Reference Ranges for Head Circumference in Ethiopian Children 0–2 Years of Age

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BACKGROUND: **Head circumference (HC) charts are important for early detection of hydrocephalus during childhood. In low-income countries where population-based HC charts are rarely available, hydrocephalus occurs more commonly than in developed countries, and is usually not diagnosed early enough to prevent severe brain damage. This applies to Ethiopia as well. The World Health Organization (WHO) has provided standard HC charts advocated for global use, but recent studies cast doubts whether these charts are equally applicable in various populations. The aim of the study was therefore to establish reference ranges for early childhood HC in Ethiopia.**

METHODS: **In this prospective, observational cross-sectional study, measurements of HC were collected from healthy children of different ethnicities between birth and 24 months, in health centers situated in 5 Ethiopian cities. Reference ranges for HC were estimated using the LMS method and compared with those recommended by WHO.**

RESULTS: **A total of 4019 children were included. Overall, 6.7% of boys and 7.1% of girls were above the +2 standard deviation (SD) of the WHO reference ranges, whereas the corresponding figures below −2 SD were 2.8% and 2.1%. Similarly, the +2 SD lines of the Ethiopian reference curves were considerably higher than those of the WHO growth standards, whereas the median and −2 SD lines were more comparable.**

CONCLUSIONS: **Ethiopian HC reference ranges for children from birth to 24 months of age were found to differ significantly from those established by WHO and should correspondingly be considered as the first choice for screening for hydrocephalus in that population.**

INTRODUCTION

Hydrocephalus in early life is a congenital or acquired condition, in which there is a mismatch between production and elimination of cerebrospinal fluid, resulting in its accumulation and increased intracranial pressure. Untreated, this condition causes permanent brain damage.

In developed countries, pediatric hydrocephalus has a rather low occurrence rate; the incidence of congenital hydrocephalus has been estimated to be about 0.5 cases per 1000 live births.[1–3] A nationwide Norwegian study showed an overall prevalence of hydrocephalus to be 0.75 cases per 1000 live births[3] and similar figures have been found for Sweden [4] and other European countries.[5]

In Sub-Saharan Africa, the incidence and prevalence of hydrocephalus is believed to be much higher, most likely because hydrocephalus in these countries appears predominantly to be caused by central nervous system infections during the first months of life.[6] High numbers of congenital neural tube defects may be another contributing factor with spina bifida representing the highest burden of disease among surgical malformations.[7]

Key words
- Developing country
- Ethiopia
- Head circumference
- Hydrocephalus
- Neurosurgery
- Occipitofrontal circumference
- Pediatrics
- Screening

Abbreviations and Acronyms
HC: Head circumference
MGRS: Multicentre Growth Reference Study
SD: Standard deviation
WHO: World Health Organization

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Conservative estimates suggest a yearly incidence of 1.25 cases of pediatric hydrocephalus per 1000 births in East Africa when infectious causes are included.[8] Based on this estimate, one can expect approximately 3.500 new cases of hydrocephalus yearly for a total of 2.8 million births in Ethiopia. Our experience is that only a small fraction of these children, possibly <1%, are detected early enough to prevent brain damage.

Routine measurements of the head circumference (HC, also termed occipitofrontal circumference) have proved effective in the early detection of hydrocephalus; such routine measurements identify children with hydrocephalus more commonly than clinical symptoms.[3]

The World Health Organization (WHO) currently recommends the reference ranges established by their Multicenter Growth Reference Study (MGRS) for monitoring growth, including HC, in infants and young children.[9] These reference ranges are based on data collected in 6 countries (Brazil, Ghana, India, Norway, Oman, USA), and only included breastfed children born to nonsmoking mothers of high social classes. Although advocated as general standards for unrestricted child growth, they have been shown to be at variance compared with national or regional HC growth references.[10–13]

Ethiopian HC reference ranges do not exist. Thus, the aim of the present study was to establish HC reference ranges for Ethiopia and to compare them with corresponding WHO ranges.

SUBJECTS AND METHODS

The Ethiopian HC study was prospective and observational cross-sectional. Participants were recruited from October 2009 to July 2013 in 3 of the 26 hospitals in Addis Ababa and in 4 other cities (Mekele, Dessie, Nazret, and Dire Dawa) to obtain an ethnic diverse sample. A census in 2007 listed more than 80 well-defined ethnic groups.[14] Marriages usually occur within the same ethnic group, but the population of the capital Addis Ababa is a mixture of people coming from all over the country that grossly mirrors the ethnic composition of the national population.[14]

Children between 0 and 24 months who visited the health clinics for the purpose of 1) vaccination, 2) participation in a follow-up program concerning nutrition and human immunodeficiency virus prophylaxis, or 3) for a medical check-up because of an intercurrent medical problem, were considered eligible for inclusion. Children were not included if they had a parent with a non-Ethiopian ethnic background, a history of chronic illness or visible malnutrition problems, suspected or diagnosed intracranial expansive condition, known congenital condition related to the head or brain, or previous treatment for intracranial lesions.

Data collection

HC was measured as the maximal fronto-occipital circumference with a disposable paper measuring tape to the nearest 0.1 cm. The measurement was repeated 3 times and the mean value was used. Disposable measuring tape was chosen because paper does not stretch with use, has the smallest intraexaminer and interexaminer variation, is cheap, accessible, and in common use.[15] HC was recorded along with date of birth, gender, and ethnic background of the child, as obtained from a parent or caretaker. All measurements were taken by 4 of the investigators (E.B.A., M.I., M.W., T.M.)

Statistics

Data on HC were converted to standard deviation (SD) scores relative to the WHO's growth standard.[5] Cutoffs for extremely large or small HC was correspondingly defined as below −2 or above +2 SD scores. For a matching reference curve, the percentage of extremes is expected to be close to 2.3% in either case. A 95% confidence interval that excludes this expected percentage is equivalent to a statistical significant difference with a test probability of 5% (χ^2 test or proportions test).

Reference curves for HC were estimated with the LMS method.[16] The LMS method is a semiparametric method that uses the box-cox power transformation to normalize the distribution of the parameter of interest (i.e., HC) conditional on age. Smooth curves for the box-cox power (L), median (M), and coefficient of variation (S) are estimated for the whole age range. Models were initially selected by the change in deviance, and goodness-of-fit is assessed using several tests for normality of the model residuals. With the LMS coefficients, smooth percentile curves can be calculated from $C = M^*(1 + S^*Z)^{(1/L)}$ when $L \neq 0$, and $C = M^*\exp(S^*Z)$ when $L = 0$; where Z is the desired percentile expressed as the SD score. Measurements are converted to SD scores or z-scores from $z = [(y/M)^L - 1]/[L^*S]$ when $L \neq 0$, and $z = \log(y/M)/S$ when $L = 0$; where y is the measurement, and L, M, and S are the corresponding parameters for the child's age and sex.

The Ethiopian and the WHO MGRS curves are compared graphically. Overlap of 95% confidence intervals is a pragmatic method commonly used for assessing differences.[17] Standard errors and confidence intervals of the Ethiopian percentiles were estimated with the bootstrap samples, by drawing 500 samples with replacement from, and of equal size as, the observed dataset, and calculating the variance of the desired percentile over these samples. No such information has been published for the WHO growth standards. Using the reasonable assumption that standard errors of the WHO reference are equal or smaller than those of the Ethiopian curve, it can be shown that a WHO percentile, which is outside the 95% confidence interval of the corresponding Ethiopian percentile, is equal to a statistically significant difference with a 2-sided test probability of ≤5%.

Ethical considerations

The study was approved by the Addis Ababa University institutional review board (MFGC/058/07). A parent or caregiver of each participant gave oral consent after having received written information that explained the purpose of the study.

RESULTS

A total of 4043 healthy children were eligible for inclusion. Twenty-two children (13 boys and 9 girls) with an incorrectly recorded HC were excluded. Additionally, 2 parents refused participation, leaving data from 4019 children (2046 boys and 1973 girls) fit for analysis. According to recommendations, the sample was larger in the first year of life (Table 1).[18] The prevalence of children with a HC below -2 SD of the WHO standards was close to the expected number of 2.3%. However, the prevalence of children above +2 SD was significantly larger than expected, except in the oldest age group (Table 1).