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Serum Insulin Like Growth Factor-1 Level in Egyptian Healthy Children from 2 to 6 Years Old

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Abstract

Background: The growth hormone (GH)–insulin-like growth factor-1 (IGF-1) axis is a master endocrine regulator for growth and development in children. GH and IGF-1 play significant roles in regular biological processes in childhood and puberty, including cell proliferation and differentiation, organ growth and development, skeletal growth, and metabolism. Although IGF-1 is mainly secreted by the liver, it may be produced in several other tissues as well. Serum IGF-1 levels increase as the child grows, reach a peak value at puberty, and decrease with aging.

Aim of Study: The current study aimed to evaluate serum insulin-like growth factor-1 (IGF-1) levels in Egyptian healthy preschool children.

Patients and Methods: This cross sectional study was conducted on 100 children admitted from Outpatient clinic, Children's Hospital, Ain Shams University in a period of 6 months starting from November 2023 till April 2024; they were 44 females (44.0%) and 56 males (56.0%) with age ranged from 2-6 years and with mean ± SD of 3.68±1.20 years.

Results: Anthropometric measurements revealed that all participants had a weight SDS within the normal range (–2 to 2), while 95% had a height SDS within the normal range. Only one child had a height SDS below -2, and four children had a height SDS above 2. Regarding BMI SDS, 97% of the children were within the normal range, and 3% had a BMI SDS above 2. The median IGF-1 level in the study population was 131.5ng/mL (IQR: 90.25-181.15), with a range of 38-300ng/mL. A significant positive correlation was found between IGF-1 levels and age (r=0.206, p=0.039). No significant correlations were found between IGF-1 levels and other parameters such as weight, height, and BMI SDS. When analyzing the relationship between IGF-1 levels and various parameters using non-parametric tests, no statistically significant differences were found based on age group, gender, height SDS, or BMI SDS.

Conclusion: Our study suggested that IGF-1 levels increase with age in this population. In our study IGF-1, levels are not significantly influenced by gender, height, or BMI.

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Key Words: *Serum Insulin Like Growth Factor-1 Level in Egyptian Healthy Children from 2 to 6 Years Old.*

Introduction

THE growth hormone (GH)–insulin-like growth factor-1 (IGF-1) axis is a master endocrine regulator for growth and development in children. GH and IGF-1 play significant roles in regular biological processes in childhood and puberty, including cell proliferation and differentiation, organ growth and development, skeletal growth, and metabolism **[1].**

Although IGF-1 is mainly secreted by the liver, it may be produced in several other tissues as well. Serum IGF-1 levels increase as the child grows, reach a peak value at puberty, and decrease with aging **[2].**

IGF-1 is a small peptide hormone and over 99% of circulating IGF-1 is bound to serum proteins including IGFBP-3 and the acid labile subunit. However, both serum IGF-1 and IGFBP-3 levels are regulated by age, sex, pubertal stage, genetic factors, social factors, nutritional status and disease **[3].**

Several studies have shown that the serum level of IGF-1 is GH-dependent. Serum IGF-1 concentration is decreased in patients with GH deficiency and increased in patients with acromegaly. GH is secreted in a pulsatile pattern, while serum IGF-1 has almost no pulsatile secretion and for that reason it is widely used in clinics **[4].**

Aim of the work:

Evaluate serum insulin-like growth factor-1 (IGF-1) levels in Egyptian healthy preschool children. A secondary aim is this study will be the first one among future studies that compare IGF-1 levels in healthy Egyptian children among different age groups.

Patients and Methods

Patients:

This cross sectional study was conducted on 100 children admitted from Outpatient clinic, Children's Hospital, Ain Shams University in a period of 6 months starting from November 2023 till April 2024 for 100 children.

Inclusion criteria:

Apparently Healthy children with normal anthropometric measurements of both sexes, aged 2-6 years old.

Method:

All included children were subjected to the following:

1- Full history: From children and their caregivers, socio-demographic data (age, gender, consanguinity of parents), detailed history suggestive of chronic systemic or autoimmune disease (cardiac, respiratory, GIT, hepatic, renal, hematological, rheumatological disorders).

2- Clinical evaluation: Weight was measured on a digital scale in kilograms and to the nearest 0.1kg with the subjects standing motionless without shoes and with minimal clothing. Weight for height SDS (standard deviation score) was calculated according to the norms of Tanner et al. **[5]**.

Height was measured to the nearest 0.1cm on a Harpenden stadiometer (Holtain Ltd, Crowell, Crymych, UK), also without shoes and with Frankfort plane parallel to the ground. Height SDS was calculated according to the norms of Tanner et al. **[5]**.

Body mass index (BMI) was calculated using the formula: Weight in kg/(height)^2 in m^2, and BMI standard deviation score (SDS) was calculated from the age -sex and specific reference values according to Cole **[6]**.

Tanner pubertal staging was done according Marshall and Tanner **[7]** for girls and Marshall and Tanner **[8]** for boys.

3- Investigational Studies:

Laboratory investigations:

5ml blood will be withdrawn from a peripheral vein after disinfecting the skin. The sample will be allowed to clot for 10min then centrifuged and the supernatant tested using kits from Bioassay Technology laboratories. This sandwich kit is for the accurate quantitative detection of Human insulin-like growth factors 1, with a sensitivity: 0.058ng/ml.

Statistical analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. Also qualitative variables were presented as number and percentages. The *p*-value was considered significant as the following: $p>0.05$: Non significant (NS), $p<0.05$: Significant (S), $p<0.01$: Highly significant (HS).

Results

This cross sectional study was conducted on 100 children admitted from Outpatient clinic, Children's Hospital, Ain Shams University in a period of 6 months starting from November 2023 till April 2024.

Table (1): Demographic data of the studied children.

		No.=100
	Median (IQR)	3.67 (2.59-4.54)
	Range	2-6
Age	(2-<2.5 yrs)	18 (18.0%)
	(2.5-<3.5 yrs)	30 (30.0)
	(3.5-<4.5 yrs)	26 (26.0%)
	(4.5-<5.5 yrs)	18 (18.0%)
	(5.5-6 yrs)	8 (8.0%)
Gender	Female	44 (44.0%)
	Male	56 (56.0%)

Table (1) shows that 44 females (44.0%) and 56 males (56.0%) with age ranged from 2-6 years and with mean ± SD of 3.68±1.20 years.

Table (2): Anthropometric measurements of the studied children.

		No.=100
Weight-KG	Mean ± SD	16.00±3.04
	Range	11-25
Weight SDS	Median (IQR)	0.22 (-0.36-0.61)
	Range	-1.51-1.68
	WT SDS <-2	0 (0.0%)
	WT SDS -2 to 2	100 (100.0%)
	WT SDS >2	0 (0.0%)
Height cm	Mean ± SD	98.53±8.96
	Range	83-119
	Median (IQR)	0.01 (-0.57-0.62)
	Range	-2.32-2.25
Height SDS	HT SDS <-2	1 (1.0%)
	HT SDS -2 to 2	95 (95.0%)
	HT SDS >2	4 (4.0%)
BMI SDS	Median (IQR)	0.52 (-0.28-1.03)
	Range	-2-2.09
	BMI SDS <-2	0 (0.0%)
	BMI SDS -2 to 2	97 (97.0%)
	BMI SDS >2	3 (3.0%)

Table (2) shows that 100 (100.0%) of the studied children have weight SDS from –2 to 2. Also, 95 of them (95.0%) have height SDS from -2 to 2 while only one of them has height SDS < –2 and 4 (4.0%) have height SDS >2. Regarding BMI SDS 97 of the studied children (97%) has BMI SDS –2 to 2 and 3 of them (3.0%) have BMI SDS >2.

Table (3): IGF-1 level of the studied patients.

IGF-1 (ng/mL)	No.=100
Median (IQR)	131.5 (90.25-181.15)
Range	38-300

Table (3) shows that the level of IGF-1 of the studied patients ranged from 38-300 with median (IQR) of 131.5 (90.25-181.15).

Table (4): Correlation of IGF-1 with other studied parameters.

	IGF-1 (ng/mL)	
	r	*p*-value
Age	0.206*	0.039
Weight-KG	0.078	0.442
WT SDS	0.125	0.217
Height cm	0.017	0.866
Height SDS	0.041	0.688
BMI SDS	0.187	0.063

*: Significant.
Spearman correlation coefficient.

The previous table shows that there was statistically significant positive correlation between the level of IGF-1 and age of the studied patients with r=0.206 and p-value = 0.039 while there was no statistically significant correlation between the level of IGF-1 and other studied parameters among the studied children.

Table (5): Relation between level of IGF-1 and the other studied parameters.

	IGF-1		Test value	*p*-value	Sig.
	Median (IQR)	Range			
Gender:					
Female	144.5 (91.85-181.05)	38-266	–0.361•	0.718	NS
Male	127.05 (88-181.5)	41-300			
Age group:					
(2-<2.5 yrs)	120.5 (93-160.4)	41-237	5.031#	0.284	NS
(2.5-<3.5 yrs)	109.15 (65-179.8)	43-269.1			
(3.5-<4.5 yrs)	142.7 (91.5-190.5	38-265.9			
(4.5-<5.5 yrs)	153.25 (103-182.3)	64.43-300			
(5.5-6 yrs)	137 (95-239.85)	87-258.4			
Height SDS group:					
HT SDS <-2	182.3 (182.3-182.3)	182.3-182.3	4.293#	0.117	NS
HT SDS -2 to 2	124.1 (89-179.8)	38-300			
HT SDS >2	191.35 (169.15-216.1)	160.6-227.7			
Weight SDS group:					
Wt SDS <-1	142 (96-155.9)	79.6-300	2.136#	0.344	NS
Wt SDS -1 to 1	122 (89-180)	38-283.5			
Wt SDS >1	165.25 (123.8-206.6)	65-255			
BMIS SDS group:					
BMI SDS -2 to 2	133 (89-180)	38-300	–0.232•	0.816	NS
BMI SDS >2	101.8 (92.6-283.5)	92.6-283.5			

p-value >0.05: Non significant (NS). *p*-value <0.05: Significant (S). *p*-value <0.01: Highly significant (HS).
•: Mann Whitney test. #: Kruskal Wallis test.

Table (5) shows that there was no statistically significant relation found between the level of IGF-1 and age groups, gender, height SDS, Weight and BMI SDS with *p*-value = 0.284, 0.718, 0.117, 0.344 and 0.816; respectively.

Discussion

Insulin-like growth factor-1 (IGF-1) is an effector hormone which is essential for normal growth in humans and has an important role in mediating the effects of growth hormone (GH) **[9]**.

Several studies have shown that the serum levels of IGF-1 are GH dependent. Serum IGF-1 concentrations are decreased in patients with GH deficiency and increased in patients with acromegaly. GH is secreted in a pulsatile pattern. On the other hand, serum IGF-1 have almost no pulsatile secretion and for that reason they are used widely in clinics **[10]**.

Although IGF-1 is mainly secreted by the liver, they may be produced in several other tissues as well. Serum IGF-1 levels increase as the child grows, reach a peak value at puberty, and decrease with aging. Although GH is the main regulator of the

production of IGF-1, other factors, such as gender, puberty, hormones, nutrition, seasonal variations, liver and renal functions, gene polymorphisms also have an effect on their levels [11].

We have no documented normal value for IGF-1 in the Egyptian population, so the current study aimed to evaluate serum insulin-like growth factor-1 (IGF-1) levels in Egyptian healthy preschool children.

This cross sectional study was conducted on 100 children admitted from Outpatient clinic, Children's Hospital, Ain Shams University in a period of 6 months starting from November. 2023 till April 2024; they were 44 females (44.0%) and 56 males (56.0%) with age ranged from 2-6 years and with mean±SD of 3.68±1.20 years.

In this study, the demographic data of the study participants showed a relatively even distribution across the age groups, with the highest percentage of children in the 3-year-old group (30%). The gender distribution was slightly skewed towards males (56%), and we reported that there was no difference between male and female in this study.

These findings are consistent with similar studies conducted on healthy preschool children in other populations [4].

Also found in Zumbado et al. [12] IGF-I there were no statistically significant differences between genders neither in the youngest group (male children between 6 and 15 years and female children between 6 and 13 years) nor in the groups of boys and girls (15–19, and 13–19 years, respectively).

In this study, the median IGF-1 level in the study population was 131.5ng/mL (IQR: 90.25-181.15), with a range of 38-300ng/mL.

These finding are similar to those of Yüksel et al. [4] who describe the normal level of IGF-1 in healthy children from 2 to 6 years old with a range of 26-333ng/mL.

In this study, a significant positive correlation was found between IGF1 levels and age (r=0.206, p=0.039).

This finding is consistent with previous studies that have reported agerelated increases in IGF-1 levels during childhood [4].

We found in Guo et al. [1] IGF-1 levels in childhood increase slowly with age, and continuously with growth until to 15 years for boys and reached a peak value at 13 years for girls.

Also in Xu et al. [3] serum levels of IGF-1 increased from early childhood into adolescence .in late puberty, IGF-1levels were maintained at platform or decreased slightly with increasing age.

Serum levels of IGF-I increased steadily with age in the prepubertal stage followed by a rapid increase in IGF-I in the early pubertal stages [13].

Another study show that Serum IGF-1 levels increased with age from the age of 1 year, peaking at around the age of 13 years in girls and 15 years in boys and then began to decline [14].

In accordance Andrade Olivié et al. [15], they reported significant positive correlation between IGF-1 and age during childhood.

Moreover, in a Korean study they reported that serum IGF-I levels increased continuously from early childhood into adolescence. Peak of serum IGF-I was observed two years earlier in girls than it was in boys 13 vs. 15 years of age, respectively [16].

One of the largest studies which established the reference levels for IGF-1 and IGFBP-3 was conducted on 353 children between 0 and 5 years of age and showed that serum IGF-1 levels decreased slowly between 0 and 24 months but increased with age thereafter. Although the decrease found during the first 24 months was not significant, the increase after 24 months was statistically significant [2].

In accordance, Dawoud et al. [17] who aimed to compare IGF-1 levels in children with down syndrome (DS) to those in healthy children. They reported that, there was a significant positive relationship between IGF-1 levels, age in both the patient and control groups.

These findings are similar to those of Barreca et al. [18] who looked at IGF-1 plasma levels in 39 children with DS and found a positive association with age. Ragusa et al. [19] also found a positive correlation between IGF-1 levels and age in DS patients. IGF-1 levels are affected by age and diet.

In agreement, Abdou et al. [20] reported that, IGF-1 showed significant positive correlations with age in both stunted children groups and with height for age z score (HAZ) in stunted underweight children.

These observations are in harmony with the study of Camurdan et al. [21] which demonstrated that serum IGF-1 values were significantly correlated with age in Turkish children with familial short stature. Furthermore, Wang et al. [22] demonstrated a significant positive correlations between the level of IGF-1 and age in Chinese children with idiopathic short stature (ISS).

In accordance Gannagé-Yared et al. [23] who aimed to establish reference values for insulin-like growth factor 1 (IGF-1) in Lebanese schoolchildren and to evaluate the relationship between IGF-1 and age, sex, body mass index (BMI), vitamin D, and ferritin. They reported that, IGF-1 was correlated with age in both sexes (p<.0001).

In this study, no significant correlations were found between IGF-1 levels and other parameters such as weight, height, and BMI SDS. These results contrast with other study that has reported weak positive correlations between IGF-1 and body mass index (BMI) in infants and young children ***[4]***.

The positive correlation between serum IGF-1 levels and BMI is most prominent in puberty ***[2,13]***.

The lack of significant correlations in this study may be due to the relatively small sample size or the narrow age range of the participants.

In a prospective study, Chellakooty et al. ***[24]*** reported that a statistically significant but weak association existed in young age between serum IGF-1 levels and postnatal growth in those at age 3 months who were appropriate for gestational age (AGA) but not in those who were small for gestational age (SGA).

Ragusa et al. ***[19]*** found no correlation between IGF-1 levels and BMI.

Abdou et al. ***[20]*** reported that, IGF-1 showed significant positive correlations with weight and height in both stunted children groups and with HAZ in stunted underweight children.

These observations are in contrary with the study of Camurdan et al. ***[21]*** which demonstrated that serum IGF-1 values were significantly correlated with weight, height, and height SDS in Turkish children with familial short stature.

Furthermore, DeBoer et al. ***[25]*** reported that IGF-1 was positively associated with height for age z score (HAZ) and weight for age z score (WAZ) in Brazilian malnourished children.

Wang et al. ***[22]*** demonstrated a significant positive correlations between the level of IGF-1, height, weight, in Chinese children with ISS.

In this study, there was no difference between males and females with IGF-1 levels.

However, some studies have reported gender-specific differences in IGF-1 levels, with higher levels observed in girls compared to boys of the same ages, but the differences were statistically significant only in pubertal ages 9-14 years ***[13,26]***.

Gannagé-Yared et al. ***[23]*** reported that, IGF-1 was higher in girls compared to boys (p=. 007) and peaked at the ages of 14 and 12 for boys and girls, respectively.

The lack of significant gender differences in our study may be due to the relatively small sample size or the young age of the participants.

Dawoud et al. ***[17]*** reported that there was no statistically significant difference in the mean IGF-1 level between male and female groups of either DS patients or the control group, but the mean IGF-1 level was significantly lower in the age group 2–6 years of DS patients than in the age group 7–12 years. The difference in the level of IGF-1 between DS children and typically developing children could be attributed to the difference in the genetic make-up, age, sex, exercise status, stress levels, nutrition level, and BMI. All these factors can be different in DS children than normal children.

Conclusion:

Our study suggested that IGF-1 levels increase with age in this population, but are not significantly influenced by gender, height, or BMI. Future studies with larger sample sizes and longitudinal designs are needed to further investigate the factors affecting IGF-1 levels in children and to establish age- and genderspecific reference values for clinical use.

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قياس مستوى عامل النمو شبيه الانسولين- ١ في الأطفال المصريين الاصحاء من عمر ٢ الى ٦ سنوات

المقدمة: يعتبر محور هرمون النمو -(GH) عامل النمو الشبيه بالأنسولين -١ (IGF-١) منظمًا رئيسيًا للغدد الصماء للنمو والتطور عند الأطفال. يلعب GH و IGF-١ دورًا مهمًا في العمليات البيولوجية المنتظمة في الطفولة والبلوغ، بما في ذلك تكاثر الخلايا وتمايزها، ونمو الأعضاء وتطورهم، ونمو الهيكل العظمي، والتمثيل الغذائي. يفرز IGF-١ بشكل رئيسي عن طريق الكبد، إلا أنه يمكن إنتاجه في العديد من الأنسجة الأخرى ايضاً وتزيد مستويات مصل IGF-١ مع نمو الطفل، وتصل إلى ذروة القيمة عند سن البلوغ، وتنخفض مع تقدم العمر.

الهدف من الدراسة: تقييم مستويات عامل النمو الشبيه بالأنسولين-١ (IGF-١) في مصل الأطفال الأصحاء في مرحلة ما قبل المدرسة في مصر.

المرضى وطرق العلاج: تم إجراء هذه الدراسة المقطعية على ١٠٠ طفل من العيادات الخارجية في مستشفى الأطفال بجامعة عين شمس على مدى ٦ أشهر بدءاً من نوفمبر ٢٠٢٣ حتى ابريل ٢٠٢٤؛ وكان من بينهم ٤٤ إناث (٤٤,٠٪) و٥٦ ذكور (٥٦,٠٪) بمتوسط أعمار ±SD يبلغ ٣,٦٨±١,٢٠ سنوات.

النتائج: كشفت القياسات البشرية أن جميع المشاركين كان لديهم وزن SDS ضمن النطاق الطبيعي (-٢ إلى ٢) ، بينما كان ٩٥٪ لديهم طول SDS ضمن النطاق الطبيعي. وكان طفل واحد فقط لديه طول SDS أقل من -٢، وأربعة أطفال لديهم طول SDS أعلى من ٢. بالنسبة لـ BMI SDS، كان ٩٧٪ من الأطفال ضمن النطاق الطبيعي، و٣٪ لديهم BMI SDS أعلى من ٢. كان متوسط مستوى IGF-١ في مجتمع الدراسة ١٣١,٥ نانوغرام/مل ٩٠,٢٥-١٨١,١٥ (IQR)، بنطاق من ٣٨ إلى ٣٠٠ نانوغرام/مل. وجد ارتباط إيجابي كبير بين مستويات IGF-١ والعمر p=٠,٠٣٩)، (r=٠,٢٠٦). - لم يتم العثور على ارتباطات كبيرة بين مستويات IGF-١ والمعايير الأخرى مثل الوزن والطول وBMI SDS. عند تحليل العلاقة بين مستويات IGF-١ والمعايير المختلفة باستخدام الاختبارات غير البارامترية، لم يتم العثور على اختلافات ذات دلالة إحصائية بناءً على الفئة العمرية أو الجنس أو طول SDS أو BMI SDS.

الاستنتاج: في الختام ،اقترحت دراستنا أن مستويات IGF-١ تزداد مع التقدم في العمر في هذه الفئة السكانية، ولكنها لا تتأثر بشكل كبير بالجنس أو الطول أو مؤشر كتلة الجسم (BMI). هناك حاجة لدراسات مستقبلية تضم عينات أكبر وتصميمات طولية لتحقيق المزيد من الفهم حول العوامل المؤثرة في مستويات IGF-١ في الأطفال وتحديد القيم المرجعية الخاصة بالعمر والجنس للاستخدام الاكلينيكي.