



COMPARISON OF PENILE LENGTH AT 6–24 MONTHS BETWEEN CHILDREN WITH UNILATERAL CRYPTORCHIDISM AND A HEALTHY NORMAL COHORT.

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ABSTRACT **PURPOSE:** Urologic diseases affected by testosterone can be associated with smaller penis size compared to the normal population. We sought to compare penile length in children with unilateral cryptorchidism and normative data from a cohort of healthy Korean boys.

MATERIALS AND METHODS: This study was performed in 259 Korean boys (212, normal cohort; 47, cryptorchidism) aged 6–24 months, each of whom had been brought to an outpatient clinic at one of five tertiary hospitals (Gyeongsangnam-do Province) between April 2014 and June 2015. Penile length was measured via stretched penile length (SPL) and testicular size was measured using orchidometry (mL).

RESULTS: SPL in children with cryptorchidism was significantly shorter compared to a cohort of healthy Korean boys aged 6–24 months (3.7 ± 0.5 cm and 4.3 ± 0.8 cm, $p < 0.001$), although there were no differences with regard to height, body weight and contralateral testicular size between the two groups. According to the stratified ages (6–12, 12–18, and 18–24 months), SPL in children with cryptorchidism was persistently shorter at their ages than those without.

CONCLUSIONS: It might be that the penile length aged 6–24 months of children with unilateral cryptorchidism is shorter than that of a cohort of healthy Korean boys.

KEYWORDS : Anthropometry; Child; Cryptorchidism; Penis

INTRODUCTION

Cryptorchidism is a potential manifestation of testicular dysgenesis syndrome at birth [1]. Androgens are essential in normal fetal descent of the testes into the scrotum, particularly during testicular descent into the inguinal and scrotal areas [2]. Androgen abnormality has been proposed as a pathogenic mechanism underlying abnormal fetal testicular development [3]. Deficient androgen exposure during fetal masculinization can result in smaller adult size of the testes, prostate, seminal vesicles and penis [4, 5]. In some reports, it is suggested that congenital cryptorchidism is associated with smaller penile length at birth [3, 6]. In contrast to previous research, another study suggested that the penile length of children with cryptorchidism might be similar to that of normal healthy boys after growth during childhood [6]. During the first 3 months after birth, the majority of infants with congenital cryptorchidism experience spontaneous testicular descent because of testosterone surge. This testosterone surge during early infancy does not affect penile length between boys with cryptorchidism and a cohort of healthy boys after the first 3 months.

In humans, there have been few reports on penile length in cryptorchidism, and how it compares to normal cohorts in infancy and childhood remains controversial. Therefore, we sought to compare the penile length of Indian children with unilateral cryptorchidism against normative data from a cohort of healthy Korean boys aged 6–24 months.

MATERIALS AND METHODS

This study was conducted in the outpatient clinics of 5 hospitals between April 2014 and June 2015. The subjects of this study were 259 Indian boys aged 6–24 months from the Tamil Nadu. Two hundred twelve healthy Indian boys were included and 47 boys with unilateral cryptorchidism were included. Exclusion criteria were other penile diseases including hypospadias, concealed penis, bilateral cryptorchidism, and other growth problems such as renal failure and endocrinologic disorders. Therefore, most children included in the current study were brought in for general periodic examinations, urinary tract infection, enuresis or lower urinary tract symptoms [7]. Children without cryptorchidism among all the children included in current study were regarded as a healthy normal cohort.

For all boys, penile length and testicular size were measured by a pediatric urologist at each hospital. Stretched penile length (SPL) was measured and testicular size was evaluated using orchidometry (mL) in the presence of their parents in a warm room. SPL was measured with a stiff ruler by compressing the fat tissue with one end of the ruler through the pubic ramus; then, the penis was fully stretched and the distance to the glans of the stretched penis was plotted [7, 8]. The

foreskin of uncircumcised children was not involved in the measurement (Fig. 1). We used contralateral testicular size in children with cryptorchidism for comparison.

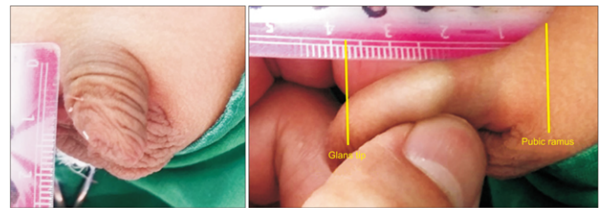


Fig. 1. Method used to measure stretched penile length (SPL) in the current study. SPL of a child with unilateral cryptorchidism (10 months old) varied from penile length without stretching.

Statistical analysis and ethics statement

Data analysis was performed using the software package SPSS ver. 17.0 K for Windows (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as the mean \pm standard deviation. Student's t-test was used to compare SPL, height, body weight and testicular size between children with cryptorchidism and a cohort of healthy boys. Between hospitals and age groups, ANOVA test was used for comparison and a p-value < 0.05 was considered statistically significant. This study was approved by the institutional review board of Ulsan University Hospital (approval number: 2017-03-020). Clinical data for all of the participants were collected by retrospectively reviewing medical records. Therefore, our institutional review board waived the need for informed consent.

RESULTS

There were no significant differences in SPL and anthropometric data between hospitals

Table 1. Patient characteristics

| Characteristic | Hospital A | Hospital B | Hospital C | Hospital D | Hospital E |
|--------------------------------|----------------|-----------------|-----------------|-----------------|-----------------|
| Number (normal:cryptorchidism) | 26 (23:3) | 79 (71:8) | 70 (64:6) | 54 (36:18) | 30 (18:12) |
| A healthy normal cohort | | | | | |
| Age (y) | 1.3 \pm 0.4 | 1.2 \pm 0.4 | 1.4 \pm 1.1 | 1.4 \pm 0.4 | 1.5 \pm 0.4 |
| Stretched penile length (cm) | 5.0 \pm 0.5 | 4.9 \pm 0.5 | 3.7 \pm 0.6 | 3.7 \pm 0.5 | 4.8 \pm 0.7 |
| Testis size (mL) | 2.3 \pm 0.3 | 2.2 \pm 0.4 | 1.7 \pm 0.4 | 2.0 \pm 0.3 | 2.1 \pm 0.4 |
| Height (cm) | 78.2 \pm 8.0 | 78.4 \pm 8.8 | 74.9 \pm 17.4 | 83.1 \pm 6.1 | 84.2 \pm 13.9 |
| Weight (kg) | 10.9 \pm 1.5 | 10.6 \pm 1.8 | 10.3 \pm 2.1 | 11.4 \pm 2.0 | 11.7 \pm 2.2 |
| Children with cryptorchidism | | | | | |
| Age (y) | 0.6 \pm 0.1 | 0.8 \pm 0.1 | 1.2 \pm 0.3 | 1.1 \pm 0.4 | 1.3 \pm 0.3 |
| Stretched penile length (cm) | 3.3 \pm 0.3 | 3.8 \pm 0.3 | 3.6 \pm 0.7 | 3.6 \pm 0.5 | 3.9 \pm 0.3 |
| Testis size (mL) | 2.0 \pm 0.0 | 1.9 \pm 0.2 | 1.7 \pm 0.3 | 2.0 \pm 0.2 | 2.0 \pm 0.3 |
| Height (cm) | 67.8 \pm 2.0 | 76.4 \pm 10.8 | 77.7 \pm 5.0 | 84.5 \pm 14.7 | 79.9 \pm 7.6 |
| Weight (kg) | 8.2 \pm 1.3 | 9.7 \pm 1.6 | 10.7 \pm 0.8 | 10.3 \pm 1.4 | 10.7 \pm 1.6 |

Values are presented as number only or mean \pm standard deviation.

SPL in children aged 6–24 months with unilateral cryptorchidism was significantly shorter than a cohort of healthy boys (3.7±0.5 cm and 4.3±0.8 cm, p<0.001). There were no differences between the two groups in terms of height or contralateral testicular size (Table 2). Age in children with cryptorchidism was earlier than those without (p=0.022); however, there was no difference in body weight between two groups.

Table 2. Comparison of penile length between children with cryptorchidism and a healthy normal cohort

| Variable | Normal cohort (n=212) | Cryptorchidism (n=47) | p-value |
|-------------------------------|-----------------------|-----------------------|---------|
| Age (y) | 0.8±0.4 | 0.6±0.5 | 0.022 |
| Stretched penile length (cm) | 4.3±0.8 | 3.7±0.5 | <0.001 |
| Testis size (mL) ^a | 2.0±0.4 | 1.9±0.3 | 0.221 |
| Height (cm) | 78.2±12.8 | 79.3±10.8 | 0.591 |
| Weight (kg) | 10.7±1.9 | 10.2±1.5 | 0.130 |

Values are presented as mean±standard deviation.

^a:Present study used contralateral testicular size in children with cryptorchidism for comparison.

According to the stratified ages (6–12, 12–18, and 18–24 months), SPL in children with cryptorchidism was shorter than those without in every group (Table 3) although there was no difference in height and body weight between children with cryptorchidism and without. SPL grew slowly bigger with age; however, there was no statistical significance.

Table 3. Comparison of penile length between children with cryptorchidism and a healthy normal cohort according to the age

| Age group | Normal cohort | Cryptorchidism | p-value |
|-------------------------------|---------------|----------------|---------|
| Age 6–12 months | | | |
| Number | 46 | 19 | |
| Age (y) | 0.7±0.2 | 0.7±0.1 | 0.392 |
| Stretched penile length (cm) | 4.2±0.8 | 3.6±0.4 | <0.001 |
| Testis size (mL) ^a | 2.1±0.4 | 2.0±0.2 | 0.315 |
| Height (cm) | 68.4±13.1 | 76.4±13.1 | 0.058 |
| Weight (kg) | 8.7±1.9 | 9.3±1.3 | 0.181 |
| Age 12–18 months | | | |
| Number | 78 | 20 | |
| Age (y) | 1.2±0.1 | 1.2±0.1 | 0.710 |
| Stretched penile length (cm) | 4.2±0.8 | 3.7±0.5 | 0.001 |
| Testis size (mL) ^a | 2.0±0.5 | 1.9±0.3 | 0.264 |
| Height (cm) | 78.8±4.1 | 80.3±9.9 | 0.556 |
| Weight (kg) | 10.7±1.2 | 10.7±1.3 | 0.967 |
| Age 18–24 months | | | |
| Number | 88 | 8 | |
| Age (y) | 1.8±0.8 | 1.6±0.1 | 0.092 |
| Stretched penile length (cm) | 4.5±0.8 | 3.8±0.7 | 0.022 |
| Testis size (mL) ^a | 2.0±0.4 | 1.9±0.3 | 0.309 |
| Height (cm) | 82.3±15.1 | 83.6±4.2 | 0.600 |
| Weight (kg) | 11.8±1.6 | 11.3±1.5 | 0.445 |

Values are presented as number only or mean±standard deviation.

^a:Present study used contralateral testicular size in children with cryptorchidism for comparison.

DISCUSSION

There have been few reports on human penile length in cryptorchidism compared with normal cohorts [3, 4, 6]. It is suggested that there was a significant difference in penile length between newborn with cryptorchidism and those without [6, 9]. The penile length of children with cryptorchidism might be similar to that of normal healthy boys after the testosterone surge during the first 3 months following birth [6]. In meticulous searching in PubMed, there were only two studies regarding the difference of penile lengths aged 6–24 months between two groups [3, 6]. Their results were different from each other (Table 4). In our study, penile length in boys with unilateral cryptorchidism aged 6–24 months was significantly shorter rather than that of a healthy cohort. The result of current study is limited, but the result is very important to parents and doctors of children with cryptorchidism.

Table 4. Comparison of penile length between children with and without cryptorchidism in the literature

| Reference | Number | Age (mo) | Penile length (cm) | Testis size (mL) | Height (cm) | Body weight (kg) |
|------------------------------|--------|----------------------|--------------------|------------------|-------------|------------------|
| Thankamony et al. [4] | | | | | | |
| Normal cohort | 487 | 11.5±6.2 | 3.6±0.5 | - | 71.8±10.2 | 8.8±2.7 |
| Cryptorchidism | 71 | 13.4±5.8 | 3.5±0.6 | - | 76.2±6.9 | 10.3±2.0 |
| p-value | | 0.012 | 0.002 ^a | | 0.52 | 0.24 |
| Acerini et al. [4] | | | | | | |
| Normal cohort | 408 | 12.0 | 3.8±0.6 | - | 76.9±2.6 | 10.3±1.1 |
| Cryptorchidism | 24 | 12.0 | 3.8±0.6 | - | 76.4±3.8 | 10.0±1.8 |
| p-value | | | >0.3 | | >0.3 | >0.3 |
| Present study | | | | | | |
| Normal cohort | 212 | 0.8±0.4 ^b | 4.3±0.8 | 2.0±0.4 | 78.2±12.8 | 10.7±1.9 |
| Cryptorchidism | 47 | 0.6±0.5 ^b | 3.7±0.5 | 1.9±0.3 | 79.3±10.8 | 10.2±1.5 |
| p-value | | 0.022 | <0.001 | 0.221 | 0.591 | 0.130 |

Values are presented as number only or mean±standard deviation.

- , not available.

^a:Standard deviation scores were used for statistical analysis. ^b:Unit, year.

Various factors can be related with the differences of SPL between children with cryptorchidism and those without. Drake et al. [10] suggested that increasing severity of cryptorchidism may be associated with reduced anogenital distance (AGD) and penile length in animals due to disruption of androgen. During weeks 8–14 of gestation in humans, genital development is critically programmed; thus, this period is called the male programming window (MPW). Disruption of androgen action during the MPW results in altered AGD and penile length as well as cryptorchidism and hypospadias [11, 12]. In human, penile length correlated with androgen levels post-natally [13]. The severity of androgen disruption in MPW according to the

severity of cryptorchidism may influence this outcome.

In a recent study of human infants, Jain and Singal [9] insisted that there was no difference in SPL between children with cryptorchidism and those without. The 71 infants with cryptorchidism included in their study had shorter ADG and SPL than the 624 infants with normal descended testes. After statistical correction of variables such as gestational age and birth body weight between children with cryptorchidism and those without, AGD varied significantly, but SPL did not. In that study, SPL and AGD appeared shorter with a higher testicular position; however, this was not statistically significant. In the current study, we could not obtain data on testicular location before orchiopexy in the cohort with cryptorchidism but also find the relation of those. A previous study reported that SPL appeared to be shorter with a higher testicular position [10].

Our study has several limitations. First, the number of children with unilateral cryptorchidism included in this study was relatively small. However, the prevalence of cryptorchidism was 2.4%–6.7% in England and 1.5% at 18 months of age in Danish and Finnish cohort studies [14]. Further studies with more patients with cryptorchidism, this factor should be considered. Second, we had no data on serum testosterone levels because this study was performed retrospectively. Third, we did not collect data about gestational age and birth weight. These factors can cause differences in SPL between children with cryptorchidism and those without at an early age [11]. Fourth, penile measurement was checked by different physicians at each hospital. Although SPL was measured in the same way in both studies, the results may have differed depending on the examiner because SPL can be affected by examiner strength. Fortunately, a previous Korean study reported no difference in SPL between two observers (3.3±0.2 cm and 3.2±0.3 cm, p=0.165) in newborn infants with normal weight [8]. In a recent study, no significant fixed or proportional bias could be found for inter-observer variation [15]. Despite these limitations, our results include important epidemic information regarding penile length in children with unilateral cryptorchidism.

CONCLUSIONS

It might be that the penile length aged 6–24 months of children with unilateral cryptorchidism is shorter than that of a cohort of healthy Korean boys. Further multicentric longitudinal studies with a larger sample size, serum testosterone level, birth weight and other information are needed to better define the exact difference between two groups.

Notes

CONFLICTS OF INTEREST: The authors have nothing to disclose.

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