Anogenital distance in human male and female newborns: A look at a cross section of a Nigerian population.

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Abstract

A cross-sectional study was conducted among the newborn children at the University of Port Harcourt Teaching Hospital and Braithwaite Memorial Hospital all in Port Harcourt, Rivers State, Nigeria. The study included 139 newborn infants (80 males and 59 females), born at term, with no congenital defects. Birth weight, length, and anogenital distance AGD, were made with tape by two independent observers. Distance was measured from the center of the anus to the posterior convergence of the fourchette in females; and from the center of the anus to the junction of the smooth perineal skin with the rugated skin of the scrotum in males. Student's T-test and analysis of variance were used to compare male-female measurements using Graph Pad Prism 3.0. The AGD in males and females were 3.02 ± 0.14 and 2.58 ± 0.11 cm respectively. There was significant difference between the AGD values in male and female babies in a Nigerian population.

INTRODUCTION

Anogenital distance results from the development of the genital tubercle, genital swellings, and cloacal membrane into the penis or clitoris, scrotum or labia majora, and anus, respectively. In multiple mammalian species, including rodents, cows, whales, monkeys, and humans, males have a longer anogenital distance than females, suggesting that this metric is under hormonal influence (1). Anogenital distance AGD is sexually dimorphic in many mammals, with males having longer anogenital distance on average than females. Alterations in human anogenital distance thought to be due to endocrine abnormalities were first noted in girls with congenital adrenal hyperplasia, who have longer anogenital distance than girls without the disorder [1] . Moreso in males with endocrine disruption like hypospadias and cryptorchidism may be associated with reduced anogenital distance.

AGD is a measure of fetal androgen action commonly used in animal studies and recently in human studies [2, 3] . Anogenital distance at birth is regarded as a useful measurement that reflects the prenatal androgenic status [4] .

Recently, Salazar-Martinez et al. (2004) [5] studied AGD in 45 male and 42 female infants. They measured the distance from the anus to the base of the scrotum in males and from the anus to the base of the genitals (the fourchette) in females. By these measures, AGD was sexually dimorphic and about twice as long in males as in females. No other studies have examined AGD among human males, although two other studies have evaluated

AGD in female infants [6, 7] . Although measurement of AGD in humans has been discussed in the literature [8-11] , it has been measured formally in only three descriptive studies of females [5, 6] . Because AGD has been an easy-to measure, sensitive outcome in animal studies, Salazar-Martinez et al 2004 [5] developed and implemented an anthropometric protocol for measurement of AGD in human males as well as females. We are not aware of any previous study that has dealt with the anthropometric measurement of anogenital distance of babies in a Nigerian population. This work constitutes a modest step towards evaluation of AGD in human infants in Nigeria.

METHODS

SUBJECTS

A cross-sectional study was conducted (in October/November 2007) among the newborn children of women admitted for delivery to the University of Port Harcourt Teaching Hospital and Braithwaite Memorial Hospital all in Port Harcourt, Rivers State, Nigeria. These hospitals provide medical care to people of different socioeconomic status and uninsured populations.

The study included 139 newborn infants (80 males and 59

females), none of whom had congenital defects or had been admitted to the neonatal intensive care unit. All infants were born at term (≥38 weeks gestation). Access

ANTHROPOMETRY

Anthropometric measurements were taken of birth weight, length, and AGD. AGD was measured as follows: the newborn infant was in the dorsal decubitus position; both hips were flexed and light pressure was exerted on the infant's thighs until the examiner's hand touched the subject's abdomen. Measurements were made with tape two independent observers. Distance was measured from the center of the anus to the posterior convergence of the fourchette (where the vestibule begins) in female infants (6); and from the center of the anus to the junction of the smooth perineal skin with the rugated skin of the scrotum in male infants.

Data analysis was performed with Graph Pad Prism 3.0.The mean, standard deviation, standard error of mean and ranges of each parameter were computed. Student‘s T-test and analysis of variance were used to compare male-female measurements.

Figure 1

Table: Anogenital Distance AGD in male and female babies

Sex	Anogenital Distance (mean ± SEM, cm)	Birth weight (kg, range)	Length at birth (cm, range)	n
Male	3.02 ± 0.14	2.4 - 5.9	43 - 58	80
Female	2.58 ± 0.11*	1.8 – 4.7	31 - 58	59

*P<0.0001

RESULT AND DISCUSSION

The anogenital distance AGD in male and female babies born in the University of Port Harcourt Teaching Hospital and Braithwaite Memorial Hospital all in Port Harcourt, Rivers State, Nigeria are shown in the table. The AGD in males and females were 3.02 ± 0.14 and 2.58 ± 0.11 cm respectively. It could be inferred from this finding that there was significant difference between the AGD values in male and female babies in a Nigerian population. This observation is similar to the work of Salazar-Martinez et al 2004 [5] .

The AGD measures employed in the present study reflect the location of the caudal border of the genital swelling, an embryologic structure that differentiates into the labia majora in females and the scrotum in males. After the indifferent stage of the external genitalia, the critical events determining the sexual dimorphism of AGD in humans begin when, relative to the anus, the genital swelling, urethral folds, and possibly the genital tubercle, move ventrally under the influence of androgens [12] . Elongation of the genital tubercle, which becomes the phallus, also occurs at this time.

Direct comparison of our results with some other studies with measures of anus-to-fourchette (AF) distance in female newborns ([6, 7]) is hampered by different eligibility criteria, and possibly different ethnicities, in the three studies. For example, Callegari et al.'s subjects had a mean weight of 2.53kg; Phillips et al. did not present birth weight but subjects were required to have a birth weight above 2.75kg; and in our study the birth weight range among females was 1.8- 4.7kg. The mean AF distance in the Callegari et al. study was 10.9 mm; in the Phillips et al. study was 16.1 mm in Jews and 16.5 in Bedouins. In the present study, we found an AGD of 2.58cm in Nigerian female babies. Callegari reported no ethnic differences in their population (62.6% Hispanic, 28.7% black, and 8.7% white). Phillips et al. reported that Jewish females had a greater AF distance than did Bedouins. The similarity of the mean AF distance measures in the present study and the Callegari et al. study is surprising given the difference in mean birth weights, and suggests ethnic differences, or a systematic difference in how the measurements were done.

In boys, AGD is measured in various ways, including from the middle of the anus to the anterior base of the penis, from the anus to the posterior base of the penis, and from the anus to the posterior base of the scrotum. The measurement to the anterior base of the penis is easier to standardize and the most reliable. In girls, AGD is measured from the center of the anus to the fourchette and from the anus to clitoris. For the male infant population, observations of markers of antiandrogen or estrogenic activity are of interest; in girls, however, the impact of androgens and estrogens is less clear. For female infants, noninvasive measurements that can be obtained reliably and biomarkers for androgen and estrogen effects need to be developed [13] .

The purported mechanism by which androgens increase AGD in females is by inducing “labioscrotal fusion” (in normal males fusion begins caudally and proceeds ventrally, presumably androgens in females act the same way) [Callegari et al 1987] [6] . This mechanism, however, does not account for why males who are not fully androgenized would have a decreased AGD, unless AGD in males is

defined as being from tip of penis to the center of the anus. A set of formal AGD measures on subjects with selected congenital endocrinopathies or birth defects could be useful in evaluating whether this outcome is uniformly responsive to gross stimuli, and may help discern details of normal embryology and the consequences of disrupting it.

In Mexico, Salazar-Martinez (Salazar-Martinez et al., 2004 [5] developed a method for reproducible evaluation of AGD in human newborns and showed that the distance from the anus to the base of the scrotum was longer than the distance from the anus to the posterior fourchette. Using these methods in a subsequent study of male infants with relatively high levels of DDE exposure, they saw no effect [2] . Swan et al., 2005 [3] showed that US boys (from the first Study for Future Families) with higher prenatal exposure to several phthalates had shorter anogenital index, defined as AGD/ body weight. There were no associated genital anomalies in either study, or the prognostic importance of AGD or AG index is not yet established. The impact of environmental pollutants on AGD in male and female babies in Nigeria is not yet known and may form the subject of a future investigation.

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