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Changes in Predicted Adult Height over Time in Girls with Early Puberty and Related Factors

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Abstract

Background: One of the most important concerns parents have about their daughters' precocious puberty is the reduction in final height. This study evaluates the changes in predicted adult height (PAH) over time in girls with early puberty.

Materials and Methods: Girls with aged 7 to 9.5 years old with the beginning of puberty after seven years were evaluated. Two non-dominant hand x-ray were taken at 6 to 24 months. The predicted adult height (PAH) was estimated using bone age and the Bayley-Pinneau method. Changes in PAH were determined. The relationship between age, height and weight at birth, target height and puberty stages, and bone age and BMI with PAH changes were investigated.

Results: Seventy girls with a mean age of 8.23 years (SD: 0.65) and an average time interval of 0.99 years (SD: 0.47) were studied. At the first evaluation, the average bone age was 8.6 years (p value=0.225 SD: 1.25), and the average predicted adult height was 158.95 cm (SD: 5.66). At the second evaluation, the average bone age was 10.06 years (P-value=0.15 SD: 1.36), and the average predicted adult height was 158 cm (SD: 6.75). The mean difference in predicted adult height is -0.94 ± 4.8 cm. The mean final height predicted in the first and second visits showed a significant relationship with PAH changes and in the group that increased PAH by more than 3 cm, the average growth rate was 69.7 cm per year. In other words, the group growth velocity was higher, the higher their PAH. Two factors associated with expected adult height changes were found: height growth velocity and bone age velocity.

Conclusion: Girls with early puberty are not altogether at risk of reduced adult height. However, if there is concern about reducing final height, the expected adult height will still need to be re-estimated at the appropriate interval.

Keywords: Puberty; Bone age; Female; Height

Abbreviations: PAH: Predicted Adult Height; SMR: Sexual Maturity Rate; CDC: Centers for Disease Control.

Introduction

Some studies indicate that the age of onset of puberty has decreased [1]. Today's girls begin puberty 5 to 12 months earlier than 30 to 50 years ago [2]. One of the most critical concerns about early puberty is reduced final height. To answer this concern, it is possible to predict the final height by the Bayley-Pinneau method if the bone age is over six years. If the calculated final height is within the normal range, the child and the parents can be reassured. If the girls have a small final size, interventions such as growth hormone and GnRH agonists may be used to improve final height [3-5]. Given that a decision to start on the treatments mentioned earlier or assure the child's parents based on these calculations, their accuracy and stability have always been a concern for pediatric endocrinologists.

In the experience of the pediatric endocrinology clinic of the Kashan University of Medical Sciences, it has been observed sometimes in children not receiving drug interventions that predicted adult height (PAH) could change over time. It is also possible for a child who has been reassured to be advised to take medication. We did not find a study that describes these changes and the factors affecting them despite an extensive search of the literature. This study determined the PAH changes over time in girls with early puberty. The results of this study may provide insight into the variability of PAH in girls with early puberty.

Materials and Methods

Population Study

This cross-sectional study was conducted between 2018-2019 at the pediatric endocrinology clinic of Kashan University of Medical Sciences. The Research and Ethics Committee of Kashan University of Medical Sciences approved the study protocol.

Inclusion Criteria

These were healthy children whose bone age was six years or greater; two non-dominant hand x-rays at least six months (maximum 24 months) apart.

Exclusion Criteria

Exclusion criteria included systemic or chronic diseases, history of exposure to sex hormones, or treatment with growth hormone or GnRH agonists.

Examination and Data Collection Instruments

All girls aged 7-9.5 with symptoms of puberty and having started puberty according to their history were evaluated with a physical examination. A pediatric endocrinologist examined all children, and their sexual maturity rate (SMR) was determined based on the Tanner staging method. The height and weight of girls were marked on the growth curve, and the percentile was determined for the child's height.

The required variables and other necessary information, such as age, sex, the reason for referral, age of onset of puberty symptoms, history of use of certain drugs, and history of systemic diseases, were collected with the help of researcher-made questionnaires.

Systemic examinations were performed for cardiopulmonary, hypertension, goiter, and hyperhypothyroid symptoms of skin, hair, abdomen, and genitalia (general health).

Height was measured in a standing position two times, and the mean was calculated. The BMI and height percentiles were determined using the Centers for Disease Control and Prevention (CDC) growth charts. Bone age was determined by the Greulich-Pile method—target height calculated as mid-parenteral height ±6.5 cm. Height and weight measurement, evaluating SMR, bone age determination, and PAH calculation were repeated at least six months later. Changes to the PAH value were determined. The children were divided into three groups based on the PAH estimates:1- PAH decreased or increased within 3 centimeters, 2- PAH increased more than 3 cm during the study, and 3- PAH dropped more than 3 cm.

Statistical Analysis

The study data were collected and entered into a computer and analyzed by SPSS software version 18. Statistical tests, T-test, Kruskal-Wallis, Fisher, Chi-square, correlation coefficient, Kolmogorov-Smirnov, Levene's test, Pearson, and Anova were used.

Ethical Considerations

Due to the subjects' relatively premature puberty and the fact that they usually visit the clinic with concerns about their final height, diagnostic evaluations such as radiographs of the left wrist are conducted at the patient's expense in order to determine the bone age. Therefore, there is no need for written consent.

Results

This study was performed on 70 girls with puberty at the age of 9.5-9 years with an average time interval (SD: 0.47) 0.99 years.

In the first stage, the average age (SD: 0.65) was 8.23 years and the average height (SD: 5.38) was 128.29 cm and the average weight (SD: 6.68) was 31.54 kg and the average bone age was (sd: 5.38) 8.6 years and the average final height predicted (SD:5.66) was 185.95 cm.

In the second stage, the average age (SD: 0.83) was 9.2 years and the average height (SD: 6.38) was 134.65 cm and the average weight (SD: 7.39) was 36.40 kg and the average bone age was (SD: 1.36) 10.06 years and the average final height predicted (SD: 6.75) was 158 cm. The average predicted final height change is -0.94 ±4.8 cm.

The girls were divided into three groups based on PAH changes. With a more than 3 cm increase in PAH during the study, the first group included 12 (17.4%) individuals. The second group, which had a PAH change of less than ±3 cm, included 37 (52.85%). The third group, in which PAH decreased by more than 3 centimeters, contains 21 (30%) individuals. Comparing the three groups, age, follow-up period, BMI SDS, height SDS, bone age, and target height showed no significant differences. The relationship among the other variables with the three groups is shown in Table 1.

Variables		Group 1	Group 2	Group 3	p-value
height	First	12(129.30±6.48)	37(127.57±5.1)	21(128.99±5.2)	0.49
	second	12(136.43±8.54)	37(134.14±6.3)	21(134.52±5.1)	0.56
	First-second[1]	12(7.12±2.92)	37(6.56±3.03)	21(5.53±2.8)	0.27
age	First	12(8.2±0.8)	37(8.21±0.66)	21(8.27±0.58)	0.9
	second	12(9.11±0.94)	37(9.21±0.87)	21(9.26±0.74)	0.89
Bon age	First	12(9.25±1.56)	37(8.54±1.23)	21(8.62±1.05)	0.225
	second	12(10.03±1.67)	37(9.81±1.40)	21(10.53±0.95)	0.15
Mean final height predict	First	12(1.57±7.26)	37(1.58±4.63)	21(1.61±5.77)	0.057
	second	12(1.62±7.3)	37(1.58±5.19)	21(1.54±6.82)	0.002
BMI SDS First		12(0.83±1.34)	37(0.71±1.18)	21(1.22±1.16)	0.297
Heights SDS First		12(0.128±0.87)	37(-0.207±0.73)	21(-0.009±0.93)	0.408
Birth height		9(48.66±2.34)	26(49.61±2.84)	13(48.84±3.5)	0.61
Weight height		12(3.08±0.5)	36(2.98±0.66)	20(3.22±0.76)	0.42
Refer interval[2]		12(10.97±3.10)	37(11.52±4.91)	21(11.86±5.91)	0.88
Grow velocity		12(7.69±56.1)	37(6.62±92.1)	21(5.96±55.2)	0.017

Table 1: Relation of changes in predicted adult height with other variables.

Seven (10.1%) of 70 individuals had less than 2.5 kg birth weight. These subjects had the same height and PAH (first and second) values as individuals with average birth weight, and PAH changes in the two groups did not differ.

Relationship between Predicted Adult Height Changes and Bone Age

In the first and second evaluations, the mean bone age was 0.45 ± 1 and 0.85 ±1 more than the calendar year. This increase in bone age progression was significant (P =0.0001). Advanced bone age (2 years or more) at the time of referral is associated with a higher risk of final height reduction (P: 0.018), and this relationship was also observed in the second evaluation (P: 0.028). But changes in PAH were not significantly associated with advanced bone age in each. Only two factors were associated with PAH changes: growth velocity and bone age progression rate (Table 1).

Relationship between Predicted Adult Height Changes and Puberty

Breast and pubic hair tanner stages have no significant relationship with PAH changes (P = 0.789 and P = 0.557, respectively). The breast tanner stage change (p-value=0.51) and the pubic hair Tanner stage (p-value=0.78) change are not significantly associated with PAH changes after two turns. The girls were divided into three groups regarding their maturity at the initial evaluation. The first group had only thelarche (39 cases), the second group had only pubarche (4 issues), and the third group had both the pubarche and thelarche (26 patients). The PAH at the first and second evaluations was not significantly different between the three groups (P = 0.221, P = 0.333, respectively).

In addition, the PAH changes in these three groups did not have a significant difference (P = 0.583). The third group (pubarche and thelarche) had higher age (P=0.012) and more advanced bone age (P=0.001), and similar BMI-SDS in comparison to the two first groups (thelarche or pubarche). The mean target height of the three groups was identical (P = 0.923), and the difference between the target height and the PAH in two turns was not significant (P = 0.946, P = 0, .222 respectively).

Relationship between Predicted Adult Height changes and age groups

These girls were divided into two groups based on age at the time of referral: 7-8 and 8-9.5 years old. There was no difference in the frequency of obesity in the two age groups (P=0.299). The prevalence of advanced bone age in both groups at both evaluations was similar (P = 0.947, P = 0.845, respectively). The relationship between the variables studied in the two groups is presented in Table 2.

Variable	Total	Years 7-8	Years 8-9.5	P-value
Number	70	29(41%)	41(58%)	----
Age(year)	8.2±0.65	7.5±0.25	8.68±0.43	0.001
Height-SDS	-0.09 ±0.8	0.1 ±0.7	-0.2 ± 0.8	0.29
BMI-SDS	0.89 ±1.2	1.12 ±1.1	0.72 ±1.2	0.29
Bone age	8.68±1.25	7.89±1.08	9.24±1.06	0.001
BA- CA (first)	0.45 ±1	0.30 ±1	0.55 ±0.9	0.23
BA- CA (second)	0.85 ±1	0.70 ± 1	0.83 ± 0.9	0.44
Bone Velocity	17±10	17±8.7	16.8± 11	0.551
First PAH (cm)	158±5.6	161±6.2	157±5.7	0.01
Second PAH (cm)	158±6.5	160±6.2	156±6.5	0.07
Target Height (cm)	156±3.4	157±3.3	155±3.4	0.259
TH-PAH (first)	-1.69 ±5.8	-2.88 ±6.2	-0.70 ± 5.4	0.357
TH-PAH (first)	-0.75 ±7.1	-2.30 ±7.8	0.54 ± 6.4	0.204
PAH change	-0.94 ±4.8	-0.96 ±5.3	-0.93 ±5.1	0.962

Table 2: Relation of changes in predicted adult height with age groups.

Discussion

Adult height prediction allows parents and physicians to predict a child's adult height at any age from birth onwards. According to current advice, parents wishing to estimate adult height should double a boy's height at age two or a girl's height at 18 months, but this is both restrictive and biased. A prediction chart fills a real need, allowing a child entering early puberty to estimate their adult height in an unbiased manner.

In this study, predicted adult height changes in girls with the onset of puberty at the age of 7 to 9.5 years were assessed

Relationship between Predicted Adult Height changes and age groups

In terms of precocious puberty, the age of 7-8 years is controversial. We compared this age group with those above eight years of age. Between 7 to 8 and 8 to 9.5 years old, there was no significant difference in PAH levels (P = 0.946). Also no difference in the prevalence of obesity between the two groups (P=0.299). In contrast, in our previous study, children aged 7 to 8 years were more obese than children aged 8 to 9.5 years, despite the fact that they had a higher percentage of subjects with only thelarche [6]. The prevalence of advanced bone age was similar in both groups (P = 0.947, P = 0.845, respectively). Although the target height of the lower age group was similar to that of the second group (P = 0.88), PAH in the first evaluation (first group) was higher than that of the older group (8-9.5year old) (P 0.01). We expected that the PAH of a group of 7 to 8-year-olds classified according to some sources as precocious puberty would be less than the target range, in which the PAH was about 2 cm better than the target height in this study. Of course, the difference between the target height and the PAH between the two age groups was not significant at either evaluation (P = 0.357 and P = 0.204, respectively), which means that in this age range, lower age at the onset of the symptoms of puberty is not a risk factor for subsequent lower PAH. On the other hand, this study showed that the 7 to the 8-year group is not at a higher risk for low PAH than the 8 to 9.5-year group. The rate of

progression of bone age, which could be a risk factor for PAH decline, was not different in the two age groups (P =0.551).

In a study conducted by Allali, et al. [7]. 52 children with precocious puberty followed without intervention up to adult height, with a mean age of 7.1 ± 0.9 years, target height, adult height, and PAH were similar. Similar results were observed in a study conducted by Cassio, et al. [8]. Furthermore, in a study by Yun, et al. [9] on 77 girls with precocious puberty with a mean age of 8.16 ± 0.76 years, the target height and PAH and final height were similar [3]. These investigators, of course, have treated a group of 57 girls with GnRHa who were in relatively early puberty with a mean age of 7.9 ± 0.93 and had a bone age of 10.12 ± 1.08. These individuals had a mean PAH of 155 cm, a mean target height of 158 cm, and a mean near-final height of 159 cm, indicating that the group benefited from treatment.

Relationship between Predicted Adult Height Changes and Bone Age

In the initial and re-evaluation, the bone age was more than chronological age (0.45 ± one year and .85 ± one year, respectively, P <0.0001). In our study, advanced bone age (2 years or more) was associated with a higher risk of low PAH at the time of referral (P=0.018), and this relation was also observed in the second evaluation (P=0.028). But PAH changes did not have a significant relationship with advanced bone age in each two-step (P = 0.509, P = 0.428).

Relationship between Predicted Adult Height Changes and Stage of Puberty

In our study, those who had both a history of both thelarche and pubarche at the time of entry had a higher age (P=0.012) and more advanced bone age (P =0.001), and the BMI SDS was the same as the two other groups (thelarche or pubarche). The target height of the three groups was similar (P = 0.93), and the difference between the target height and the PAH in the two evaluations was not meaningful (P = 0.946, P = 0.222, respectively).

Relationship between Predicted Adult Height Changes and Obesity

We have not found any relationship between predicted adult height changes and obesity. The relationship between obesity and early puberty is discussed in several studies [4-5]. A review study conducted by Papadimitriou, et al. [10] showed that growth acceleration in the first year of life and childhood obesity is a prerequisite for relatively early maturity. A Swedish cohort study of 99 monozygotic and 76 dizygotic twin pairs showed a close relationship between BMI and the age at onset of puberty. It has been shown that higher BMI is associated with the early onset of puberty of 0.6 years for boys and 0.7 years for girls, but no direct relationship was found between childhood BMI and ultimate height [11]. In our current study, the prevalence of obesity and overweight was 25.7% and 27.1%, respectively. In our other study, the percentage of obesity and overweight in 110 girls with precocious puberty was 38.5% and 20.2%, respectively. While the percentage of obesity and overweight in healthy Iranian girls was reported to be 5.1% and 10.8% [12].

Relationship between Predicted Adult Height Changes and birth indexes

The study also indicates that 7 (10.1%) of 70 individuals had less than 2.5 kg birth weight. Their height and the first and second PAH were the same as individuals with average birth weight, and PAH changes in the two groups did not differ. In our previous study, 17 (9.4%) of 181 individuals' had birth weights less than 2.5 kg, their target height was the same as normal birth weight children, but they had lower PAH (P = 0.001) [13]. Several studies have shown that small for gestational age SGA girls start puberty at a younger age, and their menarche occurs earlier [14]. Some studies suggest that SGA children who have rapid growth after birth are at risk of early maturity, polycystic ovary, dyslipidemia, and hyperinsulinism [15,16].

The previous study indicated that the factors influencing the changes in predicted final height were studied in 81 children with idiopathic short stature. The mean predicted height was 160.15 ± 8.79 cm in the first evaluation, and 159.4 ± 9.5 cm in the second time, with a mean time interval of 17 ±9.36 months (P = 0.002). And in detail, 53 (53.7%) individuals have minor changes in predicted height (3 ± cm). In comparison, 23 (28.8%) individuals experienced more than a 3 cm decline in predicted height, the maximum of which was 12.53 cm, and 14 (17.5%) individuals experienced more than a 3 cm increase in predicted height, with a maximum of 9.87 cm. In our current and previous studies, factors such as height-SDS, birth indexes, the height of parents, changes in pubertal stage, the interval between two evaluations, and the difference between calendar age and bone age in the first and second turns were not related to the predicted height change. Our current study found only two factors associated with expected final height changes: height velocity and bone age velocity rate. In our previous study, we found two factors related to predicted final height variations: bone age velocity and age at the time of the first visit; those with higher bone age velocity had a higher decline in PAH so that more than 95 % of patients who experienced PAH decline had bone age velocity of more than one.

On the other hand, lower bone age velocity was associated with an increase in predicted height. In our current and previous studies, there was no significant relationship between predicted height changes and the change in the pubertal stage and between the maturity stage and the predicted final height in the first and second evaluations. Also, there was no significant relationship between change in puberty stage and bone age velocity in both studies.

The interesting result of this study is the lack of correlation between predicted height and bone age in terms of delay or being advanced. In a survey by Desalvo, et al. [17], 121 children aged 5 to 9 were evaluated for precocious adrenarche. It was found that the effect of advanced bone age on predicted height was negligible.

Furthermore, the most changes in predicted height were seen in the age group of fewer than ten years, with only one (4.5%) in the group with modest changes. The most changes in PAH in this age group were decreased, while in the age group older than ten years, most children had subtle differences in PAH. It could be expected because the higher the bone age, the closest person is to his ultimate height, and, of course, there is less time to grow.

In a study conducted by Chonchaiya, et al. [18], 62 obese children aged between 5 and 17 (38 boys, 24 girls) have shown that the severity of obesity has a positive correlation with advanced bone age and the PAH is lower than the target height. In a study conducted by Benso, et al. [19], 407 Italian boys between 7 and 12 were studied to determine bone age progression factors. A weak correlation was found between bone age progression and height velocity rate. There was a weak relationship between skeletal maturity and puberty.

Conclusion

In girls with early puberty, the higher the bone age velocity, the more significant decline in PAH. Girls whose puberty starts at the age of 7 to 8 years are not expected to be at a higher risk of low PAH, or a drop of PAH, more than those whose puberty starts at the age of 8-9.5 years. In girls with early puberty, the harm of decline in PAH is not related to the rate of puberty progression. Suppose there are worries about reducing the predicted ultimate height in girls with early puberty. In that case, the PAH will still need to be repeated to predict the maximum height at appropriate intervals.

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