

## Analysis of the Potential for Height Growth at Different Stages of Puberty Based on Bone Age in Healthy Girls

Kobra Shiasi <sup>1</sup>, \* Seyed-Amirabbas Ahadiat <sup>2</sup>, Minoo Chenari <sup>3</sup>, Mansor Sayyah <sup>3</sup>

<sup>1</sup> Prof., Research Center for Biochemistry and Nutrition in metabolic diseases, Kashan University of Medical Sciences, Iran.

<sup>2</sup> MD., Orde Van Artsen, Brussel, Belgium

<sup>3</sup> Kashan University of medical science, Kashan, Iran.

### Abstract

**Background:** Many parents are concerned about their child's final height with the onset of the larche. We decided to investigate the height potential in different stages of puberty.

**Method:** 731 healthy girls who had not yet completed puberty were studied. Bone age and predicted final height were assessed. The correlation of height potential with various indices has been investigated.

**Results:** The Mean age was  $9.88 \pm 1.3$  years. The girls have a mean height potential of 28.90, 25.64, 20.89, and 13.76 cm in thelarche stages of 1, 2, 3, and 4, respectively ( $p = 0.001$ ), and a mean height potential of 27.19, 21.46, 15.51 and 11.02 cm in pubarche stages of 1, 2, 3 and 4, respectively ( $p = 0.001$ ). Height potential was inversely related to pubarche stage ( $p$ -value = 0.004), chronological age ( $r = 0.74$ ,  $p$ -value = 0.001), bone age ( $p$ -value < 0.001) and Height Standard Deviation score (SDS) ( $p < 0.001$ ). It was not related to the thelarche stage, target height, or BMI SDS. Linear regression showed that the height potential has a significant relationship with pubarche stage ( $P = 0.004$ ) but not with the thelarche stage ( $P = 0.267$ ).

**Conclusion:** This study found that potential height has no significant relationship with the thelarche stage. On the other hand, pubarche is associated with advanced bone age and lower height potential.

**Key Words:** Bone age, Height potential, Predicted final height, Pubarche, Puberty, Thelarche.

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### \* Corresponding Author:

Seyed-Amirabbas Ahadiat, Dr., Kashan University of medical science, Kashan University of medical science, Iran. Email: [dr.ahadiat61@gmail.com](mailto:dr.ahadiat61@gmail.com)

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## 1- INTRODUCTION

Concern about short stature is a common cause of visits to pediatric and endocrinology clinics (1). Growth is a complex process and is influenced by various factors. Disruption of any of these can lead to stunted growth and short stature. Regular use of a growth chart and sequential height recording from infancy is the key to detecting abnormal growth and initiating preventive and curative measures (1, 2). Bone age assessment is frequently used to examine children who present with short stature or concern for short stature in adulthood.

Pediatric endocrinologists commonly use x-ray images to determine bone age or growth delay (3). With the Bayley- Pinneau method, we can predict the future height of a child whose bone age is greater than six years (3).

If the estimated final height is within the normal range, the child and parents will be reassured. The estimated final height of less than 150 cm for girls and 160 cm for boys is defined as short stature in adults. We can use interventions such as growth hormone injections and suppressing puberty through GnRH agonists.

The Grulich-Pyle (GP) and Tanner-Whitehouse (TW) methods are most commonly used to determine bone age. The FELS method is less common. Both GP and TW methods have limitations because observers (examiners) with different levels of training usually perform analyses (4). According to the GH Research Society's (GRS) guideline for 2000, as part of routine evaluation of children with growth failure over 1 yr of age, an x-ray of the non-dominant hand should be taken and read by an experienced radiologist (5). MRI and ultrasound are still in their early stages and need further research (4).

Short height of a parent or family member is the most important reason leading to

their concerns about their children being short (6). In an endocrinology clinic, the doctor makes a clinical guess about the height and stage of puberty for such people. If there is a concern about the final height, a non-dominant hand x-ray is used to determine the final height more accurately.

In this study, we aim to calculate the height potential according to the stage of puberty by considering the bone age and the predicted final height. It should be noted that no similar study has been conducted.

## 2- MATERIALS AND METHODS

### 2-1. Design and sampling

This study was prospective and conducted from June 2012 to May 2021; we collected data of all healthy girls referred to the Kashan University of Medical Sciences endocrinology clinic, concerning their final height. A simple convenience sampling method was used. Seven hundred thirty-one samples aged 7 years or older were enrolled.

### 2-2. Inclusion and exclusion criteria

Participants are included in the study if they are healthy and excluded if they have precocious puberty, chronic medication use, short stature, or genetic conditions.

### 2-3. Clinical examination

A pediatric endocrinologist examined all children and measured their sexual maturity (SMR) and bone age using a Greulich-Pyle atlas and height using a SECA stadiometer. A checklist was set up to collect data. Variables such as age, bone age, height, puberty stage, and date of referral, history of certain drugs, and chronic disease history were considered.

### 2-4. Technical Information

Height potential is defined as the difference between height at the time of study and predicted final height.

Height potential in different stages of thelarche and pubarche was measured based on bone age.

Height potential was measured in different age groups in healthy girls.

Correlational analyses were performed between height potential, the standard deviation of body mass index, and bone age in healthy girls.

### 2-5. Data analysis

Data was analyzed by the use of SPSS version 18. After calculating the descriptive statistics indicators, the prediction equation of the desired quantities was calculated using multivariate linear regression analysis. The statistical tests were performed considering the 95% confidence level and 80% statistical power.

## 3- RESULTS

731 healthy girls seven years and older with a mean age of  $9.78 \pm 1.32$  years, and mean weight of  $34.61 \pm 9.42$  kg, and a mean height of  $135.29 \pm 7.18$  cm were studied. The mean birth height was  $49.36 \pm 4.27$  cm, and the mean birth weight was  $3.09 \pm 0.51$  kg.

Characteristics of cases and the potential for height increase in different stages of puberty are shown in **Tables 1, 2, and 3**.

### 3-1. Evaluation of potential height in a child at thelarche stage and varying pubarche stages

Girls with thelarche with varying stages of pubarche, compared with girls with only thelarche (no pubarche), had lower potential height, lower predicted final height, lower BMI SDS, more advanced chronological and bone age, and higher height SDS. While target height and height and weight at birth were not significantly different between the two groups.

### 3-2. Evaluation of potential height in a child at Pubarche stage and varying thelarche stages

Girls with pubarche with varying stages of the larche than girls with pubarche (no thelarche) had lower potential height, more advanced bone age, and lower BMI SDS. In contrast, the target height predicted final height; and height and weight at birth were insignificant between the two groups.

### 3-3. Comparing only Thelarche with only Pubarche stages

There was no significant difference between girls with only thelarche and girls with only pubarche in terms of chronological and bone age and potential height; however, the BMI SDS of girls with only Thelarche was higher than that of girls with only pubarche (Mean BMI SDS =0.69 in contrast to 0.07,  $p=0.018$ )

### 3-4. Correlation between potential height and other variables

The height potential was inversely related to chronological age, bone age, and height SDS, but not with target height ( $P= 0.687$ ) or BMI SDS ( $P=0.847$ ).

There was an inverse relationship between potential height with the pubarche stage ( $r = -0.48$  and  $P=0.001$ ) and the thelarche stage ( $r = -0.46$ ). The difference in the height potential in different stages of thelarche and pubarche and age groups was significant ( $P=0.001$ ). Linear regression showed that the height potential has a significant relationship with chronological age ( $P=0.001$ ), bone age ( $P=0.001$ ), the difference between bone age and chronological age ( $P=0.001$ ), the height SDS ( $P=0.001$ ), predicted final height ( $P=0.001$ ), and pubarche stage ( $P=0.004$ ), but had no significant relationship with thelarche stage ( $P=0.267$ ).

**Table-1:** Characteristics and potential for height increase in different thelarche stages

Variable		Chronologica l1 age (CA)	BMI SDS	.Height SDS	Bone age (BA)	BA-CA	PFH	PH	Target height
		(Year)			(Year)				
Thelarche stages	Stage 1	9.14±1.11	(-0.19)+1.29	(-1.04+0.85)	8.68+1.47	(-0.46+1.22)	7.46±156.58	8.29±28.90	7.22±154.73
	Number	(120)	(120)	(120)	(120)	(120)	(120)	(120)	(69)
	Stage 2	1.09±9.19	1.17±0.29	0.81±(-0.57)	1.28±9.35	1.10±0.15	6.21±156.49	7.67±25.64	3.73±156.16
	number	(208)	(207)	(208)	(208)	(208)	(208)	(208)	(128)
	Stage 3	1.21±9.78	1.42±0.83	0.90±(-0.38)	1.38±10.18	1.06 ±0.39	5.62±156.06	7.87±20.89	6.26±156.33
	number	(216)	(216)	(216)	(216)	(216)	(216)	(216)	(125)
	Stage 4	1.07±10.74	1.17±0.57	0.89±(-0.32)	1.02±11.62	1.06±0.88	5.39±154.78	4.98±13.76	3.90±155.50
	number	(187)	(185)	(187)	(187)	(187)	(187)	(187)	(112)
	P-value	0.001	0.001	0.001	0.001	0.001	0.021	0.001	0.166

SDS: standard deviation score, BA-CA: Difference between bone age and chronological age (in years), PFH: predicted final height, PH: potential for height increase

**Table-2:** Characteristics and potential for height increase in different pubarche stages

Variable		Chronological age (CA)	BMI SDS	Height SDS	Bone age	BA-CA	PFH	HP	Target height
		(Year)	(KSM)	(Cm)	(Year)	(Year)	(Cm)	(Cm)	(Cm)
Pubarche stages	Stage	1.11±9.13	1.46±0.42	0.89±(-0.70)	1.48±9.04	1.18±(-0.08)	6.81±156.97	8.60±27.19	3.96±155.93
	number	(297)	(297)	(297)	(297)	(297)	(297)	(297)	(171)
	Stage 2	1.14±9.66	1.10±0.49	0.83±0.45-	1.26±10.09	1.04±0.43	5.33±155.51	6.96±21.46	7.39±155.67
	number	(232)	(231)	(232)	(232)	(232)	(232)	(232)	(139)
	Stage 3	1.08±10.62	1.07±0.29	0.96± (-0.41)	1.00±11.20	1.15±0.58	5.52±155.10	5.12±15.51	3.62±156.01
	number	(136)	(136)	(136)	(136)	(136)	(136)	(136)	(80)
	Stage 4	0.95±11.11	1.70±0.67	0.88±(-0.27)	0.93±12.21	1.05±1.09	5.91±154.57	4.39±11.02	4.13±155.43
	number	(65)	(63)	(65)	(65)	(65)	(65)	(65)	(44)
P-value	0.001	0.278	0.001	0.001	0.001	0.003	0.001	0.912	

SDS: standard deviation score, BA-CA: Difference between bone age and chronological age (in years), PFH: predicted final height, PH: The potential for height increase

**Table-3:** Potential height increase based on puberty stage and age group

Age Groups	Both Pubarche and thelarche	Pubarche, without Thelarche	Thelarche without Pubarche	Pubarche, Without Thelarche	All cases	p-value
7-8 yr Number	29.98±3.30 (7)	28.26±10.19 (5)	34.10±6.33 (32)	38±3.69 (16)	34.17±6.45 (60)	0.003
8-9 yr Number	26.15±5.9 (71)	28.18±4.69 (15)	29.97±6.36 (74)	32.92±6.58 (20)	28.64±6.46 (180)	0.001
9-10 yr Number	18.66±5.72 (116)	25.01±4.12 (9)	23.82±6.66 (62)	28.64±6.62 (21)	21.48±6.92 (208)	0.001
10-11 yr Number	15.39±4.78 ((113)	17.15±1.34 (3)(3)	19.26±7.25 (26)(26)	22.85±5.09 (13)(13)	16.7±5.72 (155)	0.001
11-12 yr Number	13.07±3.93 (72)	18.98±8.71 (5)	1373±1.78 (10)	14.82±4.84 (4)	13.54±4.3 (91)	0.024
12<year Number	10.58±4.18 (33)	-	10.74±3.46 (4)	-	10.6±4.06 (37)	0.942
p-value	0.001	0.011	0.001	0.001	0.001	-

### 3-5. Comparing potential height in different age groups

The mean potential height has decreased with the increase in chronological age; and the difference between different age groups has been significant. Moreover, the difference in the mean potential height in each age group was significant in terms of puberty status.

### 3-6. Correlation between advanced bone age and other variables

Chronological and bone age difference is directly related to height SDS ( $r = 0.59$ ,  $p = 0.001$ ) and BMI SDS ( $r = 0.34$ ,  $p = 0.001$ ), and inversely to the predicted final height ( $r = -0.37$ ,  $p$ -value = 0.001), and potential height ( $r = -0.54$ ,  $p = 0.001$ ); but not with target height ( $p = 0.173$ ).

### 3-7. Correlation between predicted final height and other variables:

Predicted final height was inversely related to the chronological and bone age, and directly related to height SDS, the potential height ( $r = 0.56$ ,  $p < 0.001$ ), target height ( $r = 0.18$ ,  $p = 0.001$ ), and BMI SDS ( $r = 0.08$ ,  $p = 0.001$ ).

### 3-8. Correlation between target height and other variables

The target height was directly related to height SDS and predicted final height but had no significant relationship with chronological and bone age, potential height, BMI SDS, and the larche or pubarche stages.

### 3-9. Correlation between BMI SDS and other variables

The standard deviation of BMI was inversely related to age. There was a direct relationship between bone age and chronological age, height SDS, and the predicted final height. Also, it was directly related to the thelarche stage ( $r = 0.17$ ,  $P = 0.001$ ) but not with bone age, potential height, target height, or pubarche stage.

## 4- DISCUSSION

Parents are commonly worried about the final height of their child, especially in girls who have symptoms of puberty and aren't satisfied with their height. Our study aimed to determine the potential for height gain at different stages of clinical maturity in healthy girls referred to the pediatric endocrinology clinic. In fact, using bone age, we expect how much height a person will gain, which is the difference between PAH (Predict Final Height) and height at study, so we can reassure people who are most likely to reach their ideal height.

Our girls' average PAH was  $155.94 \pm 6.07$  cm, which is lower than the average height of 164 cm in the study by Koepke et al. (7). In the study by Razzaqi Azar et al. (8), it was reported that the height of Asian girls was one percentile shorter than that of the standard growth charts. It should also be borne in mind that the people we studied were those who were concerned about their final height and were not a random sample from the general population. In our study, the final predicted height was  $155.94 \pm 6.11$  cm and the target height, based on the height of the parents, was  $155.81 \pm 5.26$  cm. According to Shiasi et al. (9), the mean final height and target height of girls with the early onset of puberty were  $156.94 \pm 6.23$  and  $156.16 \pm 3.73$ , respectively. In our study, the final height was predicted and the target height was  $6.23 \pm 156.94$  and  $3.73 \pm 156.16$  in girls with the larch 2, respectively. This similarity of PAH and TH indicates that the girls studied were healthy, and no factors damaged their final height.

### 4-1. The relationship between height potential, thelarche, and pubarche stages

Pubarche usually occurs 6 to 12 months after thelarche, but in a significant minority of girls, pubarche occurs earlier than thelarche. (10) In our study, girls with

pubarche with varying degrees of thelarche had more advanced bone age and lower height potential compared to girls with thelarche but no pubarche. In a study by Soliman et al.(11), Healthy girls increased their height by an average of 28.5 cm during puberty; in our study, for 120 healthy girls without puberty symptoms, the average height potential of 28.90 cm was predicted. The girls had an average height potential of 28.90, 25.64, 20.89, and 13.76 cm in thelarche stages 1, 2, 3, and 4, respectively (P:0.001); and the average height potentials in pubarche stages 1, 2, 3 and 4, were, respectively, 27.19, 21.46, 15.51 and 11.02 cm (P=0.001). Girls with only thelarche or pubarche had a higher potential for height compared to girls with only thelarche or pubarche and had less chronological and bone age. Height potential was inversely related to chronological age and bone age. The potential height was reversely related to different age groups (P= 0.001), thelarche stage ( $r = -0.46$ ,  $p = 0.001$ ) and pubarche stage ( $r = -0.48$ ,  $p = 0.001$ ). So the linear regression performed to assess which of these factors is more important and interestingly found a significant relationship between the potential height and chronological and skeletal age, as well as pubarche stage but it was not correlated with thelarche stage. In the study of Yousefi et al. (12), an inverse association was expressed between the potential for height increase and calendar age, which is consistent with the findings of our study and shows that along with the increase in age, the growth rate decreases.

Nakamoto et al. (13) also reported an inverse relationship between the thelarche stage and the potential height. Thelarche-only girls and pubarche-only girls did not differ in terms of chronological age, skeletal age, or potential height, significantly. However, BMI SDS in girls who had only the larche was more than that in girls who only had pubarche (mean

BMI SDS was 0.69 vs. 0.07 with P-value = 0.018). Our study population had a mean age of 9.19 years and a breast SMR of 2, while in 1997, the mean age at onset of thelarche was 10 to 10.4 years, simultaneously declining compared to studies from 1948 to 1981, which had an average age of 10.6 to 11.2 years (10). The decline in the larche age is partly explained by childhood obesity as well as exposure to estrogen-like environmental toxins (10). In our study, BMI SDS was directly related to different stages of the larche ( $R = 0.17$ ,  $p < 0.001$ ). Girls with higher BMI deviations had more advanced bone age ( $R = 0.34$ ,  $p = 0.001$ ) but had no relationship with height potential or pubarche stage. Other studies also support that an increase in BMI causes puberty to begin earlier (14, 15).

According to the study by Holmgren et al. (16), girls with higher BMI SDS had more advanced bone ages ( $R = 0.34$ ,  $p = 0.001$ ) but had no relationship with height potential or pubarche stage. Other studies also state that an increase in BMI causes puberty to begin earlier. Holmgren's study in 2017 assessed how BMI affected puberty and height in children between 3.5 and 8 years of age. Higher childhood BMI SDS was associated with more growth before the onset of puberty, earlier puberty, and less pubertal height gain, resulting in similar adult heights.

#### **4-2. Limitations of the study**

The impossibility of studying the general population and the inability to reach the final height of children were the main limitations of this study.

#### **5- CONCLUSION**

Many parents worry about their child's final height when the larche occurs at an early age. However, it is interesting that height potential in healthy girls is not related to the thelarche stage but has a significant and inverse relationship with the pubarche stage.

According to the results of this study, the potential for height increase in girls is not related to the thelarche stage, and we should not worry about the final height of these people with the onset of the Thelarche. These girls can be exempted from having x-rays if they are healthy.

Using the potential for height increase obtained from this study, it is possible to predict healthy girls' final height at different puberty stages. If it is normal, they can be exempted from having X-rays.

## 6- ETHICAL CONSIDERATIONS

Ethical considerations in this study included obtaining permission from the Ethics Committee of the Kashan University of medical science (Ethical code:96139) and obtaining written consent to participate in the survey from the participants.

As patients are usually referred to the clinic due to concerns about final short stature, diagnostic tests such as radiography of the left wrist are typically performed at the patient's expense. Research is conducted based on the patient's file, so there is no need to consent. All information about cases remains confidential.

## 7- CONFLICT OF INTEREST

None.

## 8- ACKNOWLEDGMENT

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## 9- AUTHORS' CONTRIBUTION

SAAA and KSA collaborated on the concept, design, and data collection. HA analyzed and interpreted the data and drafted the manuscript.

The manuscript was revised for intellectual content and technical support by SAAA. MC and KSA did the final approval and supervision.

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