



# Which of the Anthropometric Parameters and Hormonal Variables in Prepubertal Children Are Correlated to True Micropenis?

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Received 2020 August 16; Revised 2020 October 05; Accepted 2020 November 05.

## Abstract

**Background:** Most issues of micropenis boys include poor body image and quality of life.

**Objectives:** The purpose of this assay was to survey the relationship of anthropometric measures, testosterone, estradiol, gonadotropins and prolactin with stretched penile length (SPL) and flaccid glans-pubis length (GPL) in pre-pubertal boys with true small penis.

**Methods:** This was prospective a cross-sectional observational study that was conducted in Imam Reza Hospital, Tehran, Iran from February 2015 to May 2020. The pre-pubertal children 7 - 14 years who referred with small penis size were evaluated by a pediatrician and urologist and, if they had true micropenis, they were enrolled in the study (n = 236). The anthropometric and hormonal measurements, SPL, GPL, and relationship of these variables were evaluated.

**Results:** Mean ages of children were  $11.65 \pm 1.59$  years. Mean SPL and GPL were  $2.95 \pm 1.23$  and  $2.29 \pm 1.06$  cm, respectively. There was a significant relationship between SPL and GPL ( $r = 0.976$ ,  $P = 0.000$ ). SPL and GPL were not correlated with BMI ( $r = -0.182$ ,  $P = 0.054$ ;  $r = -0.161$ ,  $P = 0.089$ , respectively). A significant correlation was found between SPL and GPL with height, FSH, LH, Testosterone and T/E ratio ( $P < 0.01$ ) but no correlation with weight, estradiol and prolactin ( $> 0.05$ ).

**Conclusions:** According to the finding of present study, the flaccid measurement can be as helpful as stretched measurement if it is done from pubic bone to tip of glans. Retraining of primary health workers about age-related penile length may be reducing the misdiagnosis of micropenis and concerns of parents, especially in obese boys. The penile length in prepubertal children was not related to BMI and weight but was significantly related to height. Furthermore, Estradiol level is not related to penile length in children with micropenis.

**Keywords:** Anthropometric Parameters, Estradiol, Gonadotropins, Micropenis, Testosterone

## 1. Background

Micropenis refers to a condition that the stretched penile length less than 2.5 standard deviation (SD) below the mean size of the related age, which is structurally normal. Its incidence is about 1.5 per 10000 children. Differential diagnosis of true micropenis includes: buried penis, trapped penis, webbed penis and penis with marked chordee (1).

Sexual differential begins in the 7th week of gestation. In the 15th week, the hypothalamic-pituitary-gonadal axis is activated and androgen secretion occurs. In fetal period, a peak level of androgen occurs in 14th - 16th weeks and after birth, testosterone rises from birth to 1 - 3 months, and then declines to prepubertal level by 4 - 6 months. That's why the highest growth of penis occurs up to three months after birth. In addition, the development of male identity is

due to the effect of testosterone on the central nervous system during fetal and early infancy (2). Micropenis may occur in association with hormonal disturbances or as an isolated disease. The most common hormonal disturbances include: hypogonadotropic hypogonadism, androgen insensitivity, testosterone, 5- $\alpha$  reductase and growth hormone deficiency (3).

Sometimes obese boys are examined for small penis because of parents' concerns. The penis size is mostly normal and this is because of an increase in pubic fat mass, which conceals the penis. Therefore, precise measure of penis length can differentiate micropenis from these cases. Furthermore, deferment in small penis diagnosis may delay treatment and cause anxiety of parents. Most issue of parents and their children include poor body image and concern about inappropriate sex relationship. Thus survey of penile size is important and decisive for family and

physicians (4, 5). Today, 35.1 percent of children suffer from obesity (6). According to this issue, study about relation of micropenis with anthropometric measures and hormones is quite obvious. The results of previous researches have been different and this is shown the significance of further investigations to attain precise and conclusive results.

## 2. Objectives

The purpose of this study was to assay the relationship between anthropometric measures, testosterone, estradiol, testosterone/estradiol ratio (T/E ratio), gonadotropins and Prolactin with stretched and non-stretched (flaccid) penile length in healthy pre-pubertal boys with true small penis to get proper and helpful results for this problem, which worries both physicians and parents.

## 3. Methods

### 3.1. Study Design

This was prospective cross-sectional observational study. Sampling method was simple convenience.

### 3.2. Setting

We assessed the boys at Imam Reza Hospital, Tehran, Iran from February 2015 to May 2020.

### 3.3. Study Populations

In our survey, 1798 pre-pubertal boys who referred with possible small penis underwent evaluation including stretched penile length (SPL) and flaccid glans-pubis length (GPL). Inclusion criteria were healthy children, age 7-14 years with true small penis (less than 2.5 standard deviation of the mean size of related age) (3) without bending, torsion, and scare of penis-surgery. Exclusion criteria were sever and persistent diseases, renal failure, endocrine illness such as adrenal, growth and thyroidal hormones insufficiency and defect, buried and trapped penis, undescending (UDT) and atrophic testis, hypospadias and past history of corticosteroid therapy, radiotherapy, chemotherapy. Patients were examined by a pediatric and urology specialist and after the true small penis was proven, they would be entered in the research. Of the 1,798 children with probably small penis, only 261 had true micropenis. Twenty-five children left the research because of reluctance to continue. Finally, 236 boys completed the research and blood sampling and anthropometric measurements were done.

All children had been circumcised and were examined in lying face upward at temperature of 21°C - 23°C. Penile lengths were measured with a flexible plastic ruler. Stretched penile length (SPL) was measured the distance

of pubic bone (by pressing on the pubic fat) to the end of stretched penile (stretched length). Also, the glans penile length (GPL) was measured the distance of pubic bone (by pressing on the Mons' pubis fat) to the end of penile head that had not been stretched (flaccid length). Penile length was measured by an urologist and the mean of two measurements was calculated and recorded.

### 3.4. Anthropometric Measurements

Anthropometric measurements of children were on the base of World Health Organization (6, 7). Weight and height were measured by scale (limit validity 100 g) and standing meter (limit validity of 0.5 cm) with little clothes, without shoe. Body mass index (BMI) = Weight (kg)/height<sup>2</sup> (m<sup>2</sup>). BMI ≥ 95th percentile was obese and between ≥ 85th and < 95th percentile was overweight. Anthropometric parameters of children were measured by a pediatrician and the mean of two measures was calculated and recorded.

### 3.5. Hormonal Measurements

Non-fasting venous blood sample was taken at the hospital laboratory in the early morning and preserved at -20°C. Testosterone (T) and estradiol (E) were measured with radioimmunoassay. FSH, LH, and prolactin were measured with Elisa. The detection limits, intra-assay and inter-assay coefficients of variation (CV) of hormonal kits were shown in Table 1. All hormonal laboratory kits belonged to Pishbaz Company, Tehran, Iran.

**Table 1.** Intra-assay and Inter-assay Coefficient of Variation (CV) of Hormonal Kits

Coefficients of Variation (CV)	Intra-assay, %	Inter-assay, %	Detective Limits
Testosterone, ng/mL	< 7.2	< 8.5	1
Estradiol, pg/mL	< 10	< 12	4.45
FSH, IU/L	< 2.9	< 3.8	1
LH, IU/L	< 4.9	< 7	1
Prolactin, mIU/L	< 5.7	< 6.5	15

Abbreviations: FSH, follicle stimulating hormone; LH, luteinizing hormone.

### 3.6. Main Outcome Measure

The BMI, hormonal measurements, SPL and GPL and penis length correlation to BMI and hormonal measurements were evaluated as the main outcomes.

### 3.7. Statistical Analyses

SPSS statistical software version 21 was used for data analysis (SPSS Inc, Chicago, IL, USA). Mean and standard deviations were assessed for quantitative factors and frequency and frequency percent for qualitative factors. Student *t*-test was performed for difference between SPL and GPL with anthropometrics and hormonal factors and the Pearson's correlation coefficient (*r*) was performed for statistical analysis. In subgroups, variables were compared by Mann-Whitney U-test. P-value < 0.05 was significant.

### 3.8. Ethical Considerations

In all stages of the study, ethical issues of observation, the name and information of participants were kept confidential. Informed consent was obtained from all subjects. The Ethics Committee of Army University of Medical Sciences approved research project of this study (code: IR.AJAUMS.REC.1399.024).

## 4. Results

Mean ages of subjects was  $11.65 \pm 1.59$  years. Mean and standard deviation (SD) of SPL and GPL were  $2.95 \pm 1.23$  and  $2.29 \pm 1.06$  cm, respectively. Anthropometric measures of subjects were height  $145.26 \pm 11.21$  cm, weight  $55.36 \pm 14.21$  kg and BMI  $27.24 \pm 5.22$  kg/m<sup>2</sup>. Hormonal assessment of children was FSH  $2.08 \pm 1.64$  IU/L, LH  $1.05 \pm 1.37$  IU/L, testosterone  $1.6 \pm 1.51$  ng/mL, estradiol  $50.31 \pm 11.26$  pg/mL, prolactin  $155.85 \pm 100.27$  mIU/L and T/E ratio  $0.02 \pm 0.029$ . Demographic property and hormones factors of children were demonstrated in Table 2.

**Table 2.** Demographic Properties and Hormonal Amounts of Micropenis subjects (N = 236)

	Min	Max	Mean $\pm$ SD
Age, y	7	14	11.65 $\pm$ 1.592
Heigh, cm	124	170	145.26 $\pm$ 11.21
Weight, kg	24	126	55.36 $\pm$ 14.21
BMI, kg/m <sup>2</sup>	17.06	38.38	27.24 $\pm$ 5.22
SPL, cm	1.3	5.2	2.95 $\pm$ 1.23
GPL, cm	1.1	3.5	2.29 $\pm$ 1.065
FSH, mIU/mL	0.01	8.2	2.08 $\pm$ 1.64
LH, mIU/mL	0.02	9.3	1.05 $\pm$ 1.37
Testosterone, ng/dL	0.07	11.9	1.6 $\pm$ 1.51
Estradiol, pg/mL	17	72	50.31 $\pm$ 11.26
Prolactin, mIU/L	32	527	155.28 $\pm$ 12.226
T/E ratio	0.001	0.19	0.02 $\pm$ 0.029

Abbreviations: FSH, follicle stimulating hormone; GPL, flaccid glans-pubis length; LH, luteinizing hormone; SD, standard deviation; SPL, stretched penile length; T/E, testosterone/estradiol.

The frequency of subgroups characteristics of the subjects was shown in Table 3. There was not statistically difference in SPL and GPL between the subgroups of subjects ( $P > 0.05$ ).

There was a significant relationship between SPL and GPL ( $r = 0.976$ ,  $P = 0.000$ ). SPL and GPL were not correlated with BMI ( $r = -0.182$ ,  $P = 0.054$ ;  $r = -0.161$ ,  $P = 0.089$ , respectively). A positive significant correlation was found between SPL with height, FSH, LH, testosterone and T/E ratio (height:  $r = 0.241$ ,  $P = 0.01$ ; FSH:  $r = 0.241$ ,  $P = 0.009$ ; LH:  $r = 0.300$ ,  $P = 0.001$ ; testosterone:  $r = 0.351$ ,  $P = 0.001$ ; T/E ratio:  $r = 0.317$ ,  $P = 0.001$ ) but no correlation with weight, estradiol and prolactin ( $r = -0.042$ ,  $P = 0.741$ ;  $r = 0.089$ ,  $P = 0.329$ ;  $r = -0.112$ ,  $P = 0.237$ , respectively). likewise, GPL was positively correlated to height, FSH, LH, Testosterone and T/E ratio (height:  $r = 0.221$ ,  $P = 0.03$ ; FSH:  $r = 0.193$ ,  $P = 0.036$ ; LH:  $r = 0.251$ ,  $P = 0.006$ ; testosterone:  $r = 0.341$ ,  $P = 0.001$ ; T/E ratio:  $r = 0.304$ ,  $P = 0.001$ ) but not correlated to weight, estradiol and prolactin ( $r = -0.038$ ,  $P = 0.712$ ;  $r = 0.084$ ,  $P = 0.353$ ;  $r = -0.139$ ,  $P = 0.139$ , respectively) (Table 4).

## 5. Discussion

Recently, the parental visits to check the size of their children's penis have increased because of their worries. Perhaps one of the reasons for this issue was the increased parental awareness and the use of media (2). Due to the prevalence of child obesity and parental concerns about small penis, we decided to determine the factors affecting in this issue. Fortunately, after careful examination by specialists, most of these children had a normal penis. However, it is important to examine children who are true small penis so that the precise treatments can be performed without delay. After puberty, hormonal treatments are not completely effective and the proper response is not achieved (7).

In this study BMI showed weakly and negatively correlated with SPL but was not correlated to GPL. SPL, and GPL had significant correlation with height, FSH, LH, testosterone and T/E ratio but not with weight, estradiol and prolactin. It seemed that in obese child, through the activity of aromatase in adipose tissue causes an increase in estradiol production and thereby changing T/E ratio. The penile length had a significant correlation to testosterone levels, but not to estradiol. Therefore, in T/E ratio, we think that testosterone level is more crucial and decisive. In addition, prolactin can affect on the testosterone levels, but it was not directly correlated to penile length (8).

The most previous studies had been performed on penile length to get new references of penile size of society in neonates and adult men, but this research was carried out to evaluate healthy prepubertal boys with small penile length. Today, few researches have studied the correlation

**Table 3.** SPL and GPL in Relation to Subgroups of Anthropometric Variables and Hormonal Levels<sup>a</sup>

Groups	No (%)	SPL, cm		GPL, cm	
		Mean ± SD	P-Value	Mean ± SD	P-Value
<b>BMI</b>			0.478		0.415
Normal	30 (12.7)	3.25 ± 1.2		2.59 ± 1.09	
Over weight	28 (11.9)	2.98 ± 1.334		2.17 ± 1.22	
Obese	178 (75.4)	2.90 ± 1.225		2.26 ± 1.04	
<b>FSH</b>			0.124		0.261
< Normal	36 (15)	2.68 ± 1.507		2.12 ± 1.347	
Normal	182 (77)	2.97 ± 1.177		2.29 ± 1.007	
> Normal	18 (8)	3.32 ± 1.182		2.62 ± 1.078	
<b>LH</b>			0.09		0.171
< Normal	26 (11)	2.57 ± 1.321		2.03 ± 1.2	
Normal	186 (79)	2.93 ± 1.193		2.26 ± 1.014	
> Normal	24 (10)	3.53 ± 1.323		2.80 ± 1.239	
<b>Testosterone</b>			0.355		0.319
< Normal	152 (64.5)	2.90 ± 1.299		2.24 ± 1.098	
Normal	84 (35.5)	3.04 ± 1.105		2.38 ± 1.012	
<b>Estradiol</b>			0.599		0.714
Normal	84 (35.5)	2.88 ± 1.235		2.22 ± 1.027	
> Normal	152 (64.5)	2.99 ± 1.234		2.33 ± 1.091	
<b>Ratio T/E</b>			0.404		0.521
< Normal	134 (56.78)	2.97 ± 1.244		2.31 ± 1.079	
Normal	51 (43.22)	2.38 ± 0.479		1.80 ± 0.356	

Abbreviations: FSH, follicle stimulating hormone; GPL, flaccid glans-pubis length; LH, luteinizing hormone; SD, standard deviation; SPL, stretched penile length; T/E, testosterone/estradiol.

<sup>a</sup>There was not statistically difference in SPL and GPL between the subgroups of subjects.

**Table 4.** Correlation Coefficients (r) of Penis Length with Anthropometric Characteristic and Hormonal Parameters in Subjects<sup>a</sup>

	Height	Weight	BMI	FSH	LH	T	E	P	T/E Ratio
SPL	r = 0.241	r = -0.042	r = -0.182	r = 0.241	r = 0.300	r = 0.351	r = 0.089	r = -0.112	r = 0.317
	P = 0.01	P = 0.741	P = 0.054	P = 0.009	P = 0.001	P = 0.001	P = 0.329	P = 0.237	P = 0.001
GPL	r = 0.221	r = -0.038	r = -0.161	r = 0.193	r = 0.251	r = 0.341	r = 0.084	r = -0.139	r = 0.304
	P = 0.03	P = 0.712	P = 0.089	P = 0.036	P = 0.006	P = 0.001	P = 0.353	P = 0.139	P = 0.001

Abbreviations: E, estradiol; FSH, follicle stimulating hormone; GPL, flaccid glans-pubis length; LH, luteinizing hormone; P, prolactin; SPL, stretched penile length; T, testosterone.

<sup>a</sup>SPL according to BMI showed weakly negatively correlated but GPL was not correlated to BMI. SPL and GPL were positively and significantly correlated to height, FSH, LH, testosterone and T/E Ratio but not correlated to weight, estradiol and prolactin.

between penile length and anthropometric property and hormonal factors. We also did not see any comprehensive consensus in this regard (9-12). Also, due to large percent of these children were obese (68.2%), we examined estradiol and T/E ratio for the first time, which did not see in any article.

In one study in Korea, penile length in children 0 - 14 years was investigated. The aim of this study was to determine the new references of penile size in these children and hormonal and anthropometric measures were not studied. This study showed that flaccid and stretched penile length was not correlated to BMI. They found that weight and height have increased in recent decay. However, SPL has not significantly increased (9). In the present study, prepubertal child with true micropenis (mean age 11.65 ± 1.59 years) was studied. Also, correlations of penile length to anthropometric measurements and differ-

ent hormonal variables were determined.

Another study in 1962 normal boys showed that flaccid penile length (not in stretched) was correlated to testosterone. Others hormones were not determined. Also, this study showed that BMI was negatively correlated to penile size. Subjects of this study were normal boys less than 3 months old (10). But we studied prepubertal children with micropenis. Our study showed that BMI was not correlated to penile size in flaccid length but SPL was weakly and negatively correlate to BMI.

One study in Sri Lankian's neonates found positive relationship between SPL and height but not correlated to weight (11). But, Soheilipour et al. (12) showed that SPL was correlated to weight and crown heel distance. Most mentioned articles were studied on neonates and did not perform a complete hormonal survey. Our study was performed on prepubertal boys with anthropometric and hor-

monal measurements. Also, we found that length of penis was related to height, but not to weight and BMI. It seemed that in different geographic and ethnics, the relation between these factors and penile length were different.

Ryu et al. (13) studied 259 Korean boys 6-24-month-old with UDT. They found that the penis size in these boys were smaller than boys without UDT. Weight, height and contralateral testis size were similar in both groups. They did not study the hormonal levels. It seems that deficient testosterone levels to maybe the trigger of this difference. In our study, low testosterone levels were seen in 64.5% of healthy micropenis children. Furthermore, the length of penis was significantly related to height.

A study on 45 micropenis infants were determined the etiologic factors. There were hypogonadotropic hypogonadism 31%, hypogonadism 24%, insensitivity of androgens 2%, idiopathic 7% and no diagnosis 36% (14). In our study, hypogonadotropic hypogonadism was determined 36% and testosterone deficiency and abnormal T/E ratio were the most common hormonal abnormality (64.5% and 56.78%, respectively). Furthermore, the purpose of this study was not to report the frequency of the etiologic causes of micropenis. There are several factors that affect penile length, but according to most common causes, we investigated the relationship ( $r$ ) between stretched penile length (SPL) and novel penile length measurement method [flaccid glans-pubis length (GPL)] with the some of the most important factors involved in micropenis (studied factors: weight, height, BMI, gonadotropins, testosterone, estradiol, prolactin and T/E ratio) in healthy prepubertal boys.

Isolated hypogonadotropia and testosterone deficiency were crucial factors in isolated true micropenis children. Gad et al. (cited in Tsang) (15) determined that dihydrotestosterone had the least role in the formation of isolated micropenis and was more common in micropenis children with ambiguous genitalia. There are several factors that affect penile length, but according to most common causes, we investigated the mentioned factors. Also, due to large percent of these children were obese (68.2%), we examined estradiol and T/E ratio for the first time.

Another study on 65 children with micropenis, who were referred to department of pediatrics, 31% (20 boys) did not have a true small penis. The etiologic causes were only determined in 44% (29 boys) which the most common cause was hypogonadotropic hypogonadism and etiological cause was not found in 25% (16 boys). Anthropometric measures, estradiol level and T/E ratio were not studied in this study (16). In present study, 1798 small penis children who were referred by general practitioners, only 261 true micropenis boys (15%) were confirmed by physicians. We conceived that the lack of knowledge about the age-related

penile size and exact measuring was the cause of this issue. Retraining program is crucial and is recommended for general practitioner and primary health care about this issue.

Habous et al. (17) determined that the flaccid penile length measurement from the junction of peno-pubic skin to tip of glans was not accurate in predicting erect penile length. After pressing the fat tissue on the pubis, we calculated the GPL from pubic bone to the glans tip of penis that had not been stretched (flaccid length) and GPL did not show a significant difference with SPL. Therefore, this measurement method was reliable in the predicting the penile length, although the SPL was better and more accurate.

Micropenis can cause psychological disorders and affect the sexual quality of life. Anxiety and affective disorders (16.4% and 27.9%, respectively) were the most common disorders that could cause fear of sexual relationship, premature ejaculation, impotence, nocturia, poor stream and eventually prostatitis (18, 19). Therefore, early diagnosis and evaluation of this problem will reduce the concern of parents and children (20).

### 5.1. Limitations and Recommendations

It was better to measure the growth hormone level. In this study, it was not measured, because there were no growth disorders in our subjects. Another limitation of this study was the lack of study of dihydrotestosterone and androstenedione. In addition, if these two hormones were examined (although these are rare) the results would be more complete. Due to diversity of the studies about correlation of the penis length with anthropometric and hormonal factors, it is recommended that a systematic review be conducted to get precise and helpful results about this problem.

### 5.2. Conclusions

According to the finding of present study, the flaccid measurement can be as helpful as stretched measurement if it is done from pubic bone to tip of glans. Retraining of primary health workers about age-related penile length may be reducing the misdiagnosis of micropenis and concerns of parents, especially in obese boys. On the other hand, early and precise diagnosis and treatment will reduce psychological distress in children and their parents. The penile length in prepubertal children was not related to BMI and weight but was significantly related to height. The isolated gonadotropins and or testosterone deficiency are most important causes in this issue. Furthermore, estradiol level is not related to penile length in children with micropenis.



## Acknowledgments

The authors appreciate faculty of Pediatric department of Imam Reza Hospital and all subjects who helped us is a way to complete this project.

## Footnotes

**Authors' Contribution:** Bijan Rezakhaniha carried out the design and coordinated the study, participated in most of the experiments, and prepared the manuscript. Soheila Siroosbakht provides assistance in the design of the study, coordinated and participated in manuscript preparation and contributed to writing up process. Sadra Rezakhaniha contributed to writing up process, prepared revisions, and editing.

**Conflict of Interests:** Authors had no conflict of interest.

**Ethical Approval:** The Ethics Committee of AJA University of Medical Sciences approved research project of this study (reg no.: IR.AJAUMS.REC.1399.024).

**Funding/Support:** This study was not sponsored.

**Informed Consent:** In all stages of the study, ethical issues of observation, the name and information of patients were kept confidential.

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