HEALTHY BIRTH, GROWTH & DEVELOPMENT

Primary Microcephaly: Do All Roads Lead to Rome?

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Objectives

- Symmetric intrauterine growth restriction (IUGR) has a growth pattern where all biometric measurements are affected to the same degree.
- Asymmetric IUGR has growth with small abdominal circumference (AC) compared with other growth parameters:
  - Abnormal head circumference/AC (HC/AC) ratio
  - Abnormal femur length/AC (FL/AC) ratio.
- The objectives of this study were:
  1) To determine the joint probability distributions of growth parameters describing Weight-Length and Head-Circumference (WT/LEN/HC) from age 0 to 24 mo,
  2) To study symmetry across the 3 growth measures to provide useful quantitative guidance to Zika clinicians and researchers on measurements of individuals with a normal/mild-to-moderate/small head relative to other anthropometric measures.

Methods

- Joint parametric nonlinear mixed effects (NLME) model built for WTLLENHC.
- Several parametric models tested such as exponential growth with and without decelerating growth rate.
- Key element: to determine the potential correlations between various growth outcomes WTLLENHC.
- Limited covariate testing done including covariates such as country site, sex, and socioeconomic factors.
- Model fitted using QRPEM fitting engine in Phoenix NLME parallelized on 20 cores.
- Model goodness-of-fit assessed using graphical tools and simulation based diagnostics (VPC).
- Parameter uncertainty obtained from bootstrap resampling over Linux Torque Grid on Global Health Analytics Platform (ghap.io).

Results

- Joint nonlinear deceleration model for WTLLENHC best fit the data (115,000 observations from 1568 subjects) with full random effects variance-covariance matrix.
- Between-subject variability: range, 50% (weight rate of growth) to 10% (length at 0 mo).
- Overall good agreement between observed and simulated data (1 to 97 percentiles).
- Country and sex kept in the model.
- Parameter uncertainty < 30%.
- Model accurately simulated correlated longitudinal data of WTLLENHC from 0-24 months.
- Model accurately predicted probability of stunting and trajectories of HC growth including microcephaly conditional on WT and LEN.
- WT/HC, LEN/HC, and WTLLEN standards were generated by simulating from the model.

Conclusions

- Results address key aspect of characterizing WTLLEN/HC relations and predicting their evolution over time for a specific child, not just the population.
- Potential application of this model includes individualized bivariate or trivariate growth trajectories for early detection of serious conditions such as stunting and microcephaly.
- Microcephaly-disproportionate subpopulation may be identified for further study and intervention.

References


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