.
- Indication for MRI where extracranial pathologic findings on ultrasonographic evaluation or suspicion of macrocephaly, and a family member with an intracranial pathology.
- MR imaging was performed with a 1.5T system (Optima scanner), section thickness of 3 or 4 mm.
- Participants: inclusion criteria were neurosonogram and labor in Sheba, a good quality MRI scan, and a full history of the patient in Chameleon. Exclusion criteria were multifetal pregnancy, cranial malformation found on MRI, and absence of a full US examination.
 Rare disease- recruitment was in clusters, according to US head circumference findings: 95th percentile and 5-95th percentile.

Variables:

- **Exposure**: Brain volume measured in MRI (95th percentile, vs. 5-95)
- Outcome: Development of the child, measured using Vineland Adaptive Behavior score
- Potential confounders: Mother age, habits (smoking), diseases, medications

METHODS

- Data collection- both categorical and continuous variables:
- Maternal characteristics: age, diseases, medications, previous pregnancies, IVF, habits.
- Mode of delivery and antenatal and postnatal complications
- Abnormal fetal Echocardiogram, Nuchal translucency, Karyotype and CMA (categorical)
- Birth weight, length, head circumference (continuous)
- Apgar score (continuous)
- Developmental disorders
- Brain volume: categorical- >95th percentile or normal.
- Vineland Adaptive Behavior score

STATISTICS

Comparison of the Vineland score between the two groups (*t*-test for independent samples, or Mann-Whitney test, if normal distribution cannot be assumed).

Categorical variables- described as frequency and percentage.

 Continuous variables- described as average and standard deviation or median and interquartile range (according to their distribution).

 Multivariable analysis- linear regression (or logistic regression- normal vineland/abnormal)

 Choice of variables: variables that are found to be associated to the outcome (Pearson/Spearman correlation for continuous vs. continuous, or *t*-test/Mann-Whitney for categorical vs. continuous).

STUDY SIZE

- According to the principles of two tailed *t*-test, 0.05 significance, and 80% power.
- 2:1 control : macrocephaly ratio
- Vineland SD=15 (according to literature), normal distribution
- In order to show a difference of 10 points in Vineland score, we need to measure:
 - 27 macrocephalic fetuses
 - 54 normocephalic fetuses.

This research is not powered to show less than 10 points of difference between the groups!