Original Article

Maternal antecedents of infants with abnormal head sizes in southwest Nigeria: A community-based study

Bolajoko O. Olusanya

Department of Community Health and Primary Care, College of Medicine, University of Lagos, Surulere, Lagos, Nigeria

Address for correspondence: Dr. Bolajoko O. Olusanya, Director, Healthy Start Initiative, 286A Corporation Drive, Dolphin Estate, Ikoyi, Lagos, Nigeria. E-mail: boolusanya@aol.com

ABSTRACT

Objective: To identify the socio-demographic antecedents and pregnancy-related history of infants with abnormal head sizes in a developing country. **Materials and Methods:** An observational study of mother–infant pairs attending routine immunization clinics in an inner-city community in Lagos, Nigeria. Age and gender-specific head circumference was determined with the current Child Growth Standards of the World Health Organization (WHO). Factors independently associated with any abnormal head size (z-score <-2SD or >2SD), based on the adjusted odds ratio (OR) and 95% confidence interval (CI), were explored with multiple logistic regression analyses. **Results:** Of the 5731 mothers studied, 730 (12.7%) had an offspring with an abnormal head size. In the final regression model, teenage mothers (OR:1.86; CI:1.26 – 2.75), mothers with primary or no education (OR:1.65; $P = 0.007$), multiple pregnancies (OR:3.88; CI:2.53 – 5.95), and delivery in either private hospitals (OR:1.54; CI:1.22 – 1.95) or residential homes (OR:1.50; CI:1.05 – 2.14), compared to government hospitals, were significantly more likely to have offsprings with abnormal head sizes. **Conclusions:** Community-oriented public health education, targeting prospective mothers with multiple pregnancies, teenage girls, and women with little or no formal education on the potential risk of delivery outside public hospitals, may curtail the burden of abnormal head size of their offspring and reduce the pressure on the already overstretched rehabilitation services in resource-poor countries.

Key words: Developing country, early detection, growth monitoring, head circumference, WHO growth standard

INTRODUCTION

Abnormal head size (very small or very large) at birth or in early infancy is a strong indicator of intrauterine disturbances accompanied by fetal growth restriction, maternal and fetal malnutrition, as well as being a precursor to diverse neurodevelopmental disorders, such as, cerebral palsy, epilepsy, mental retardation and autistic spectrum disorders, in childhood, as well as, a poor quality of life in adulthood.[1-6] This poor growth status is underpinned by a cluster of genetic and environmental factors that cannot be completely prevented or effectively addressed in many developing countries,[4,5] while routine screening for genetic disorders are generally lacking, partly as a result of socio-cultural barriers.[7] However, an understanding of the maternal antecedents of this condition could be valuable in designing intervention programs toward curtailing the overall burden, including reducing the demand on the already overstretched and poorly funded community-based rehabilitation services in developing countries.[8]

The bulk of evidence in the literature on abnormal head sizes is derived from case reports or studies with small samples, predominantly in hospital settings.[8] For example, a simple query of major databases such as PubMed with the search terms, 'head size', 'head circumference', 'microcephaly' or 'macrocephaly,' and 'developing country' yields very limited population / community-based studies, particularly in such regions as South Asia and Sub-Saharan Africa, where the vast majority (up to 90%) of babies are born outside hospitals.[9] Available reports are also based on various local growth standards and classification methods that make comparison difficult.

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In 2007, the World Health Organization released an international Child Growth Standard for head circumference (termed 'WHO-CGS'), to facilitate comparable studies worldwide and draw attention to the needs of children with abnormal head sizes from birth to the age of five years.[10] This study, therefore, sets out to estimate the prevalence of abnormal head sizes in early infancy using the WHO-CGS, and to identify the maternal socio-demographic antecedents of the affected infants, in a community-based setting in Southwest Nigeria.

MATERIALS AND METHODS

Study design and population

This is a cross-sectional, observational study of mother–infant pairs recruited under a previously reported universal newborn / infant hearing screening (UNHS) program in an inner-city community in Lagos, Nigeria, from July 2005 to April 2008![11] This community of about 250,000 people is served by one general hospital, one children's hospital, one specialist maternity hospital, and seven primary healthcare centers, all of which are State-owned. There are also several private hospitals and traditional maternity homes. The participants consisted of all infants (0 – 3 months old) attending their first immunization clinics for Bacille Calmette-Guérin (BCG) shortly after birth, at four primary healthcare or well-child centers. As previously reported, because of the clashes in the times of the immunization clinics, these four centers with the highest number of immunizations, based on the official health records, were selected.[11] The BCG and Diphtheria-Pertussis-Tetanus (DPT) vaccinations in the first three months of life have the highest uptake in sub-Saharan Africa, usually in excess of 80%.[9] Considering that the WHO-CGS is designed for full-term infants, all preterm infants (< 37 weeks gestation) were excluded from the current study. Ethical approval was obtained from the Lagos State Health Management Board, Nigeria, and University College London, UK, as part of the primary UNHS program. Informed consent was obtained from all participating mothers in writing or with their thumb prints before enrolment.

Anthropometry and case definition

Head circumference (occipitofrontal circumference) for each child was measured with a standard non-stretchable lasso tape (1 mm increments) [Child Growth Foundation, London, UK], at enrolment. One research assistant recruited and trained by this author (a developmental pediatrician) carried out the measurement throughout the study period. The head circumference was measured by passing the tape between the supraorbital ridges and the maximum occipital prominence. Gender-specific z-scores for head circumference were obtained from the macro provided by the WHO.[12] Each z-score represented the difference between the head circumference of a child and the mean 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. Infants with z-score < - 2SD (microcephaly) or > 2SD (macrocephaly) were considered as having abnormal head sizes and constituted the cases for this study.[4-6]

Independent variables

Maternal socio-demographic and pregnancy-related factors were considered. The socio-demographic factors included maternal age, marital status, ethnicity (based on the three most predominant ethnic groups in Nigeria, Hausa, Ibo, and Yoruba; and others), religion, educational attainment, occupation (formal / regular employment, self-employed or none), social class, type of accommodation (rented or owned), and quality of accommodation (with own or shared toilet facilities). Determination of the social classes of the participants was based on mother's education and father's occupation, as previously validated in this population.[13] Social class I was termed as 'high', II and III as 'middle,' and IV and V as 'low'. Pregnancy-related factors included parity, antenatal care visits, herbal drug use in pregnancy, gestational type (singleton or multiple), and place of delivery (public / government, private hospitals, family homes, herbal / traditional maternity homes run by traditional birth attendants, and other locations).

Statistical analysis

Continuous variables (maternal age and parity) were categorized according to the established risk threshold in the literature. Factors significantly associated (two-tailed $P <$ 0.05) with any abnormal head size in the univariate analysis were first considered for inclusion in the multiple logistic regression model. A second model consisting of all factors based on biological plausibility was built and compared with the first model to determine the effects of the non-significant variables. The strength of association was estimated by the odds ratios (OR) and the corresponding 95% confidence intervals (CI). There were no *a priori* hypotheses for the interaction terms, so these were not investigated. Missing data were managed by exclusion in all of the analyses. Model calibration was verified with the Hosmer-Lemeshow test. All statistical analyses were done with SPSS Windows version 16.0 (SPSS Inc, Chicago, IL, USA).[14]

RESULTS

A total of 5731 term infants (mean ± SD age: 16.0 ± 16.5 days), with complete anthropometric data over the study period, 730 (12.7%) of whom had abnormal head sizes [Table 1] and their mothers were enrolled. From this group, 623 (85.3%) had microcephaly. The distribution of abnormal

Table 1: Maternal socio-demographic correlates of infants with abnormal head sizes

Factors	Total (%) *n* = 5731	Abnormal head size (%) *n* = 730	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)
Age (Years) [a]				
< 20	198	44 (22.2)	2.04 (1.44 – 2.88)	1.86 (1.26 – 2.75)
20 – 35	5039	619 (12.3)	1.0	1.0
> 35	483	62 (12.8)	1.05 (0.80 – 1.39)	1.12 (0.84 – 1.50)
Marital status				
Married	5531	692 (12.5)	1.0	1.0
Unmarried	200	38 (19.0)	1.64 (1.14 – 2.36)	1.23 (0.82 – 1.84)
Ethnicity				
Hausa	123	12 (9.8)	1.0	
Ibo	409	54 (13.2)	1.41 (0.73 – 2.73)	
Yoruba	5144	654 (12.7)	1.35 (0.74 – 2.46)	
Others	55	10 (18.2)	2.06 (0.83 – 5.10)	
Religion				
Muslim	3786	471 (12.4)	1.0	
Christian	1945	259 (13.3)	1.08 (0.92 – 1.27)	
Education				
Tertiary	939	98 (10.4)	1.0	1.0
Secondary	3774	479 (12.7)	1.25 (0.99 – 1.57)	1.31 (0.96 – 1.80)
Primary / None	1018	153 (15.0)	1.52 (1.16 – 1.99)	1.65 (1.15 – 2.37)
Occupation				
Regular employment	1240	160 (12.9)	1.0	
Self-employed	3704	471 (12.7)	0.98 (0.81 – 1.19)	
None	787	99 (12.6)	0.97 (0.74 – 1.27)	
Social class				
High (I)	368	39(10.6)	1.0	
Middle (II and III)	4388	561 (12.8)	1.24 (0.88 – 1.74)	
Low (IV and V)	975	130 (13.3)	1.30 (0.89 – 1.90)	
Home ownership				
Owned	238	23 (9.7)	1.0	
Rented	5493	707 (12.9)	1.38 (0.89 – 2.14)	
Housing sanitation				
Self-contained	765	99 (12.9)	1.0	
Shared	4966	631 (12.7)	0.98 (0.78 – 1.23)	
Parity				
Primiparous	2361	320 (13.6)	1.0	
Multiparous	3370	410 (12.2)	0.88 (0.76 – 1.03)	
Antenatal care				
One or more visits	5636	718 (12.7)	1.0	
None	95	12 (12.6)	0.99 (0.54 – 1.82)	
Herbal drug use in pregnancy				
No	2147	260 (12.1)	1.0	
Yes	3584	470 (13.1)	1.10 (0.93 – 1.29)	
Multiple pregnancy				
No	5630	696 (12.4)	1.0	1.0
Yes	101	34 (33.7)	3.60 (2.36 – 5.48)	3.88 (2.53 – 5.95)
Place of delivery				
Public hospital	1389	142 (10.2)	1.0	1.0
Private hospital	1401	206 (14.7)	1.51 (1.21 – 1.90)	1.54 (1.22 – 1.95)
Traditional maternity home	2276	293 (12.9)	1.30 (1.05 – 1.61)	1.23 (0.96 – 1.58)
Residential home	359	53 (14.8)	1.52 (1.08 – 2.14)	1.50 (1.05 – 2.14)
Others	306	36 (11.8)	1.17 (0.79 – 1.73)	1.15 (0.77 – 1.72)

Missing data [a] = 11 (0.2%); Hosmer-Lemeshow test: $\chi^2 = 4.21$, df = 8, $P = 0.838$ *Adjusted for all factors

head sizes across the age groups in the study population is presented in Figure 1. More than half (56.2%) of the infants with abnormal head sizes were male. About one-fifth (22.2%) of the teenage mothers and one-third (33.7%) of mothers with multiple pregnancies had offspring with abnormal head sizes. Over three-quarters of the mothers belonged to the middle class, attended antenatal clinics, and lived in rented accommodation with shared facilities. Delivery in traditional maternity homes was highest (39.7%), while each of those in both public and private hospitals accounted for 24% of the total deliveries. In the entire study population, only six (0.1%) mothers reported alcohol use and two (0.03%) smoked.

In the univariate analysis, maternal age, marital status, education, multiple pregnancies, and place of delivery were significantly associated with abnormal head size in the offspring. In the first model, using only statistically significant factors, maternal age, education, multiple pregnancies, and place of delivery were independently associated with abnormal head size. The model was well-calibrated (Hosmer-Lemeshow test: $P = 0.930$). These factors were not materially affected in the second model containing all the factors, regardless of their univariate association with abnormal head size. In this second and preferred model, abnormal head sizes were significantly associated with teenage mothers (OR:1.86; 95% CI:1.26 – 2.75; $P = 0.002$), mothers with primary or no education (OR:1.65; 95% CI:1.15 – 2.37; $P = 0.007$), multiple pregnancies (OR:3.88; 95% CI:2.53 – 5.95; $P < 0.001$), and delivery in either private hospitals (OR:1.54 95% CI:1.22 – 1.95; $P < 0.001$) or at home (OR:1.50; 95% CI:1.05 – 2.14; $P = 0.025$). This regression model was also satisfactorily calibrated (Hosmer-Lemeshow test: $P = 0.853$). Marital status was not a significant factor in either model after adjustment for other confounders. Although there was an elevated risk among infants delivered in traditional maternity homes, the difference did not reach statistical significance.

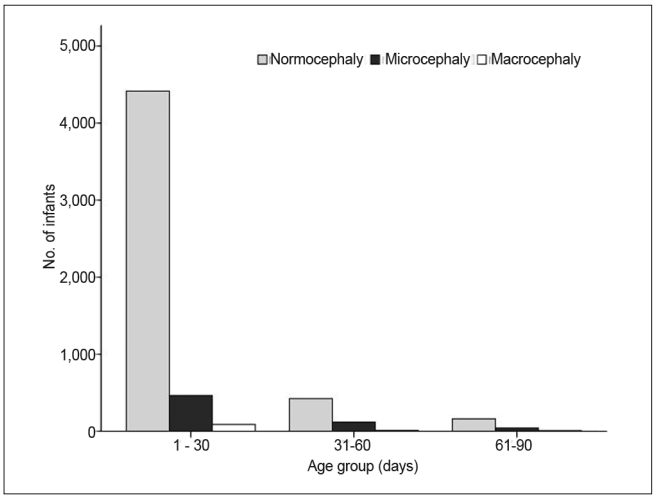

Figure 1: Distribution of abnormal head sizes in the study population

DISCUSSION

Several studies have shown that abnormal head sizes are among the most common genetic disorders and birth defects worldwide.[8] The current study is one of the earliest emerging reports worldwide exploring the socio-demographic and pregnancy-related antecedents of infants with abnormal head sizes, based on the latest WHO-CGS, but with specific reference to a country with low income. The principal findings from this community-based study are that maternal age, educational level, pregnancy type, and place of delivery are significantly associated with abnormal head size in early infancy. Even when adjusted for place of delivery, the socio-demographic factors still remain significant. These findings are in contrast with a related hospital-based study in which a comparable incidence of abnormal head sizes (12.9%) was observed, but no association was established between the maternal socio-demographic profile and abnormal sizes at birth.[15] Taken together, the current study would suggest that the socio-demographic factors were more predictive of acquired or progressive rather than congenital abnormal head sizes. Barring the lack of evidence from a more robust longitudinal study from birth, the current findings are quite plausible, considering the potential role of asymptomatic and ubiquitous infections like the *Cytomegalovirus*, which is characteristically progressive.[16,17] Perhaps, more notably is an indication that adverse environmental or early postnatal conditions are likely to play a more dominant role than genetic factors in the etiology of abnormal head sizes in countries with low income, such as Nigeria.

Perhaps the most striking observation from this study is that infants delivered outside government-run public hospitals, especially in private hospitals or in homes, were at 50% increased risk of having abnormal head sizes. The exact mechanism underlying this association is unclear and merits further investigation, considering the high proportion of such deliveries in many resource-poor countries. For example, public hospitals are usually better equipped and better staffed with various levels of obstetric professionals than what most private hospitals in low-income countries can afford. Thus, the quality of puerperal and perinatal care, especially resuscitation practices available outside public hospitals is often lower, exacerbated by the lack of, or poorly enforced regulatory standards. The lesser risk of abnormal head size among infants delivered in traditional maternity homes may not be unconnected, with the practice of the traditional birth attendants to refer high-risk pregnancies, including first-time parturients, in this population to public hospitals.

The association with teenage mothers contrasts with findings from developed countries where older mothers

(≥35 years old) have been associated with microcephalic offspring.[18] It is plausible that the finding among teenagers in the current study may be attributable to the competing nutritional needs of pregnancy underpinned by the mother's biological immaturity and growth. This situation is likely to be exacerbated in nutritionally deprived adolescent girls in poor communities, with poor micronutrient intake, resulting in reduced placental growth and fetal size.[19] The high risk of abnormal head size among mothers with no or low education is in agreement with other studies,[18] while the highest risk reported among infants in multiple gestation is not unexpected, based on the extensive evidence in literature on the associated congenital malformations.[8]

Overall, this study suggests that the maternal socio-demographic profile, including the place of delivery, is crucially relevant toward any efforts to curtail the burden of abnormal head sizes and the demand for scarce community-based rehabilitation services in low-income countries. The high uptake of antenatal visits offers an opportunity to educate mothers on the avoidable risk factors for abnormal head sizes. In particular, poor interpersonal encounters with maternity staff and long waiting times in public hospitals are not uncommon, and have been noted as major incentives for delivery in private hospitals or at home. These issues also need to be addressed. Although it was impracticable to examine the perinatal or early postnatal outcomes associated with abnormal head sizes in this community-based setting, this study complements the hospital-based study, which identified intrauterine growth restriction, under-nutrition, hyperbilirubinemia, and neonatal sepsis as probable outcomes.[15]

A few limitations of this retrospective and essentially exploratory study are worth noting. For example, the study sample was restricted to survivors during the enrolment period, which would have made it impossible to ascertain the true incidence of abnormal head sizes. The study also excluded preterm infants, as they would have required modification to the WHO-CGS standards designed for term infants. Case finding was based solely on WHO-CGS standards and no attempt was made to compare the results with other growth standards. As a cross-sectional study, it was difficult to accurately discriminate between congenital, acquired, progressive, or even arrested abnormal head sizes. Additionally, the community-based design of this study precluded reliable data on important variables such as mode of delivery, maternal nutritional status, and non-pregnancy related factors such as exposure to drugs, infections, and radiation. Nonetheless, the study provides initial evidence on the application of the WHO-CGS for early detection and intervention for infants at risk of diverse neurodevelopmental disorders, underpinned by abnormal head sizes, in developing countries.

CONCLUSION

Abnormal head sizes are highly prevalent in this study population and are significantly associated with teenage mothers, mothers with primary or no education, multiple pregnancies, and delivery in either private hospitals or residential homes. Community-oriented public health education targeting prospective mothers with multiple pregnancies, teenage girls, and women with little or no formal education on the potential risk of delivery outside public hospitals should be considered in this and other comparable populations, to curtail the burden of abnormal head sizes in the their offsprings. Such initiatives are also likely to reduce the pressure on the overstretched rehabilitation services in resource-poor countries.

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