Serum Insulin-like Growth Factor-1 (IGF-I) and Insulin-like Growth Factor Binding Protein-3 (IGFBP-3) in Healthy Thai Children and Adolescents: Relation to Height, Weight, and Body Mass Index

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Abstract

The objective of this study was to evaluate the correlation between serum concentrations of insulin-like growth factor-1 (IGF-1), insulin-like growth factor binding protein-3 (IGFBP-3) and growth parameters (height, weight, and body mass index) in 260 healthy children and adolescents aged 5-20 years. The subjects were divided into 2 groups according to the age achieving final height. Group 1 included children with active growth consisting of girls aged under 14 years (N = 80) and boys aged under 16 years (n = 74). Group 2 included adolescents who achieved final height consisting of females aged at and over 14 years (n = 82), and males aged at and over 16 years (n = 24). In group 1, the serum concentrations of IGF-1 and IGFBP-3 were significantly positive correlated with all growth parameters. In group 2, although the correlation was insignificant, the concentrations of IGF-1 and IGFBP-3 seemed to be greater in individuals who were relatively taller and had lean body mass than those who were relatively short and overaverage body mass.

Key word : Body Mass Index (BMI), Height, Insulin-like Growth Factor-1 (IGF-1), Insulin-like Growth Factor Binding Protein-3 (IGFBP-3), Weight

Determination of the serum insulin-like growth factor-1 (IGF-1) and insulin-like growth factor binding protein-3 (IGFBP-3) has proven to be an important screening test in evaluation of a growth-retarded child[1-3]. The serum levels of IGF-1 and IGFBP-3 have been widely studied in Western countries and found to be related to spontaneous growth hormone secretion as well as to

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height and height velocity[4-8]. In Thailand, data concerning the levels of IGF-1 and IGFBP-3 are limited to only a few studies which demonstrated the age, sex, and pubertal status dependency[9,10]. Therefore, we wish to add more information of the relationships between IGF-1, IGFBP-3 concentrations to the growth parameters such as height, weight, and body mass index (BMI).

SUBJECTS AND METHOD
Subjects

The subjects were 260 healthy children and adolescents aged 5-20 years as previously described[10]. We divided the subjects into 2 groups according to age when final height was achieved

as defined by height velocity less than 1 cm per year[11,12]. Group 1 consisted of prepubertal and pubertal children which included under 14 year-old girls (n = 80) and under 16 year-old boys (n = 74). Group 2 was post-pubertal subjects which included at and over 14 year-old females (n = 82), and at and over 16 year-old males (n = 24). Height was measured in a standing position using a stadiometer. Weight was measured using a beam balance scale. Body mass index (BMI) was calculated by weight in kilograms divided by the square of height in meters (kg/m^2).

The concentrations of the IGF-1 and IGFBP-3 were measured by immunoradiometric assay (IRMA) which was previously described[10].

Table 1. The mean ± standard deviation of growth parameters in group 2 subjects.

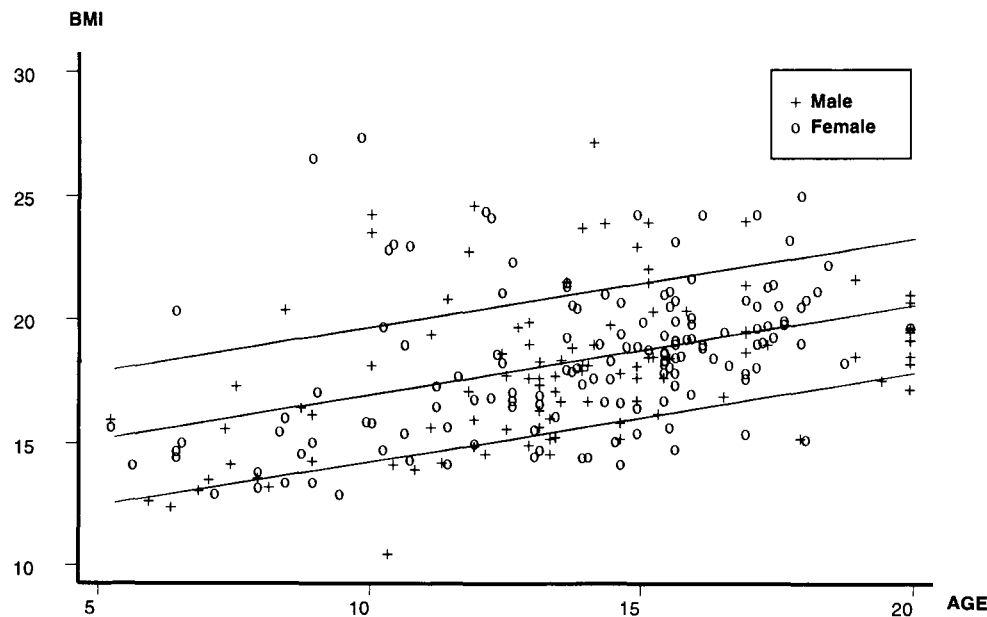| Growth parameters	Males (≥16 years old) (n = 24)	Females (≥14 years old) (n = 82)
Height (cm.)	169.6 ± 4.2	157.0 ± 4.8
Weight (kg.)	55.8 ± 6.2	47.3 ± 5.8
BMI (kg/m^2)	19.5 ± 2.2	19.7 ± 2.3

Fig. 1. The mean and standard deviation of body mass index (BMI). The middle line represents the mean, the upper and lower lines represent ±1 standard deviation.

Method

In group 1, or the prepubertal and pubertal subjects, the concentrations of IGF-1 and IGFBP-3 were plotted against the height, weight, and BMI in boys and girls. In group 2, or the post-pubertal subjects, the standard deviation score (SDS) of IGF-1 and IGFBP-3 concentrations were plotted against the SDS of height, weight, and BMI. The SDS was calculated based on the formula of[13]

$$SDS = \frac{actual\ measurement\ -\ mean}{standard\ deviation\ (SD)}$$

For the SDS calculation of each growth parameter, in this study we used the mean and SD of our studied population (Table 1) for the purpose of balanced distribution of the scores. The mean height and weight of our population were slightly greater than those of normal Thai adolescents[14] (169.6 *vs* 165.4 cm and 55.8 *vs* 53.5 kg in males, 157.0 *vs* 154.4 cm and 47.3 *vs* 47.0 kg in females). For the SDS calculation of IGF-1 and IGFBP-3, we used the mean and SD in our previous study in order to account for the age-dependency[10]. For

BMI, the mean and SD showed no difference between sexes as shown in Fig. 1. Therefore, BMI-SDS was calculated using the mean and SD of the total subjects.

Statistical analysis

Correlation coefficient (r) was used to demonstrate the relationship between the IGF-1, IGFBP-3 concentrations and the growth parameters. The statistical significance was stated when the p value was less than 0.05.

RESULTS

In group 1, the concentrations of IGF-1 and IGFBP-3 showed significant positive correlation with height, weight, and BMI in both boys and girls as shown in Fig. 2-4. In group 2, there was no correlation between the SDS of IGF-1, IGFBP-3 and the SDS of each growth parameter with the correlation coefficient 0.01-0.03 and the p value 0.41-0.84. We then compared the mean concentration of IGF-1 between subjects whose SDS of each
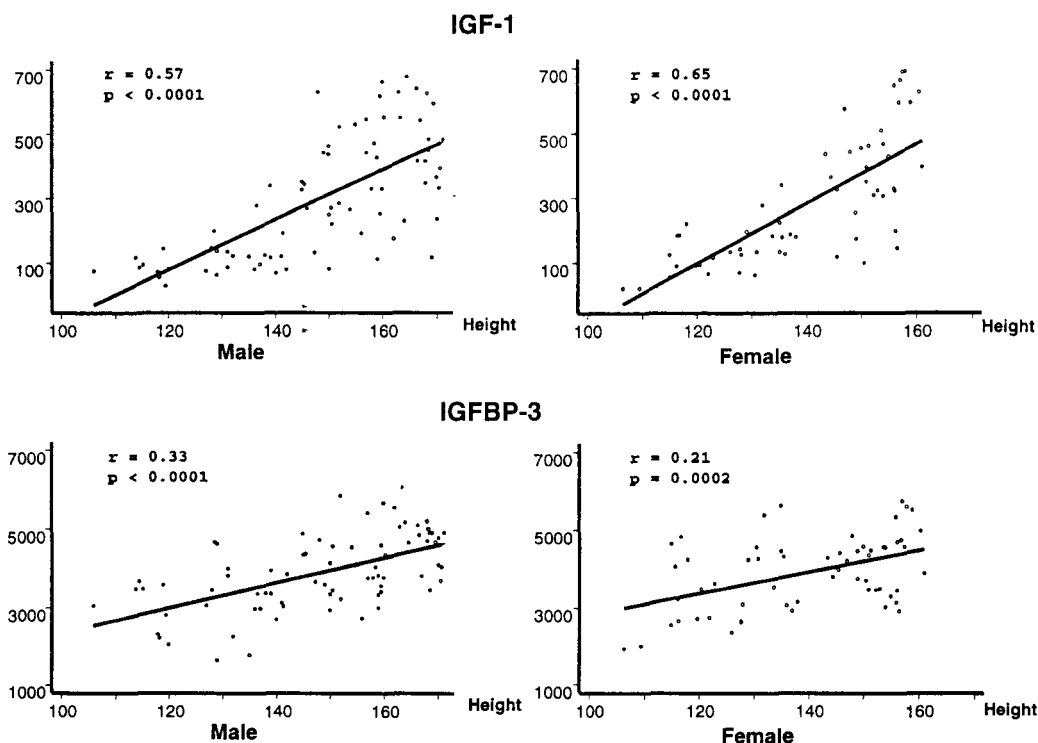

Fig. 2. The correlation of IGF-1, IGFBP-3 concentrations and height in <16 year-old boys and <14 year-old girls.
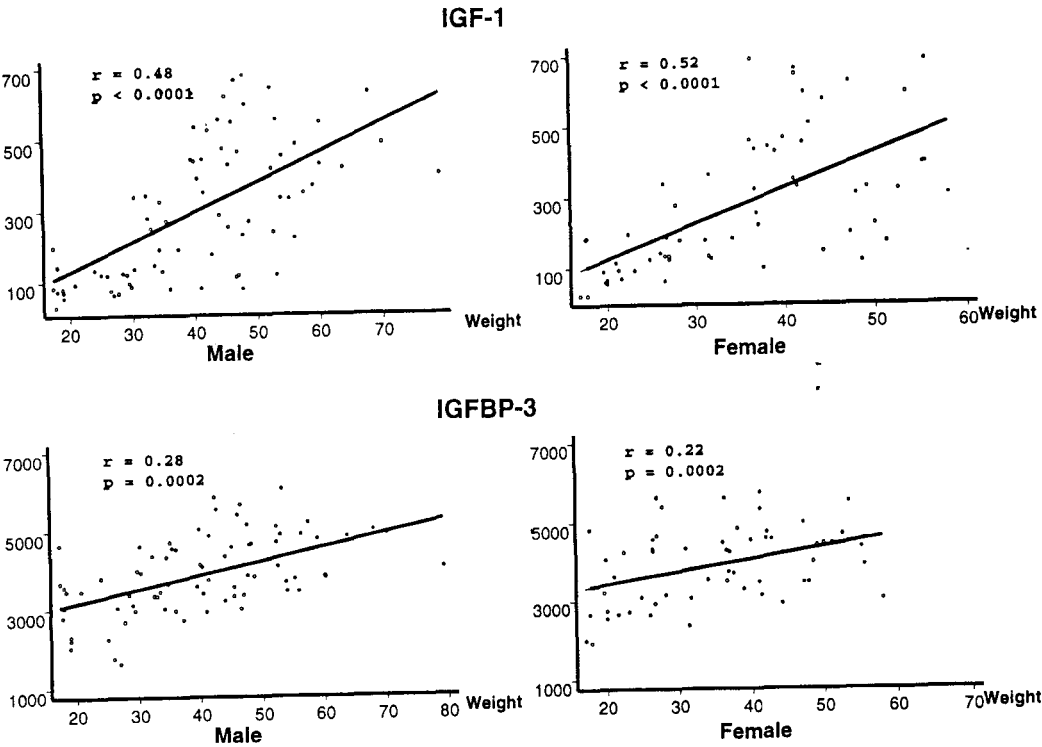
IGF-1

IGFBP-3

Fig. 3. The correlation of IGF-1, IGFBP-3 concentrations and weight in <16 year-old boys and <14 year-old girls.
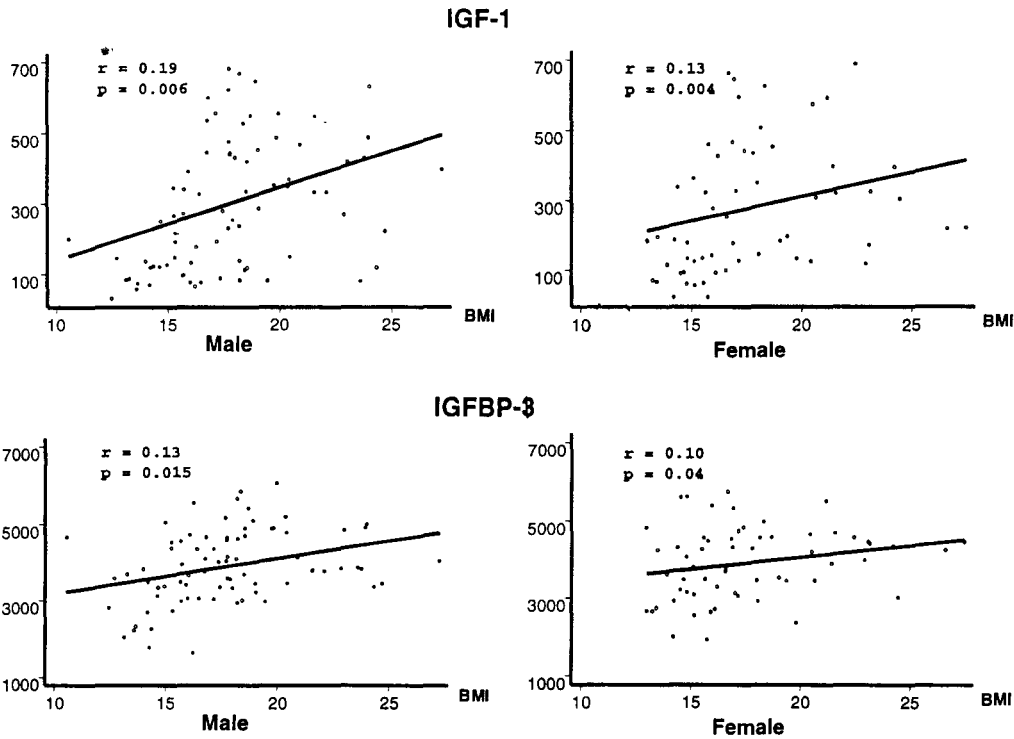
IGF-1

IGFBP-3

Fig. 4. The correlation of IGF-1, IGFBP-3 concentrations and BMI in <16 year-old boys and <14 year-old girls.

Table 2. The mean ± standard deviation of IGF-1, IGFBP-3 in group 2 subjects according to SDS of growth parameters in males and females.

Growth parameters	N	IGF-1		IGFBP-3	
		X ± SD	p value	X ± SD	p value
Males					
Height SDS < 0	10	240.4 ± 28.3		3305 ± 289	
> 0	14	267.9 ± 37.4	0.23	3565 ± 201	0.26
Weight SDS < 0	11	268.7 ± 46.7		3458 ± 278	
> 0	13	265.3 ± 22.8	0.61	3433 ± 206	0.84
Females					
Height SDS < 0	39	403.4 ± 20.2		4204 ± 85	
> 0	43	436.6 ± 22.7	0.37	4285 ± 95	0.53
Weight SDS < 0	40	402.4 ± 21.9		4278 ± 98	
> 0	42	410.7 ± 21.3	0.69	4311 ± 82	0.42
Males and Females					
BMI-SDS < 0	61	386.9 ± 17.7		4270 ± 86	
> 0	45	346.9 ± 24.3	0.21	3988 ± 116	0.34

growth parameter above zero and those below zero (Table 2). For height SDS, the IGF-1 and IGFBP-3 concentrations seemed to be modestly greater in subjects with height SDS above 0 than those below 0, however it was statistically insignificant. For weight SDS, the IGF-1 and IGFBP-3 concentrations were at the same levels between those with weight SDS above 0 and those below 0. For BMI-SDS, the IGF-1 and IGFBP-3 tended to be lower in subjects with BMI-SDS above 0 than those below 0, again without statistical significance.

DISCUSSION

The results of our study showed a significant positive correlation between the IGF-1, IGFBP-3 concentrations and all growth parameters in prepubertal and pubertal boys and girls. After puberty, or in subjects who had reached their final height, there was no significant difference of IGF-1, IGFBP-3 concentrations between individuals with growth parameter above average and those below average. However, individuals who were relatively tall (height SDS > 0) and lean (BMI-SDS < 0) tended to have greater concentrations of IGF-1, IGFBP-3 than those who were relatively short (height SDS < 0) and above average BMI (BMI-SDS > 0).

The significant positive correlation between IGF-1, IGFBP-3 concentrations and growth parameters in prepubertal and pubertal subjects can be explained by the stimulating effect of growth

hormone (GH)-IGF-1-IGFBP-3 axis during the period of active growth. It has been known that height and height velocity correlates positively with spontaneous GH secretion and that GH secretion correlates positively with IGF-1 and IGFBP-3 levels[15,16]. The stimulating effect of GH-IGF-1-IGFBP-3 axis leads to the increasing IGF-1 and IGFBP-3 levels with age during the childhood and pubertal period.

In post-puberty, the stage in which individuals had no furthur height increment, whereas, the concentrations of IGF-1, IGFBP-3 declined with age, particularly in males. Therefore, the study of correlation between growth and IGF-1, IGFBP-3 concentrations should be calculated in SDS to account for the age dependency of IGF-1, IGFBP-3. The study by Blum et al demonstrated the significant positive correlation between height SDS and the IGF-1, IGFBP-3 SDS. They concluded that short healthy children had significantly lower IGF-1, IGFBP-3 concentrations which was probably due to the difference in GH secretion contributing to the growth variability in the normal population[8]. Our results demonstrated no significant correlation of IGF-1, IGFBP-3 concentrations between individuals with growth parameters either height, weight or BMI above average and those below average. However, the mean concentrations of IGF-1 and IGFBP-3 in individuals who were relatively tall (height SDS > 0) and lean (BMI-SDS < 0) showed a modestly greater level than those who were rela-

tively short (height SDS < 0) and overweight (BMI-SDS > 0), although the difference was statistically insignificant. This was probably due to our inclusion criteria of subjects whose height and weight was between the 10th-97th centile resulting in a narrow distribution of growth of subjects. Secondly, the sample size in our study was not large enough to demonstrate the significant difference, eventhough it may exist. Therefore, a larger number of subjects along with a wider variation of growth of normal subjects is needed in a further study to demonstrate the correlation between growth parameters and IGF-1, IGFBP-3 concentrations.

In conclusion, we demonstrated the positive correlation between the IGF-1, IGFBP-3 concentrations and growth parameters during the period of active growth in prepubertal and pubertal stages. In adulthood, the concentrations of IGF-1, IGFBP-3 tended to be greater in individuals who were relatively tall and had a lean body mass than those who were relatively short and overweight, although the difference was not statistically significant.

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ระดับของ insulin–like growth factor–1 (IGF–1) และ insulin–like growth factor binding protein–3 (IGFBP–3) ในซีรั่มของเด็กและวัยรุ่นไทยปกติ: ความสัมพันธ์กับความสูง น้ำหนัก และมวลดัชนีกาย

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     ได้ทำการศึกษาถึงความสัมพันธ์ระหว่างค่า insulin–like growth factor–1 (IGF–1), insulin–like growth factor binding protein–3 (IGFBP–3) และความสูง น้ำหนัก มวลดัชนีกาย ในเด็กและวัยรุ่นที่มีสุขภาพดีจำนวน 260 ราย อายุระหว่าง 5-20 ปี แบ่งกลุ่มตัวอย่างเป็น 2 กลุ่มตามอายุของการเจริญเติบโต กลุ่มแรกได้แก่ เด็กที่ยังอยู่ในวัยของการเจริญเติบโต ซึ่งรวมเด็กหญิงอายุต่ำกว่า 14 ปี (จำนวน 80 ราย) และเด็กชายอายุต่ำกว่า 16 ปี (จำนวน 74 ราย) กลุ่มที่สอง ได้แก่กลุ่มที่มีความสูงเท่าวัยผู้ใหญ่ ซึ่งรวมถึงหญิงที่มีอายุมากกว่า 14 ปี (จำนวน 82 ราย) และเด็กชายที่อายุมากกว่า 16 ปี (จำนวน 24 ราย) ผลการศึกษาพบว่า ในกลุ่มแรก ระดับของ IGF-1, IGFBP-3 มีความสัมพันธ์ในทางบวกกับความสูง น้ำหนัก และมวลดัชนีกาย อย่างมีนัยสำคัญทางสถิติ ในกลุ่มที่สอง ระดับ IGF-1, IGFBP-3 ไม่มีความสัมพันธ์กับความสูง น้ำหนัก และมวลดัชนีกาย อย่างไรก็ตามผู้ที่รูปร่างค่อนข้างตัวสูงและค่อนข้างผอม มีแนวโน้มที่จะมีระดับ IGF-1, IGFBP-3 สูงกว่าผู้ที่มีรูปร่างค่อนข้างเตี้ยและน้ำหนักเกิน ถึงแม้ว่าจะไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติก็ตาม

คำสำคัญ : ดัชนีมวลกาย, น้ำหนัก, ความสูง, ไอจีเอฟ-1, ไอจีเอฟบีพี-3

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