Normal Reference Range of Serum Insulin-Like Growth Factor (IGF)-I in Healthy Thai Adults

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Background: *Serum insulin-like growth factor (IGF)-I level is growth hormone (GH) dependent and reflects GH secretion. Analysis of IGF-I is a component in the diagnosis of GH-related disorders and is going to be of interest in determining the risk of many disorders such as cancer or atherosclerosis. The diagnosis value of IGF-I is dependent on the establishment of an accurate reference ranges, which can be affected by parameters such as age, gender, ethnicity, medications, chronic illness, or assay methodologies.*
Objective: *To determine reference ranges of IGF-I for healthy Thai adults.*
Material and Method: *Eight hundred sixteen healthy Thai adults aged between 21-70 years were recruited in the present study. Serum IGF-I was measured by using immunochemiluminescent (ICMA; Roche, USA). Subjects were recorded by their age and gender groups. Data were presented in mean and $\pm$ 2 standard deviation (SD). Correlation analysis between serum IGF-I and physical parameters including sex, age, weight, height, and body mass index (BMI) was also made.*
Results: *The present study demonstrated normal reference range of serum IGF-I by using mean $\pm$ 2SD value. The well-known age dependency of serum IGF-I levels was also revealed. Levels decreased with increasing age in both genders. The mean value of serum IGF-I was slightly higher in women at the age of 30-40 years compared with men in the same age group, but not statistically insignificant. In addition, serum IGF-I was found to correlate directly with the height and negatively with BMI. However, age-adjusted IGF-I level did not show correlation with these physical parameters.*
Conclusion: *This reference range will be beneficial for using IGF-I assay as a tool in the diagnosis of GH function abnormalities in Thai subjects.*

Keywords*: IGF-I, Growth Hormone*

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Assessment of growth hormone (GH) disorder requires the provocation or suppression tests of GH release. Unfortunately, these tests are expensive, uncomfortable, invasive, and risky. Insulin-like growth factor (IGF)-I is a small circulating peptide, which mainly reflects the secretion of GH[1]. Moreover, IGF-I has a stable circadian serum levels and reliable assays for IGF-I are available[2]. Thus, the measurement of serum IGF-I has been proposed for the evaluation of GH secretion in acromegaly or GH deficiency[3,4]. The diagnostic value of IGF-I in GH-related disease is dependent on the establishment of appropriate reference[5]. IGF-I reference range has correlated with many parameters such as age, gender, or ethnicity and can be affected by concomitant diseases and assay methodologies[6-8].

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The objective of the present study was to establish a reference level of serum IGF-I in Thai adult populations. In addition, possible variables with significant effect on IGF-I concentrations were analyzed.

Material and Method

The present study was carried out in 816 healthy Thai volunteers using blood donors from Thai Red Cross and medical staffs from Chulalongkorn University. The study protocol had been approved by the appropriate university authorities and informed consent was obtained from each subject. Subjects with diseases or taking medications, which may affect serum IGF-I level, in particular renal diseases, liver diseases, diabetes mellitus, malignant disorders, diseases of pituitary glands, critical illness, smoking, heavy alcoholic drinking, and steroid usage, were excluded by medical history, physical examination, and laboratory tests. To construct a reference model of normal populations, the only adults included were those with height and weight within $\pm$3 SD of normal Thai population mean. Because of the well-known age- and gender-dependence of IGF-I level, 334 men and 482 women were stratified into different age groups: 21-30, 31-40, 41-50, 51-60, and 61-70 years, respectively.

Blood samples were separated by centrifugation at 2000g for 15 min with a maximal time interval of 60 min between sampling and freezing. Sera were frozen and stored at -80°C until assay. IGF-I was determined by immunochemiluminescent (ICMA; Roche, USA) method. The assay has been calibrated against the World Health Organization International Reference Range 87/518. The mean intra-batch coefficients of variation were 1.6% for an IGF-I concentration of 150 ng/ml and the mean inter-batch coefficients of variation for the same concentrations were 4.6%.

Statistic analysis

Due to normal distribution, the data are shown as mean ($\bar{x}$) and standard deviation (SD). Physical parameters including sex, age, weight, height, and body mass index (BMI) were also analyzed with Pearson correlation and simple linear regression (SPSS version 15.0). A p-value less than 0.05 was considered significant.

Results

Physical data of the study populations are presented in Table 1. Men were slightly younger than women. Mean height and BMI values were significantly higher in men compared with women ($p < 0.001$); whereas the women were heavier than the men ($p < 0.001$). As anticipated, serum IGF-I level decreased with increasing age, $r = -0.54$, $p < 0.001$ (Fig. 1). IGF-I level was slightly higher in women than men in a group

Table 1. Mean age and physical characteristics of our study population (means $\pm$ 2SD)

	Total	Male	Female	t-test for equality of means
Number	816	334	482	-
Age (years)	43.11 $\pm$ 24.79	40.64 $\pm$ 22.62	44.82 $\pm$ 25.66	$p < 0.01$
Body weight (kg)	61.58 $\pm$ 24.08	68.92 $\pm$ 22.78	56.50 $\pm$ 19.24	$p < 0.01$
Height (cm)	161.35 $\pm$ 15.11	168.36 $\pm$ 9.94	156.49 $\pm$ 9.32	$p < 0.01$
BMI (kg/m^2)	23.60 $\pm$ 8.00	24.31 $\pm$ 7.7	23.10 $\pm$ 8.06	$p < 0.01$

Table 2. Reference values of serum IGF-I levels in relation to age (means $\pm$ 2SD)

Age (years)	Total		Male		Female	
	No.	IGF-I	No.	IGF-I	No.	IGF-I
21-30	164	184.46 $\pm$ 124.96	74	186.31 $\pm$ 117.12	90	182.94 $\pm$ 131.64
31-40	186	151.99 $\pm$ 101.10	91	146.64 $\pm$ 94.48	95	157.11 $\pm$ 106.54
41-50	218	129.52 $\pm$ 97.22	101	129.94 $\pm$ 82.26	117	129.16 $\pm$ 108.84
51-60	177	109.94 $\pm$ 79.10	55	111.13 $\pm$ 73.92	122	109.41 $\pm$ 81.60
61-70	71	81.65 $\pm$ 52.06	13	86.52 $\pm$ 59.82	58	80.56 $\pm$ 50.48

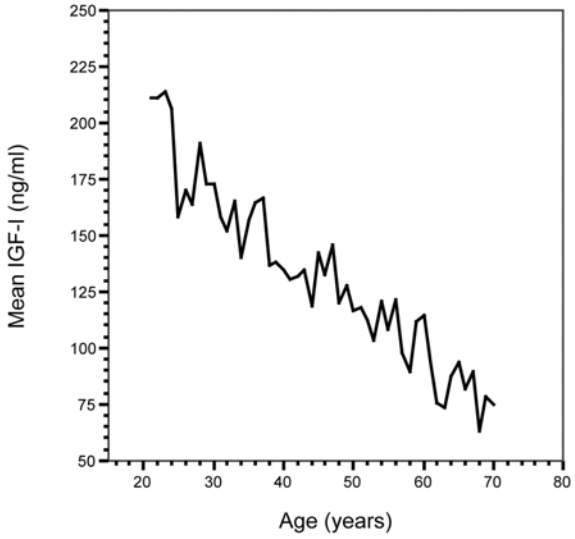

Fig. 1 Mean serum IGF-I concentrations of all participants by age; IGF-I (ng/ml) = 245.43 - 2.51 x Age (years)

of age 31-40 years but not at statistical significance (Table 2). Serum IGF-I correlated directly with the subject's height; $r = 0.18$, $p < 0.001$, and negatively with BMI, $p < 0.005$. Age-adjusted IGF-I did not show correlation with the physical parameters.

Discussion

The diagnostic value of IGF-I assay is dependent upon the establishment of accurate normal range with which to compare patient data. In the present study, the authors constructed the reference values of serum IGF-I level based on a large number of healthy Thai adults between 21-70 years of age by using mean $\pm$ 2SD. To the authors' knowledge, this is the largest study to date documenting the age-related changes in IGF-I levels in Thai adults.

Concurrent with the data from previous studies, IGF-I levels showed a peak during puberty and appeared to be a gradual decrement with increasing age[5,8]. The decline was steeper in women at the age over 50 years. A possible explanation for these findings may be the effect of estrogen in females, which is well known to influence serum IGF-I levels[9]. Nevertheless, this gender difference is small and the use of a common adult serum IGF-I reference range is applicable in clinical practice. The present study also shows an association between serum IGF-I and the height and BMI of the subjects. However, these correlations were not found in age-adjusted serum IGF-I levels.

IGF-I is mainly secreted by the liver. It circulates as a complex with its binding proteins, IGF-binding proteins (IGFBPs). The measurement of serum IGF-I has become a screening and diagnostic tools for GH disorders in children and adults. In recent studies, the serum IGF-I is going to be of interest in determining the risk for disorders such as cancer or atherosclerosis[10-12]. One needs to be aware when utilizing IGF-I performance that various physiologic and pathological states affect levels including pregnancy, nutritional intake, liver, or renal diseases and other hormones such as thyroid hormones, cortisol, sex steroids, and insulin[9]. Racial variations in serum IGF-I level have also been mentioned. A higher level of serum IGF-I levels were found in Africans and Caucasians compared with those of Asians. That may explain the incidence of the IGF-I related tumors such as prostate cancer are higher among these populations[13].

Normal IGF-I values should be obtained from a large number of healthy populations with normal GH secretion. However, it is non-practical to perform GH provocative tests on all subjects. Therefore, the authors used healthy adult subjects who have normal physical parameters and no evidence of diseases or medications affecting the values of IGF-I. A limitation of the present study is that it was based on hormone measurements performed on blood specimens obtained at a single point of time. It is likely that the observed associations had been somewhat attenuated as a result of physiological within-subject fluctuations in hormone concentrations at any given point in time and variability related to laboratory error.

Conclusion

The present result supported other previous studies that showed the IGF-I level was age-dependent. Concentrations increased from birth through mid-puberty and then declined during the adult life. Other physical factors such as height, weight, and BMI were not found to affect on age-adjusted IGF-I levels. Our reference values may assist the use of IGF-I assay as a tool in the diagnosis of GH function abnormality in Thai subjects.

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ค่าอ้างอิงของระดับ insuline growth factor-1 ของประชากรไทยผู้ใหญ่

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Insuline growth factor-1 เป็นฮอร์โมนหลักในระบบการทำงานของ growth hormone ซึ่งพบว่าสามารถนำมาใช้ในการประเมินความผิดปกติที่เกิดขึ้นเนื่องจากการทำงานของ growth hormone แต่ระดับ insuline growth factor-1 ขึ้นกับปัจจัยทางกายภาพอื่น ๆ เช่น อายุ เพศ ส่วนสูง น้ำหนัก ดัชนีมวลกาย และเชื้อชาติ ดังนั้นจึงจะต้องมีค่าอ้างอิง ของระดับ insuline growth factor-1 ในประชากรผู้ใหญ่ชาวไทยเพื่อใช้ ในการศึกษาเปรียบเทียบการศึกษานี้เพื่อหาค่าอ้างอิงของ insuline growth factor-1 ในประชากรไทยช่วงอายุ 20 ถึง 70 ปี จำนวนประชากร ศึกษา 816 คน แบ่งแยกตามเพศ และอายุ นำมาวัดระดับ insuline growth factor-1 ผลการศึกษา พบว่าอายุเป็นปัจจัยที่มีความสัมพันธ์กับระดับ insuline growth factor-1 แต่ไม่พบความสัมพันธ์ระหว่างระดับ insuline growth factor-1 กับเพศ น้ำหนัก และดัชนีมวลกาย จากการศึกษานี้ ได้ค่าอ้างอิงของระดับ insuline growth factor-1 สำหรับประชากรผู้ใหญ่ชาวไทยโดยแบ่งตามช่วงอายุ ค่าที่ได้จากการศึกษานี้สามารถนำมาใช้ในทางคลินิกเพื่อประเมินความผิดปกติของ growth hormone และเป็นข้อมูลพื้นฐานในการศึกษาความสัมพันธ์ระหว่างระดับ insuline growth factor-1 และภาวะความผิดปกติต่าง ๆ ต่อไป