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ORIGINAL ARTICLE

Pattern of head growth and nutritional status of microcephalic infants at early postnatal assessment in a low-income country

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Abstract

Objective: To determine the pattern of head growth and the early postnatal nutritional status of microcephalic infants in a low-income country.

Materials and Methods: A cohort study in Lagos, Nigeria in which the head growth of full-term singletons within the first postnatal check-up at 6-8weeks was evaluated using the latest World Health Organization (WHO)'s Child Growth Standards (WHO-CGS) for head circumference. Nutritional status of microcephalic infants at follow-up was also determined after adjustments for potential confounders.

Results: Of the 452 infants (male: 227) enrolled, microcephalic infants were 32 (7.1%) at birth and 34 (7.5%) at follow-up. However, while 401 (88.7%) remained normocephalic and 15 (3.3%) remained microcephalic at follow-up, 19 (4.2%) became microcephalic and 17 (3.8%) became normocephalic. Microcephalic infants were significantly underweight ($P < 0.001$), stunted ($P < 0.001$) and wasted ($P < 0.001$) at follow-up.

Conclusions: Regardless of their status at birth, microcephalic infants at 6-8weeks are likely to be undernourished by all nutritional indices suggesting that head circumference may serve as a complementary or default screening tool for early detection of undernourished infants in resource-constrained settings.

Key words: Developing country, early detection, head circumference, postnatal examination, undernutrition

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Introduction

Head circumference is well-established as a strong indicator for both brain development and nutritional status from birth to adulthood.[1,2] Microcephaly, defined as age/sex-specific head circumference more than 2 standard deviations (SDs) below the mean, is therefore, indicative of poor brain development and associated with several neurodevelopmental problems such as mental retardation, cerebral palsy, epilepsy and intellectual disabilities.[2-5] By the time of onset, microcephaly can be congenital or postnatal underpinned by several genetic and environmental factors.[1] For example, undernutrition during infancy causes delayed head growth and impairs brain development while poverty and deprivation exacerbate these adverse effects in poorly-resourced settings.[2,4,5] Children particularly with severe and protracted undernutrition as infants are likely to remain microcephalic as adults.[2] There is also ample evidence to suggest that microcephalic infants may be at risk of undernutrition especially as a result of inappropriate dietary intake and oral motor dysfunction.[6]

Very limited studies from the developing world have been published describing the trajectory of head growth from birth in individual infants or ascertaining the nutritional status of infants at various stages of head growth after birth.[3,4]

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Additionally, studies based on the latest child growth standards of the World Health Organization (WHO-CGS) for head sizes derived from exclusively breastfed reference populations are sparse.[7] This study therefore set out to partly address these gaps based on secondary analysis of a previously reported cohort of infants recruited during one of the earliest universal newborn hearing screening (UNHS) programs in Africa.[8]

Materials and Methods

This retrospective cohort study was conducted at the Lagos Island Maternity Hospital (LIMH), Lagos, Nigeria from May 2005 to December 2006. LIMH is a tertiary hospital located in an inner-city area with an estimated population of 250,000. The hospital is owned and managed by the state government as a public health institution. It is the oldest maternity hospital in metropolitan Lagos providing specialist services to several private and public hospitals within and outside its catchment area. The eligibility criterion was full-term (37 or more gestational weeks) singletons over the study period who returned for the routine post-natal check at 6-8 weeks or for any other reason within the first three months of life. Preterm infants were excluded as no provision has been made for them in the WHO-CGS while multiple gestations were excluded because of their confounding effects. Ethical approval was obtained from the Lagos State Health Management Board, Nigeria and University College London, UK.[8]

Anthropometric measurements (head circumference, weight and length) were obtained at enrolment shortly after birth and at follow-up visit by a research assistant trained by the principal investigator (a pediatrician) and specifically assigned to this task throughout the duration of the study. Head circumference (occipito-frontal circumference) was measured with a standard non-stretchable lasso tape (1mm increments) [Child Growth Foundation, London, UK]. The head circumference was measured by passing the tape between the supraorbital ridges and the maximum occipital prominence. Weight was measured with a digital scale (10 g increments) [TANITA Baby Scale, Model 1583; Tanita Corporation, Tokyo, Japan] while length was measured supine using graduated polyurethane plastic mats (1mm increments) [Child Growth Foundation, UK] with the baby naked and feet uncovered.

Gender-specific *z*-scores for head circumference were obtained from the software macro provided by WHO for all child growth standards. Each *z*-score represents the difference between the head circumference of a child and the median head circumference of a reference population (for the same age and sex) divided by the standard deviation of the reference population used by the WHO-CGS. Default settings in the software regarding cut-offs for out-of-range or biologically improbable values were used in the data analysis and all such values were recorded as missing data. Microcephaly was defined as *z*-score < -2 while macrocephaly was defined as *z*-score > 2. Z-scores between -2 and 2 were considered to be within the "normal" range or "normocephalic". Similarly, the nutritional status of the infants at follow-up was determined with the appropriate WHO growth standards. Nutritional indices of interest were length-for-age (HAZ), weight-for-age (WAZ) and body-mass-index (zBMI) expressed as *z*-scores. WAZ, HAZ and zBMI < -2 were termed as "underweight", "stunting" and "wasting" respectively. In order to reflect the comorbidity of all the three nutritional deficits a composite variable termed "any undernutrition" was introduced.

The characteristics of the study participants of interest were maternal age, height, marital status, education, social class, parity, antenatal care, hypertensive conditions (including pre-eclampsia, eclampsia and pregnancy induced hypertension), HIV status as well as infant factors such as intrauterine growth restriction (IUGR), Apgar scores at 5 min, hyperbilirubinemia, admission into special care baby unit (SCBU) at birth and mode of feeding. Maternal height below 152.4 cm (5ft) was classified as short stature. Social classes were determined based on mother's education and father's occupation as validated by Olusanya *et al.*[9] SCBU admission is a useful surrogate for adverse perinatal conditions that cannot be readily ascertained in hospital-settings with limited facilities for clinical/laboratory investigations.

Statistical analysis

The postnatal status of the infants were categorized into four: infants with normal head size at birth and at follow-up (termed "nomocephalic"), infants with small head size at birth and at follow-up (termed "congenital microcephaly"), infants with normal head size at birth but small head size at follow-up (termed "acquired microcephaly") and infants with small head size at birth but normal head size at follow-up (indicative of "catch-up growth" or "normalized microcephaly"). Maternal and infant characteristics associated with these four groups were first explored by descriptive analysis. Thereafter, separate logistic regression models were built to determine the relationship between microcephaly (congenital and acquired) at follow-up with each of the nutritional indices adjusting for maternal age, maternal height, antenatal care, IUGR, SCBU admission and mode of feeding. The choice of factors was guided by biological plausibility and evidence from the literature.[10-12] Strength of association was estimated by odds ratios (OR) and the corresponding 95% confidence intervals (CI). Significance level was set at 5 percent and only two-tailed p-values were reported. Model calibration was assessed with Hosmer-Lemeshow

test. SPSS for Windows version 16.0 (SPSS Inc, Chicago, IL, USA) was used for all statistical analyses.

Results

Of the 3196 term singletons enrolled at birth, 503 (15.7%) presented for the first routine postnatal checkup within the study period. The analysis suggests that the mother-infant pairs who returned at follow-up were significantly less likely to be associated with lack of antenatal care, hypertensive disorders, IUGR, hyperbilirubinemia and SCBU admission. After excluding those with complete anthropometric data or macrocephalic infants and one infant with craniofacial anomaly a total of 452 (male: 227) infants were studied. Of this group, 401 (88.7%) were normocephalic, 15 (3.3%) had congenital microcephaly, 19 (4.2%) had acquired microcephaly and 17 (3.8%) exhibited catch-up growth to normocephaly. In this same cohort, 32 (7.1%) overall were microcephalic at birth and 34 (7.5%) at follow-up. The mean (±SD) age at enrolment and follow-up was 1.5±2.3 days and 47.9±13.9 days respectively. Of the 11 infants detected with macrocephaly at follow-up, none was microcephalic at birth.

The profile of these four groups is presented in Table 1. A descriptive analysis suggests that teenagers were less likely to have microcephalic offspring at follow-up while mothers with short stature were more likely to have offspring with acquired microcephaly. Infants without catch-up growth were likely to belong to mothers with primary or no education and mothers with hypertensive disorders. Offspring of HIV-positive mothers were only likely to be associated with congenital microcephaly. Microcephalic infants not exclusively breastfed were unlikely to experience catch-up growth. Of the microcephalic infants who returned for follow-up none had hyperbilirubinemia. At least half of the infants with microcephaly or catch-up growth were delivered by primiparous mothers while almost one-third (31.6%) of infants with catch-up growth had 5-min Apgar scores, which are low.

Regardless of their status at birth, microcephalic infants at follow-up were significantly ($P < 0.001$) associated with undernutrition based on all nutritional indices with or without adjustment for confounders [Table 2]. The odds for being underweight were highest. All the logistic models were satisfactorily calibrated as shown by the p-values for Hosmer-Lemeshow test.

Discussion

This study has demonstrated that the overall prevalence rates of microcephaly at two time intervals are likely to mask clinically important individual variations in the pattern of head growth status of some infants and the underlying etiological factors. For instance, while only a marginal increase was recorded in the prevalence of microcephaly at follow-up, the affected infants actually consisted of a heterogeneous group of those with congenital and acquired microcephaly but without providing information on the group who experienced catch-up growth. This finding underscores the need for close monitoring of the pattern of growth from birth for the early detection of those with persistent subnormal head size that is either congenital or of post-natal onset. It is pertinent to mention that small head size may also be constitutional and inevitable in some infants and highly correlated with maternal head circumference which though was not elicited in this study.[2] While special efforts were made to minimize measurement errors resulting from possible shape distortion and scalp edema in the newborns at birth, it was not unlikely that excessive molding in some infants would have contributed to the reported incidence of congenital microcephaly considering that over half of the mothers of microcephalic infants were primiparous.

Another notable finding is that infants with congenital or acquired microcephaly were significantly associated with all measures of nutritional deficits consistent with the established link between head size, brain function and body growth.[1,2,13] Skull et al, also reported a significant association between wasting and microcephaly independent of IUGR in a cohort of aboriginal children admitted into a tertiary Australian hospital within the first two years of life but did not investigate the relationship with underweight.[14] Early infancy undoubtedly constitutes a window of vulnerability during which nutritional deprivation may have irreversible consequences in the absence of timely intervention. However, a major challenge in many resource-poor countries is the lack of reliable scales requiring periodic calibration for accurate weight monitoring especially outside hospital settings. The evidence from this study would suggest that the use of standard inexpensive non-stretchable lasso tape for measuring head circumference can serve as a valuable default screening tool for the early detection of undernourished infants. Head size monitoring also has additional utility because of its high correlation not just with brain volume but equally with a child's intelligence quotient and scholastic achievement in subsequent years.[2,5]

A key limitation of this study is the selection bias as there were significant differences between infants who returned for the postnatal check-up in the same hospital and those who did not. The fact that a significant proportion of SCBU graduates and infants who were treated for hyperbilirubinemia prior to discharge did not return is not altogether surprising because it may be possibly due to the extended stay after delivery or death of the infant. For example, it is most likely that the poor return rate

Table 1: Maternal and infant characteristics associated with early head growth changes in full-term singletons at 6-8 weeks postnatal assessment based on WHO-CGS

Factors	Total (n = 452)	Pattern of head size between birth and at follow-up			
		Normocephaly[1] n = 401	Congenital microcephaly[2] n = 15	Acquired microcephaly[3] n = 19	Normalized microcephaly[4] n = 17
Maternal					
Age (years)[a]					
< 20	6	5 (83.3)	0 (0.0)	0 (0.0)	1 (16.7)
20-35	383	344 (89.8)	12 (3.1)	15 (3.9)	12 (3.1)
> 35	61	50 (82.0)	3 (4.9)	4 (6.6)	4 (6.6)
Short stature (< 152.4 cm)[b]					
Yes	24	21 (87.5)	0 (0.0)	3 (12.5)	0 (0.0)
No	422	374 (88.6)	15 (3.6)	16 (3.8)	17 (4.0)
Marital status					
Unmarried	5	1 (20.0)	2 (40.0)	1 (20.0)	1 (20.0)
Married	447	400 (8.9)	13 (2.9)	18 (4.0)	16 (3.6)
Education					
None/primary	32	30 (93.8)	1 (3.1)	1 (3.1)	0 (0.0)
Secondary	227	197 (86.8)	10 (4.4)	11 (4.8)	9 (4.0)
Tertiary	193	174 (1.0)	4 (2.1)	7 (3.6)	8 (4.1)
Social class					
Low	61	53 (86.9)	1 (1.6)	4 (6.6)	3 (4.9)
Middle	308	272 (88.3)	12 (3.9)	13 (2.0)	11 (3.6)
High	83	76 (91.6)	2 (2.4)	2 (2.4)	3 (3.6)
Parity					
Primiparous	264	231 (87.5)	8 (3.0)	16 (6.1)	9 (3.4)
Multiparous	188	170 (90.4)	7 (3.7)	3 (1.6)	8 (4.3)
Antenatal care					
None	80	67 (83.8)	4 (5.0)	8 (10.0)	1 (1.2)
One or more visits	372	334 (89.8)	11 (3.0)	11 (3.0)	16 (4.3)
Hypertensive disorders					
Yes	12	10 (83.3)	1 (8.3)	1 (8.3)	0 (0.0)
No	440	391 (88.9)	14 (3.2)	18 (4.1)	17 (3.9)
HIV-positive					
Yes	17	15 (88.2)	2 (11.8)	0 (0.0)	0 (0.0)
No	435	386 (88.7)	13 (3.0)	19 (4.4)	17 (3.9)
Infant Fetal growth restriction					
Yes	20	11 (55.0)	2 (10.0)	4 (20.0)	3 (15.0)
No	432	390 (90.3)	13 (3.0)	15 (3.5)	14 (3.2)
Apgar < 7 at 5 min					
Yes	111	98 (88.3)	3 (2.7)	4 (3.6)	6 (5.4)
No	341	303 (88.9)	12 (3.5)	15 (4.4)	11 (3.2)
Hyperbilirubinemia					
Yes	7	7 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No	445	394 (88.5)	15 (3.4)	19 (4.3)	17 (3.8)
Admission for special care					
Yes	29	26 (89.7)	1 (3.4)	1 (3.4)	1 (3.4)
No	423	375 (88.7)	14 (3.3)	18 (4.3)	16 (3.8)
Feeding mode					
Non-exclusive breast	69	60 (87.0)	6 (8.7)	3 (4.3)	0 (0.0)
Exclusive breast	383	341 (89.0)	9 (2.3)	16 (4.2)	17 (4.4)

1 = Normal head size at birth and at follow-up; 2 = Small head size at birth and at follow-up; 3 = Normal head size at birth but small head size at follow-up; 4 = Small head size at birth but normal at follow-up. Missing data: [a] = 2 (0.4%); [b] = 6 (1.3%)

Table 2: Nutritional status of infants with congenital and acquired microcephaly compared with normocephalic infants at 6-8 weeks postnatal checkup

Nutritional indices	Unadjusted models		Adjusted models	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Underweight (zWAZ < -2)[1]	25.21 (11.19-56.80)	< 0.001	22.70 (9.39-54.89)	< 0.001
Stunted (zHAZ < -2)[2]	12.72 (6.00-27.03)	< 0.001	10.48 (4.66-23.59)	< 0.001
Wasted (zBMI < -2)[3]	9.00 (3.62-22.38)	< 0.001	9.13 (3.34-24.93)	< 0.001
Any undernourishment[4]	15.51 (7.04-34.17)	< 0.001	13.61 (5.90-31.40)	< 0.001

[1,2,3,4]Models adjusted for maternal age, maternal height, antenatal care, Fetal growth restriction, Admission into special care baby unit and feeding mode; CI = Confidence interval. Hosmer-Lemeshow test: Model 1 [*P* = 0.305]; Model 2 [*P* = 0.617]; Model 3 [*P* = 0.960] and Model 4 [*P* = 0.603]

accounted for the lack of hyperbilirubinemia among microcephalic infants at follow-up in this study and in sharp contrast to an earlier finding (unpublished data) in which infants with congenital microcephaly out of a total enrolment of 3196 were significantly associated with hyperbilirubinemia. It was most likely that infants who were (still) sick after discharge would have been taken to the nearby exclusive children's hospital rather than return to this specialist maternity hospital with limited in-patient pediatric facilities. It may also be useful in future studies to explore the relationship between the quality of antenatal care received and failure to return for the postnatal checkup. However, the effects of the selection bias were adequately accounted for in the logistic regression modeling for the nutritional deficits.

Another limitation is that the study was not adequately powered to explore the factors significantly associated with the four groups of head growth. For example, it would have been useful to identify predictors or contributors to catch-up growth between birth and the early postnatal follow-up to guide intervention for infants detected with microcephaly at birth. Similarly, the knowledge of the risk factors for acquired microcephaly would have facilitated the proactive management of infants with early warning signs. Mothers who are likely to default in presenting for the routine postnatal visits as demonstrated in this study should be specially tracked before and after discharge for the benefit of their offspring. Finally, while early-postnatal growth status at approximately 6-8 weeks provide opportunity for early detection and intervention, not all cases of progressive or acquired microcephaly would be detected within this time interval. Although the first year often represents the period of the fastest growth and greatest vulnerability for head size and brain development, postnatal onset microcephaly in some infants may only be apparent by 2 years of age.[3] On-going surveillance especially in the first two years of life should therefore be considered as far as practicable. Overall, this study demonstrates the value of routine monitoring of head size besides its well-established utility as surrogate for birth weight in poorly-resource settings.

References

1. Illingworth RS, Eid EE. The head circumference in infants and other measurements to which it may be related. Acta Paediatr Scand 1971;60:333-7.
2. Ivanovic DM, Leiva BP, Pérez HT, Olivares MG, Díaz NS, Urrutia MS, *et al*. Head size and intelligence, learning, nutritional status and brain development. Head, IQ, learning, nutrition and brain. Neuropsychologia 2004;42:1118-31.
3. Ashwal S, Michelson D, Plawner L, Dobyns WB; Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Practice parameter: Evaluation of the child with microcephaly (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2009;73:887-97.
4. Committee on Nervous System Disorders in Developing Countries (CNSDDC), Board on Global Health. Neurological, psychiatric and developmental disorders: Meeting the challenge in the developing world. Washington DC: National Academy Press; 2001. p. 113-76.
5. Stoch MB, Smythe PM, Moodie AD, Bradshaw D. Psychosocial outcome and CT findings after gross undernourishment during infancy: A 20-year developmental study. Dev Med Child Neurol 1982;24:419-36.
6. Marchand V, Motil KJ; NASPGHAN Committee on Nutrition. Nutrition support for neurologically impaired children: a clinical report of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr 2006;43:123-35.
7. WHO Multicentre Growth Reference Study Group. WHO child growth standards: head circumference-for-age, arm circumference-for-age, triceps skinfold-for-age and subscapular skinfold-for-age: methods and development. Geneva: WHO; 2007. Available from: http://www.who.int/childgrowth/standards/second_set/technical_report_2.pdf. [Last accessed on 2011 Apr 26].
8. Olusanya BO. Newborns at risk of sensorineural hearing loss in low-income countries. Arch Dis Child 2009;94:227-30.
9. Olusanya O, Okpere E, Ezimokhai M. The importance of social class in voluntary fertility. West Afr J Med 1985;4:205-12.
10. Krauss MJ, Morrissey AE, Winn HN, Amon E, Leet TL. Microcephaly: an epidemiologic analysis. Am J Obstet Gynecol 2003;188:1484-9; discussion 1489-90.
11. McElrath TF, Allred EN, Kuban K, Hecht JL, Onderdonk A, O'Shea TM, *et al*. Factors associated with small head circumference at birth among infants born before the 28th week. Am J Obstet Gynecol 2010;203:138.e1-8.
12. Wolf MJ, Wolf B, Bijleveld C, Beunen G, Casaer P. Acquired microcephaly after low Apgar score in Zimbabwe. J Trop Pediatr 1999;45:281-6.
13. Rosman NP, Tarquinio DC, Datseris M, Hou W, Mannheim GB, Emigh CE, *et al*. Postnatal-onset microcephaly: pathogenesis, patterns of growth, and prediction of outcome. Pediatrics 2011;127:665-71.
14. Skull SA, Ruben AR, Walker AC. Malnutrition and microcephaly in Australian aboriginal children. Med J Aust 1997;166:412-4.

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