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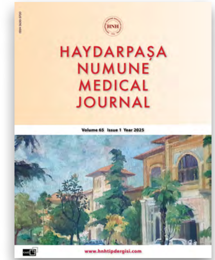

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ORIGINAL ARTICLE

A Current Perspective on Variations in Male Urogenital Development under Changing Environmental Conditions

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Abstract

Introduction: In recent years, the deterioration of male reproductive health and the increasing incidence of urogenital anomalies such as hypospadias, cryptorchidism, and micropenis have been associated with environmental endocrine disruptors. This study aimed to assess the prevalence of micropenis and other urogenital anomalies in healthy full-term male newborns in our country. A secondary aim of the study was to contribute further to national data by recording penile measurements, along with gestational age, in infants in whom micropenis was not detected.

Methods: In this study, the findings of urogenital examinations performed by the same physician during routine neonatal check-ups were evaluated in healthy male infants born at term (38–42 weeks of gestation) within a one-month period, at Zeynep Kamil Women and Children's Hospital.

Results: Among the 230 newborns examined, the incidence of hypospadias was 0.43%, and hydrocele 8.2%, while no cases of cryptorchidism were observed. The mean penile length was found to be 3.14±0.36 cm, and the mean penile diameter was 1.5±0.24 cm, with no cases of micropenis detected.

Discussion and Conclusion: No significant increase in the prevalence of hypospadias and cryptorchidism was observed. A significant correlation was found between penile length and birth weight, but no such relationship was identified with gestational age. The findings emphasize the need for ethnic-specific reference standards and larger-scale studies to better understand the impact of endocrine disruptors on male reproductive health.

Keywords: Endocrine disruptors; hypospadias; mean penile length; micropenis; urogenital anomalies.

In recent years, reports from all over the world have highlighted a decline in male reproductive health [1–5]. These publications describe a drop in sperm quality together with a rising incidence of urogenital anomalies such as hypospadias and cryptorchidism, as well as an increase in testicular cancer. The principal culprit is thought to be growing exposure to environmental endocrine disruptors—synthetic hormones, plastic components, and pesticides being the best-known examples. Today's newborn is already exposed in utero to chemicals that infants born before 1920 never encountered.

According to current literature, a thorough urogenital examination is a critical component of the routine neonatal physical assessment [6]. This examination is indispensable

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for distinguishing disorders of sex development, identifying life-threatening conditions such as congenital adrenal hyperplasia, and detecting urogenital anomalies such as micropenis, undescended testes, and hypospadias.

Micropenis is defined as a stretched penile length that falls more than 2.5 standard deviations below the mean for a given age [7,8]. Age-specific reference ranges for penile length have been established and serve as the benchmark in the diagnosis of micropenis. According to current data, the average penile length in full-term newborns is 3.5±0.7 cm, and the average penile diameter is 1.1±0.2 cm [7,8]. Values below 1.9 cm are considered indicative of micropenis and should prompt further investigation for underlying conditions [8]. These reference values are based on international data, but average measurements may vary by ethnic background [9]. However, studies conducted within our country on this topic remain limited.

Hypospadias is among the most common urogenital anomalies and is defined as an incomplete fusion of the penile urethra. Hypospadias is classified as Type I when the urethral meatus is located at the glans or subcoronal region, Type II when it is along the ventral penile shaft, and Type III when it is in proximal positions such as the penoscrotal, scrotal, or perineal region [10]. The incidence of hypospadias, reported as 2.02 per 1000 live births in 1970, increased to 3.97 per 1000 by 1993, corresponding to approximately 1 in every 250 live births [11,12]. Some researchers have linked the development of hypospadias to prenatal exposure to exogenous progestins, a type of endocrine disruptor [13]. The increased incidence of hypospadias in infants conceived through *in vitro* fertilization (IVF) further supports the potential role of endocrine disruptors in its etiology, although current evidence is not yet sufficient to establish a definitive causal relationship [14].

Cryptorchidism is another common congenital anomaly. Early recognition and appropriate treatment are crucial in preventing long-term complications such as infertility and malignancy [15,16].

Other conditions evaluated during routine neonatal urogenital examination include phimosis, paraphimosis, and hydrocele, which may signal underlying congenital adrenal hyperplasia [6,7].

This study aimed to determine the prevalence of micropenis and other urogenital anomalies in healthy full-term male newborns under local conditions. Additionally, penile length and diameter measurements, obtained during the assessment of infants without micropenis, were recorded alongside gestational age to provide supplementary data for national reference values.

Materials and Methods

This study was conducted at Zeynep Kamil Women and Children Diseases Training and Research Hospital. The gestational age of the neonates was determined based on the last menstrual period (LMP) as reported by the mothers.

Inclusion Criteria

1. Healthy male neonates born at term (38–42 weeks' gestation) based on LMP were included.

Exclusion Criteria

1. Premature infants were excluded.
2. Neonates with a history of undetermined maternal LMP were excluded.

Urogenital findings from the routine neonatal examination, all performed by the same physician, were analyzed.

This study was conducted following the ethical principles of the 1964 Declaration of Helsinki and its subsequent amendments, as well as comparable ethical standards. The measurements were performed as part of the routine physical examination of the neonates, with prior parental information and consent obtained. A total of 230 newborn boys met the inclusion criteria. For each infant, gestational age, mode of delivery, birth weight, and maternal data—age, gravidity, parity, number of miscarriages or terminations, illnesses during pregnancy, and use of iron, multivitamins, or other medications—were recorded. Family history variables (consanguinity, urogenital anomalies in male siblings or other relatives) were also documented.

During the standard physical examination, the urogenital system was assessed by inspection and palpation. Penile length and diameter were measured; a stretched penile length more than 2.5 SD below the mean for gestational age was classified as micropenis [7,8]. Additional findings such as hydrocele, hypospadias, epispadias, and cryptorchidism were noted. Hypospadias was defined by the presence of incomplete fusion of the penile urethra during clinical examination. Cases with any urogenital anomaly were referred, as per routine practice, to pediatric endocrinology and pediatric surgery.

Statistical Analysis

Data were analyzed with SPSS version 10.0 (SPSS Inc., Chicago IL, USA). Descriptive statistics (mean, SD, frequency, percentile) were calculated. Because continuous variables followed a normal distribution, Pearson correlation assessed relationships between continuous variables, and the chi-square test compared categorical variables. Results were considered significant at $p<0.05$ (95% confidence level).

Table 1. Penile length and diameter values in full-term male neonates

	Min-max (cm.s)	Mean±SD (cm.s)
Penile length	2.30-4.50	3.14±0.36
Penile diameter	0.90-1.70	1.15±0.12

Penile length and diameter are presented as mean±SD, with corresponding minimum and maximum values (cm). SD: Standard deviation.

Table 2. Correlation between penile length and birth weight & gestational age

	Penile Length	
	r	p
Birth weight	0.279	0.001**
Gestational age	0.046	0.485

**: p<0.01 indicates a statistically highly significant correlation. r: Pearson correlation coefficient.

Results

The mothers' mean age was 25.52±4.70 years (range 17–40). Mean gravidity was 1.99±1.11 (range 1–8) and mean parity 1.75±0.97 (range 1–7). Consanguinity was present in 28.7% of cases, and 3.0% had a male sibling with a urogenital disorder. Vaginal delivery accounted for 90.9% of births. Mean birth weight was 3371±453.9 g.

Measured penile lengths ranged from 2.30 cm to 4.50 cm, with a mean of 3.14±0.36 cm. Mean penile diameter was 1.5±0.24 cm (range 0.90–1.70). The minimum, maximum, and mean values of penile length and diameter (in centimeters) are presented in Table 1. Hydrocele was identified in 8.2% of cases (3.9% bilateral, 3% right-sided, and 1.3% left-sided). Hypospadias was detected in a single case (0.43%), and no instances of cryptorchidism were found.

A highly significant correlation emerged between penile length and birth weight (p<0.001), but not between penile length and gestational age (p=0.485; Table 2).

Discussion

A thorough urogenital examination is an essential component of the neonatal examination, enabling the early detection of conditions that can affect future health. As demonstrated in our cohort, such an approach facilitates the detection of urogenital anomalies.

Only one infant (0.43%) presented with hypospadias, classified as type 2. The case was evaluated by pediatric surgery, and corrective surgery was scheduled for age one year; no additional urogenital anomalies were present. Apart from a medically supervised course of antibiotics during pregnancy, the maternal history was unremarkable.

No cases of cryptorchidism were recorded, even though cryptorchidism is generally considered the most common congenital anomaly, with reported prevalences of 4–8% [7]. The absence of cryptorchidism in our 230 infants contrasts with both these figures and studies suggesting an increasing incidence.

In our cohort, hydrocele was identified as an additional physical examination finding in about 8% of infants assessed for insufficient virilization. All were placed under pediatric surgical follow-up; persisting hydroceles were slated for elective repair.

Current reference values for neonatal penile size derive mainly from international data: with lengths below 1.9 cm regarded as micropenis [8]. Ethnic variation clearly influences these parameters, yet local data remain limited [17–21]. In a 2005 Turkish study conducted in Diyarbakır by Akarsu et al. [22], mean penile length in 1,522 healthy term newborns was 3.5±0.7 cm (range 2.1–4.9 cm), with a minimum of 1.9 cm.

In our series, no cases of micropenis were identified. Mean length in our study is slightly lower than both the commonly used reference and the value reported by Akarsu et al. [22], whereas mean diameter aligns with the literature. Our analysis revealed that penile length showed a correlation with birth weight, but not with gestational age.

Endocrine disruptors are exogenous substances or mixtures that alter endocrine function in a healthy organism—or in its offspring—and thereby cause adverse health effects. The agents most frequently implicated include diethylstilbestrol (DES), persistent organochlorines (DDT, PCBs, bisphenol A), methoxychlor, alkylphenols, phthalates, anti-androgenic fungicides, and phytoestrogens [23–26]. DES, once used to prevent miscarriage, is known to increase the incidence of urogenital anomalies in male infants and vaginal adenocarcinoma in females [27]. Contemporary data documenting the rising prevalence of urogenital anomalies and the deterioration of male reproductive health often implicate endocrine disruptors. Multiple studies have demonstrated measurable levels of toxic substances in amniotic fluid, cord blood, placenta, and breast milk [28–31]. Epidemiologic evidence also indicates an elevated relative risk of cryptorchidism in boys whose mothers work in pesticide-treated environments [31].

Our study did not include direct assessment of exposure to these compounds; future research should adopt prospective designs with larger cohorts and objective measures of endocrine disruptor exposure.

Conclusion

The impact of endocrine disruptors on the male reproductive system remains a timely and compelling topic. This study offers a current investigation into the prevalence of urogenital anomalies in male infants in the setting of increasing environmental exposure to endocrine-disrupting chemicals. Our findings indicate that there has been no significant increase in the prevalence of hypospadias and cryptorchidism, which are well-recognized clinical indicators of impaired virilization associated with endocrine disruptors.

Ethics Committee Approval: The study was approved by Haydarpaşa Numune Training and Research Hospital Ethics Committee (No: 771/7/2025, Date: 29.07.2025).

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