

Penile Length and Anogenital Distance in Male Newborns From Different Iranian Ethnicities in Golestan Province

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Background: Anogenital distance (AGD) is a feasible and accepted parameter of exogenous or endogenous androgens effects on development of reproductive system.

Objectives: Since there is no report on penile length (PL) and AGD in our region, we investigated these parameters in male newborns in Golestan Province, Iran.

Patients and Methods: In this cross-sectional study, we measured stretched PL and AGD in term newborns from different races in Dezyani Gynecologic Hospital of Gorgan, Iran. We also recorded the anthropometric parameters and maternal age. The data was analyzed using the SPSS 14.

Results: Means of PL and AGD of 427 healthy term newborns were 32.1 ± 3.5 and 24.5 ± 2.5 mm, respectively. There was a positive correlation between PL and AGD ($r = 0.097$, $P = 0.046$). According to their ethnicity, there were 166 Fars (38.9%), 129 Turkmen (30.2%), and 132 Sistani (30.9%) infants with mean PL of respectively 31.8 ± 3.9 , 32.3 ± 3.3 , and 32.4 ± 3.3 mm and mean AGD of respectively 25 ± 2.5 , 24.3 ± 2.5 , and 24 ± 2.5 mm. One Fars neonate (0.23%) had micropenis (PL = 21.3 mm).

Conclusions: Using -2.5 standard deviations as the cutoff for micropenis, a newborn infant in Golestan Province with a PL of < 23.3 mm had micropenis; however, more investigations are needed to clarify this issue.

Keywords: Ethnic Groups; Anthropometry; Male; Iran

1. Background

Examination of the genitalia is part of the physical examination of all neonates. Size abnormalities of the external genitalia in male and female newborns might be the first sign of underlying endocrine or genetic disorders such as congenital hypopituitarism (1). Micropenis is a condition, in which a penis is abnormally small while perfectly formed without hypospadias or epispadias and is usually defined as a penis that has a stretched length of shorter than 2.5 standard deviations (SD) below the mean (2). Isolated micropenis is an inadequate virilization disorder that results from a hormone defect arising after week 14 of embryonic development (3). It might be presented in Noonan and Robinow syndromes as well as in chromosomal abnormalities such as Klinefelter's and Prader-Willi syndromes (4). Nowadays, anogenital distance (AGD) is used for investigations on fetal androgen activity and reproductive toxicities in experimental animals and humans (5-8). Several studies have shown that males have a greater AGD than females, in both animals and humans (9-11). Comorbidity of shorter AGD with hypospadias and cryptorchidism was seen in human males (9). Recently, Mendiola et al. reported a strong correlation of AGD with all semen parameters and its predictive

value for low sperm concentration in adult males (8). Therefore, early measurement of penile length (PL) and AGD can help us find underlying masculinization defects and predict future reproductive health of newborns. PL is reported to vary between different races and ethnicities in several studies (1, 12-16). Reference values based on local normative data for PL are important for the early diagnosis and treatment of potential diseases. To our knowledge, there are no published studies from our region establishing normal values for PL and AGD of newborn males.

2. Objectives

This study aimed to demonstrate and compare the norms of PL and AGD in term newborn infants in Golestan Province, northern Iran, and assess inter-racial differences in our population. We also evaluated the association between PL and anthropometric measures such as body weight and length.

3. Patients and Methods

This cross-sectional study was conducted in Dezyani Hospital of Gorgan, Golestan Province, northern Iran. A total of 427 full-term (37-42 weeks) healthy male infants,

who were born between March 2011 and March 2012, were included. While there is a rich cultural and racial variety in the Golestan Province, we measured PL and AGD in newborns from three main ethnicities including Fars, Turkmen, and Sistani to compare the results among them. Written informed consent was obtained from parents before all evaluations. The Ethics Committee of Golestan University of Medical Sciences approved this study (code, 6309102319). Neonates with ambiguous genitalia, hypospadias, undescended testis, multiple maternal anomalies, endocrine disorders, admission in NICU, and neonates of mothers who took androgens during pregnancy were excluded. Three patients were excluded from the study because of some congenital urological malformations, two with undescended testes and one with hypospadias. Gestational age was calculated according to the last menstrual period or the age based on sonography before the week 20. In case of uncertain gestational age, the Ballard score examination was performed within the first 24 hours of life to determine the gestational age. Sampling was done by screening method; we included every single healthy male newborn who was born in our hospital. The stretched PL and AGD were measured in supine position. For measuring PL, the penis was gently stretched to the point of maximum resistance and a ruler (VYCON) was pressed alongside the penis onto the pubic bone. The PL was measured at the level of the top of the glans penis excluding the foreskin (10, 11). For measurement of AGD, both hip and knee joints were in flexion and gentle pressure was applied on both legs towards the abdomen and the distance between the center of anus and posterior base of scrotum was recorded (10, 11). All measurements were performed by a single examiner whose proficiency was validated before the study. Measurements were repeated three times for each newborn in the first day of life and the mean was recorded as the final value.

The results were expressed as means and standard de-

viations (SD). Micropenis was calculated and defined as $PL < [\text{mean PL} - (2.5 \times \text{SD})]$ in each ethnic group and total study population. According to Ting et al. (15) and results of a pilot study with sample size of 18, $\alpha = 0.05$, $\beta = 0.1$, maximum error of 0.9 sample size for each ethnic group (Fars, Turkmen), $\mu_1 = 32$, $\mu_2 = 33.6$, and $\delta_1 = 4.4$, $\delta_2 = 3.4$, the sample size in each ethnic group was calculated at 129. The expected power of study was 90%. Normal distribution of data was evaluated by Shapiro-Wilk's test. The one-way ANOVA was used for comparisons and the Pearson's correlation test was applied to assess the associations among parameters. The data was analyzed using the SPSS 14 (SPSS Inc, Chicago, IL, USA). $P < 0.05$ was regarded as statistically significant.

4. Results

A total of 427 term male newborns were included in the study. Mean and SD of weight, height and head circumference in the first day of birth were 3.3 ± 0.4 kg, 49.2 ± 2.1 cm, and 35 ± 1.2 cm, respectively. Mean maternal age was 26.9 ± 5.5 years. Mean PL and AGD in study subjects were 32.1 ± 3.5 mm and 24.4 ± 2.5 mm, respectively (Figure 1). There was a statistically significant positive correlation between PL and AGD ($r = 0.097$, $P = 0.046$) and there was a significant negative correlation between PL and infants' head circumference ($r = -0.098$, $P = 0.043$). According to their ethnicity, there were 166 Fars (38.9%), 129 Turkmen (30.2%), and 132 Sistani (30.9%). Mean \pm SD and range of PL and AGD in different ethnic groups are shown in Table 1. There was no significant difference in PL among ethnic groups but AGD in Fars neonates was the highest and statistically different from Turkmen ($P = 0.04$) and Sistani ($P = 0.003$) neonates. As previously described, micropenis definition was calculated for each ethnicity and total study population as shown in Table 1. In our study, one Fars neonate (0.23%) was had micropenis (PL = 21.3 mm) that diagnostic and therapeutic approach was started for him.

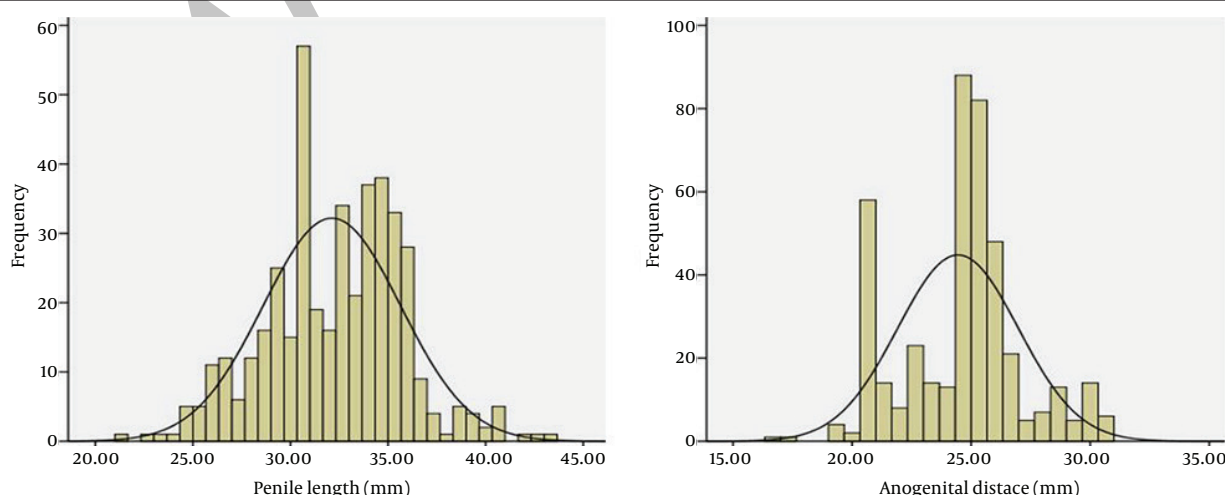


Figure 1. Distribution of Penile Length and Anogenital Distance of Iranian Newborn Infants From Golestan Province, Iran

Table 1. Penile Length and Anogenital Distance of Male Neonates According to Ethnicity in Golestan Province, Iran ^{a,b}

Parameter	Fars (n = 166)	Turkmen (n = 129)	Sistani (n = 132)	Total (n = 427)
Penile Length, mm	31.8 ± 3.9 [21.3-41.3]	32.3 ± 3.3 [24.7-40.7]	32.4 ± 3.3 [24.3-40.7]	32.1 ± 3.5 [21.3-43.3]
P Value	Compared to Turkmen (P = 0.543)	Compared to Sistani (P = 0.981)	Compared to Fars (P = 0.418)	P = 0.388
Anogenital Distance, mm	25 ± 2.5 [17.3-30.3]	24.3 ± 2.5 [20.7-29.7]	24 ± 2.5 [16.7-29.7]	24.5 ± 2.5 [16.7-30.3]
P Value	Compared to Turkmen (P = 0.04)	Compared to Sistani (P = 0.673)	Compared to Fars (P = 0.03)	P = 0.002
Micropenis Definition, mm ^a	PL < 22.2	PL < 24.1	PL < 24.1	PL < 23.3

^a Data are presented as mean ± SD [range].^b Micropenis is defined as follows: mean PL - (2.5 × SD).

5. Discussion

In comparison with other parts of the world, the mean PL of term newborns from Golestan Province seemed to be more similar to European newborns. Specifically, Kutlu et al. (4) and Thankamony et al. (10) reported a mean PL of 31.5 ± 5 and 30 ± 4 mm from Turkey and England, respectively. Moreover, Ting et al. reported PL of 35 ± 4 mm in Malaysia (15), Al-Herbish reported 36.5 ± 5 mm in 379 Saudi Arabian infants (17), Feldman and Smith reported a mean PL of 35 ± 7 mm in 37 Caucasian term newborn infants in the United States (18), and Vasudevan et al. from India reported PL of 36 ± 5 mm in 135 South Indian infants (19). Our measurements of AGD were similar to the reports from the United States and Nigeria (23 ± 3.8 and 25.8 ± 1.1 mm, respectively) (20, 21). Salazar-Martinez et al. reported mean AGD of 21 ± 3 mm from Mexico (11) and Thankamony et al. reported AGD of 19.8 ± 6.1 mm (10), both different from our results. According to the results of our study, the ethnicity had no significant effect on PL but would affect AGD. Ting et al. (15) also reported no difference between PL of Chinese, Malay, and Indian infants (PL = 35 ± 4 mm) but other studies by Lian et al. (12) reported of 35 ± 3 mm for Chinese, 36 ± 4 mm for Malay, and 38 ± 4 mm for Indian infants and Cheng et al. (14) showed significant difference between races. Regarding the significant difference of AGD between races, our findings were similar to report of Sathyanarayana et al. (20) who reported longer AGD in Caucasian male infants in comparison to compared to Asian or native American (P = 0.033). In this study, PL < 23.3 mm in an Iranian newborn was determined as micropenis and necessitated further laboratory and clinical evaluations. Specifically in Fars, Turkmen, and Sistani neonates in whom the micropenis was defined as PL < 22.2, < 24.1, and < 24.1 mm, respectively. In other reports from Singapore, Malaysia, Turkey, and England, the micropenis was defined as PL < 26, < 25, < 21.9, and < 20 mm, respectively (10, 12, 15, 22). Numerous studies have demonstrated validity of AGD as a sensitive marker for the effects of intrauterine exposure to androgens and chemicals with anti-androgen effects (23-25). Consequently, AGD has been identified as one of the endpoints in the United States Environmental Protection

Agency guidelines for reproductive toxicity studies in humans (26). Therefore, its changes in comparison to normal population might predict future sexual and fertility disorders (10). According to the results of our study, there is a positive correlation between PL and AGD. Romano-Riquer et al. reported a positive correlation between PL and AGD (r = 0.03, P = 0.046) in a group of 781 Mexican infants (27). Thankamony et al. also reported positive correlation between PL and AGD (r = 0.18, P = 0.003) (10). Observed differences in reported PL and AGD might be due to inter-racial differences between different study populations. Thankamony et al. suggested systematic error measurements as a reason of differences between reported values (10). Considering the results of present study along with similar reports, the correlation between PL and AGD might suggest using AGD as a measure of genital development in males, as previously was shown for PL.

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Authors' Contributions

Ehsan Alaee and Mahnaz Fouladinejad designed and coordinated the study, participated in most of the experiments, and prepared the manuscript. Mohammad Javad Gharib coordinated and performed all the experiments and participated in manuscript preparation. All authors have read and approved the content of the manuscript.

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