The routine value of anogenital distance as an anthropometric measurement in newborns

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Summary

Objective: Anogenital distance (AGD) is a sexually dimorphic trait; AGD is an external marker of sexual differentiation at birth in animals. *Study Design:* The present study used a prospective, cross-sectional design. Data were collected from newborn infants that were delivered at hospital in Bucheon between March and September 2009. The mothers of the infants provided sociodemographic information and obstetric history. The relationships between AGD and other anthropometric measures (i.e., weight, height, and head circumference) were analyzed. Moreover adjusted AGD values were compared with obstetric characteristics, including number of deliveries, abortion history, preterm history, and duration of gestation. *Results:* Significant correlations were noted for all anthropometric measures in male and female newborns ($p < 0.0001$). The adjusted AGD values in males and females were also significantly associated with the duration of gestation ($p = 0.0008$ and $p = 0.0148$, respectively). Moreover, the adjusted AGD in female newborns, but not in males, was significantly associated with maternal abortion history ($p = 0.0242$). *Conclusion:* The AGD is a valuable anthropometric marker in term infants.

Key words: CRH; Progesterone; Phases of labor; Term labor; Latent phase of labor; Active labor; Postpartum.

Introduction

The anogenital distance (AGD) is an external marker of sexual differentiation at birth. Specifically, the AGD is a measure of the caudal border of the genital swelling [1]. During the embryonic stage, the genital swelling differentiates into the labia majora in females and the scrotum in males [1]. AGD measurements are routinely used as an indicator of endocrine function in animal studies. The United States Environment Protection Agency (USEPA) recommends measuring the AGD to determine reproductive toxicity and fertility effects. However, very few human studies have used AGD measurements.

Anthropometric measurements are easy to measure and represent an infant's nutritional status (i.e., body weight, height, and head circumference). Knowing the endocrine status of a newborn immediately after deliver would be advantageous. The AGD is a representative measurement of androgen action during the embryonic stage. The present study aims to confirm that AGD is an easy measurement and a valuable anthropometric marker for endocrine problems in newborn infants. The AGD in infants has not been published in the Republic of Korea. Therefore, the aim of the present study is to provide data on AGD as a reference value of Korean newborns.

Materials and Methods

Study subjects and measurements

Data were collected from newborn infants that were born at a hospital in Bucheon. A cross-sectional study was conducted from March to September 2009. The present study was approved by the Ethics Committee for the Protection of Persons in Biochemical Research at the Institute of Medical Science of Soonchunhyang University Bucheon Hospital. One hundred and sixty pregnant women were enrolled in the study. A questionnaire was administered to the mothers regarding sociodemographic characteristics and maternal obstetric history. Maternal and infant body weight and height were measured.

The adjusted AGD values were classified into four groups: short (adjusted AGD < 25th percentile), first intermediate (25th percentile ≤ adjusted AGD < 50th percentile), second intermediate (50th percentile ≤ adjusted AGD < 75th percentile), and long (adjusted AGD ≥ 75th percentile). The proportion of mothers in each of the four groups that had a history of abortions was calculated, as well as the duration of gestation.

Physical examination

All AGD measurements were taken by a trained nurse. A detailed examination of the anthropometric measurements was performed under the direction of a trained obstetrician. Anthropometric items were measured in the infants (i.e., body weight, length, head circumference, and AGD) (n = 61 females and n = 99 males). The protocol for AGD measurements was based on a previously published study [1]. The AGD was measured as follows: 1) the newborn infant was placed in the dorsal decubitus position with both hips flexed; 2) light pressure was exerted on the infant's thighs until the examiners hand touched the subject's abdomen; 3) measurements were made with Vernier calipers; 4) the distance was measured from the center of the anus to the posterior convergence of the fourchette (where the vestibule begins) in female newborns [2] and from the center of the anus to

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the junction of the smooth perineal skin with the skin of the scrotum in male newborns (Figure 1).

Statistical analysis

AGD measurements were divided by body weight (mm/kg). Preterm (gestation < 37 weeks) and low-birth weight (birth weight < 2,500 g) newborns were not excluded from the analysis. Correlations were calculated between the AGD and the other anthropometric measures (i.e., weight, height, and head circumference). Moreover, the adjusted AGD was compared with the obstetric characteristics of the mother. Specifically, the number of deliveries, abortion history, preterm history, and duration of gestation were recorded. The adjusted AGD in newborns was classified into the following three groups: short (adjusted AGD < 25th percentile), intermediate (25th percentile ≤ adjusted AGD < 75th percentile), and long (adjusted AGD ≥ 75th percentile). The proportion of male and female newborns in each of the four groups was also calculated, as well as the maternal history of abortions and the duration of gestation. The differences among the variables were determined using STATA version 10. Statistical significance was set at $p < 0.05$.

Results

General characteristics

The age of the mothers in the present study ranged from 16–44 years, with a median age of 32 years (Table 1). The median body mass index (BMI) was 21.7 kg/m^2. The majority of the mothers (67.6 %) had other children. One hundred nine of the subjects (68.1%) lived in a rural area. Nearly one-half (46.1%) of the subjects graduated from a college or university. A history of preterm births was not reported by most of the mothers (89.4 %). Moreover 65.0% of the mothers reported never having an abortion. Cesarean section (58.1%) was the main method of delivery and most of the subjects were > 37 weeks gestation (66.2 %).

General and anthropometric characteristics in newborns

AGD measurements were obtained from 160 newborns (males = 99; females = 61). The characteristics of the newborns are listed in Table 2. No neurological or behavioral disorders were noted in the newborns with genital measurements. The average AGD in male infants was 19.8 ± 3.2 mm and 15.1 ± 3.1 mm in female infants. The AGDs in males were greater than females ($p < 0.0001$; Figure 2). Specifically, males displayed a 1.3-fold greater AGD as compared with females. No significant differences were noted in body weight, height, head circumference, Apgar scores, or gestational duration between male and female infants.

Correlations between AGDs and anthropometric measures

The associations between the AGDs and anthropometric measures in newborns are shown in Table 3. In males, the AGD was correlated with height (r = 0.328), weight (r = 0.3564), and head circumference (r = 0.2124). The AGD in females was only correlated with weight (r = 0.2929). Moreover, AGD was positively correlated with weight in male and female infants. These results are consistent with previous studies that have demonstrated that body weight is a known predictor of AGD [3]. As a result, AGD values were adjusted according to weight in the present study. Significant correlations were noted for all of the anthropometric measurements in males and females ($p < 0.0001$).

Table 1. — *General characteristics of mothers (n = 160).*

Variable		n (%)
Median age (year)		32.0 (16-44)
Median BMI (kg/m^2)		21.7 (16.2-39.9)
No. of children (no.)	0	51 (31.9)
	1	62 (38.8)
	2~	46 (28.8)
	No answer	1 (0.5)
Residence area	Rural area	109 (68.1)
	Urban area	51 (31.9)
Education	Below high school	47 (29.4)
	College or university	77 (48.1)
	No answer	36 (22.5)
Experience of preterm	No	143 (89.4)
	Yes	17 (10.6)
Experience of abortion	No	104 (65.0)
	Yes	56 (35.0)
Types of delivery	Normal delivery	59 (36.8)
	Cesarean section	93 (58.1)
	No answer	8 (0.1)
Duration of gestation	< 37 weeks	54 (33.8)
	≥ 37 weeks	106 (66.2)

BMI: body mass index.

Table 2. — *Means and standard deviations of anthropometric indices, Apgar score, and gestational duration of newborns.*

Items	Males (n = 99)	Females (n = 61)
AGD (mm)	19.8 ± 3.2	15.1 ± 3.1
Adjusted AGD (mm/kg)	6.92 ± 1.8	5.19 ± 1.4
Body weight (g)	2982.8 ± 637.9	2995.1 ± 534.1
Height (cm)	49.1 ± 3.2	49.0 ± 2.6
Head circumstance (cm)	34.4 ± 2.5	34.0 ± 2.0
Apgar score	8.3 ± 1.2	8.5 ± 1.0
Gestation duration (week)	37.5 ± 2.6	38.0 ± 1.9

AGD, anogenital distance.

Table 3. — *The Pearson's correlation matrix between anogenital distance and anthropometric measures (height, weight, and head circumference) in newborns.*

	Female			
Items \ Items	AGD	Height	Weight	Head circumference
AGD		0.1851 (0.1534)	0.2929 (0.0220)	0.1664 (0.2120)
Height	0.3282 (0.0009)		0.8255 (< 0.0001)	0.6240 (< 0.0001)
Weight	0.3564 (0.0003)	0.8755 (< 0.0001)		0.7380 (< 0.0001)
Head circumference	0.2124 (0.0378)	0.5611 (< 0.0001)	0.6097 (< 0.0001)	
	Male			

AGD, anogenital distance.

Table 4. — *A comparison of adjusted anogenital distance (mm/kg) according to experience of abortion.*

Adjusted AGD (mm/kg)	Males (n = 99) No (n [%])	Yes (n [%])	χ^2 *p* value	Females (n = 64) No (n (%)]	Yes (n [%])	χ^2 *p* value
Short	12 (16.2)	13 (37.1)	Referent	6 (15.0)	9 (42.9)	Referent
Intermediate	35 (54.7)	15 (42.9)	3.448 (0.0633)	20 (50.0)	10 (47.6)	2.915 (0.088)
Long	17 (26.6)	7 (20.0)	2.643 (0.1040)	14 (35.0)	2 (9.5)	7.630 (0.0057)

AGD: anogenital distance.

Table 5. — *A comparison of adjusted anogenital distance (mm/kg) according to duration of gestation in newborns.*

Adjusted AGD (mm/kg)	Males (n = 99) No (n [%])	Yes (n [%])	χ^2 *p* value	Females (n = 64) No (n (%)]	Yes (n [%])	χ^2 *p* value
Below 25%	4 (10.8)	21 (33.9)	Referent	2 (11.8)	13 (29.6)	Referent
25-50%	18 (48.7)	32 (51.6)	3.216 (0.0729)	6 (35.3)	24 (54.6)	0.3041 (0.6992*)
50-75%	15 (40.54)	9 (14.5)	11.153 (0.0008)	9 (52.9)	7 (15.9)	6.2288 (0.0126)

* Fisher's exact test.

Adjusted AGD and maternal obstetric characteristics

The adjusted AGD (mm/kg) was examined in relation to a previous maternal history of preterm delivery and abortion, as well as the current delivery type and duration of gestation (Figure 3). In male infants, a significant difference was noted between the adjusted AGD and the duration of gestation. The adjusted AGD in males born at < 37 weeks gestation was longer ($p < 0.0001$) as compared with term infants. These differences were also noted in female infants ($p = 0.464$). In addition, the adjusted AGD in females was significantly different in mothers with a history of abortions ($p = 0.0028$). The adjusted AGD in female newborns born at > 37 weeks gestation was not significantly different as compared with female infant's born to mothers with a history of abortions (data was not shown). Therefore, these results suggest that the duration of gestation may be impacted in female infants born to mothers with a history of abortions.

Statistical analyses were used to determine the relationship between abortion history and duration of gestation. Newborns were classified into three groups. The short adjusted AGD group consisted of infants with AGD measurements below the 25th percentile. The long adjusted AGD group included infants with AGD measurements in the 75th percentile. The intermediate group included infants with AGD measurements between the 25th and 75th percentile. The intermediate adjusted AGD group and the long adjusted AGD group were compared to the short adjusted AGD group.

Abortion frequency in the intermediate and long adjusted AGD groups was compared with the short adjusted AGD group (Table 4). Significantly differences were noted in females in the long adjusted AGD group as compared with females in the short group ($p = 0.088$). No significant differences were noted in males. The frequency analysis of gestational duration was also analyzed (Table 5). Significant differences were noted in the long adjusted AGD group as compared with the short adjusted AGD group in males and females ($p = 0.0008$ and $p = 0.0126$, respectively). Differences were noted in AGD values between preterm and term delivered infants.

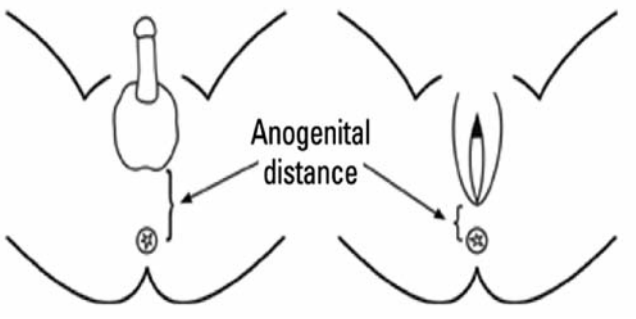

Figure 1. — Schematic diagram of the anatomical landmarks used to measure the AGD. (Reproduced from Salazar-Martinez et al. 2004, originally published in Environmental Health by Biomed Central).

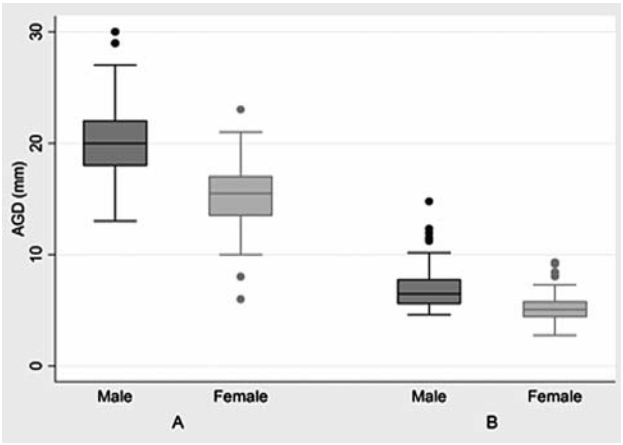

Figure 2. — Box plots of the (A) anogenital distance (AGD [mm]) and (B) adjusted AGD (mm/kg) in newborns (number of males = 102, number of females = 64).

Discussion

The aims of the present study were to determine the anthropometric value of AGD in Korean infants. The authors hypothesized that fetal weight gain occurs late in gestation after sexual organ development, which occurs during the early fetal period. They found that AGD was correlated with height, weight, and head circumference in term infants. Therefore, AGD is a valuable anthropometric measurement in term newborns, but not premature infants.

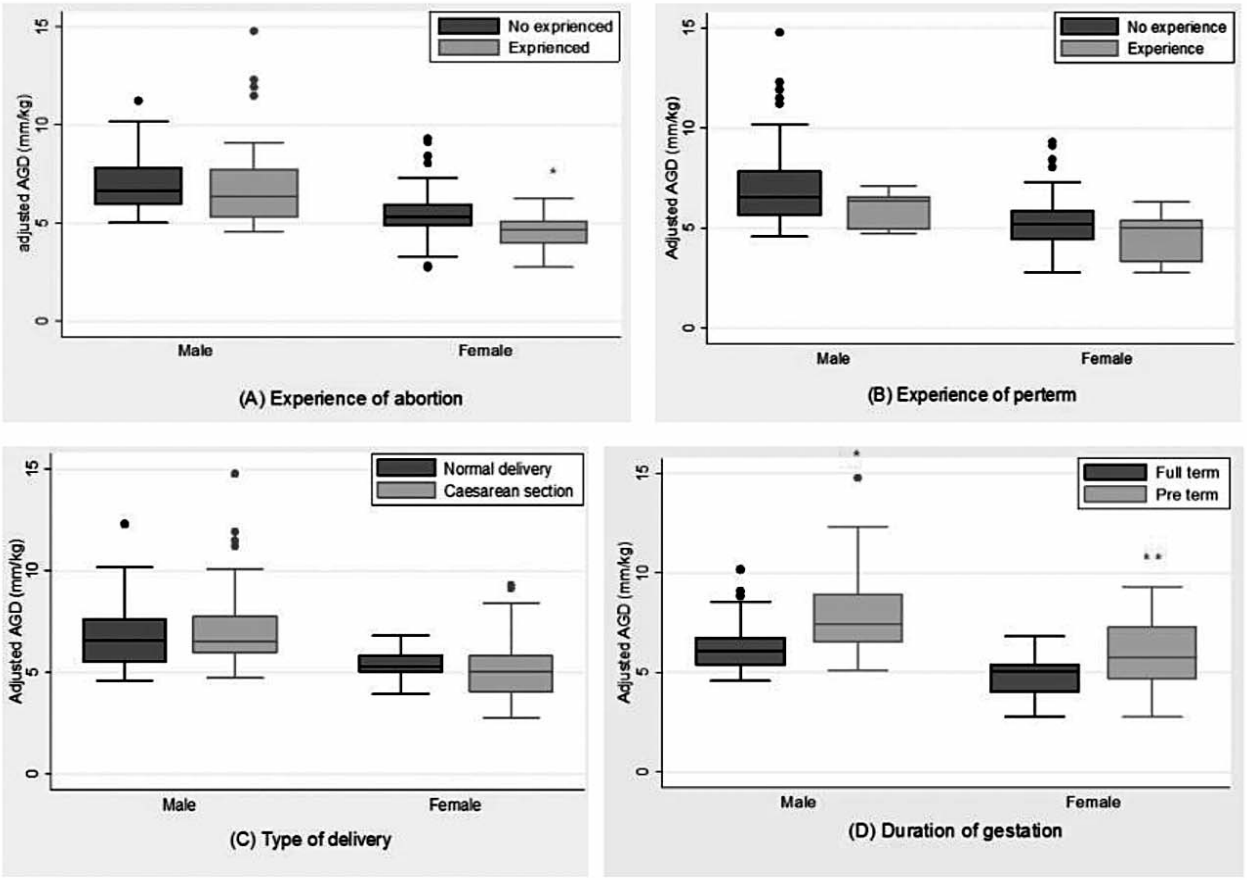

Figure 3. — Comparisons of adjusted anogenital distance in male and female newborns according to maternal obstetrical characteristics: (A) experience of abortion, (B) experience of preterm, (C) type of delivery and (D) duration of gestation (*p < -0.05, **p < 0.005).

Moreover, the authors found that their AGD measurements in males were consistent with other reports, but their AGD measurements in females were longer than previously reported [1]. This difference in AGD values in the present study provides a reference sample for Korean infants. Furthermore, they found that the adjusted AGD in females was statistically significant in mothers with a history of abortions. While the underlying cause for this result is unknown, it may be due to a maternal hormonal effect. Future studies should evaluate the relationship between previous abortions and AGD values. AGDs are sexually dimorphic in animals, with longer AGDs reported in males as compared with females. This difference suggests the action of androgens on the undifferentiated tissues during fetal developmental. The relationship between endocrine disruptors and AGDs in male animals has been previously studied. In male rats, perinatal administration of vinclozolin and ethane dimethane sulphonate (EDS) induced female-like AGD values [4, 5]. Moreover, anti-androgen action in male animals was significantly correlated with AGDs. AGD was the most sensitive parameter when anti-androgenic properties were measured in pregnant rats [6]. Female rats that were exposed to polychlorinated biphenyls (PCBs) displayed significantly increased AGDs, which may be due to androgen responsiveness in female rats during fetal developmental [7]. A decrease in the AGD and an increase in the incidence of undescended testes have been reported following exposure to monobenzyl phthalate (MBeP) [8]. AGDs may be reflective of prenatal androgen or anti-androgen endocrine disruptors in both sexes. Endocrine disruptors may interrupt sexual organ differentiation. Therefore, AGDs represent the effect of endocrine disruptor exposure during the prenatal period. In human studies, the anogenital ratio is a useful method to diagnose androgen-induced labioscrotal fusion in premature and full-term female infants [2]. A decrease in size, feminization of the AGD, and incomplete testicular descent is associated with anti-androgen action, including phthalate levels in the mother's urine.[9] In another study, AGD measurements were not correlated with intrauterine exposure to dichlorodiphenyldi-chloroethylene (DDE), an androgenic compound [10].

Physical exams in male newborns should be required within 24 hours of birth (i.e., testis position, penile length, and AGD to genitalia length) [11]. Previous studies have reported that phthalate levels were higher in males with short AGDs [12]. Thus, effects of endocrine disruptors should be evaluated after delivery.

Salazar-Martinez *et al*. [1] and Callegari *et al.* [3] reported that the AGD in females was shorter than what was reported in the present study; however, the AGD values in males were consistent between studies. In the previous study, the AGD measurement was two-fold greater in males than in females. The present data were inconsistent with this finding [1]. Therefore, the data in the present study may be specific to the Korean population. Moreover, differences in the AGD were noted in the present study between preterm and full-term newborns. Based on the present study, the adjusted AGD in full-term newborns was shorter as compared with premature newborns, indicating that full-term infants have increases in weight rather than other anthropometric factors. As a result, AGD is a good anthropometric method that is easily measured in full-term infants. The present data showed that the adjusted AGD in females was associated with maternal abortion history. Hormone levels were not evaluated in the present study. Interestingly, there are no previous reports on the relationship between adjusted AGD in females and maternal abortion history. The limitation of the current study is that there was a small sample from one hospital. However, this is the first report in the Republic of Korea in which AGD was assessed in newborns. The present study is the first evaluation of AGD that took into account the obstetrical history of the mothers. The aim of the present study was to provide information regarding a new anthropometric method for infants. This method should be further evaluated in a larger sample of newborns.

The AGD data in the current study represents an anthropometric index for AGD. Newborns in the present study did not have any congenital sexual organ issues. Endocrine disruptors in relation to AGD were not evaluated. If congenital sexual organ anomalies were present, endocrine disruptor levels and AGD values should be measured.

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