

Insulin-like growth factor-I and fast growth-hormone levels in mild and moderately malnourished children

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Insulin-like growth factor-I (IGF-I) and fasting growth hormone levels were measured in a group of 255 children (163 males and 92 females, age ranged 6-17 years) of varying pubertal development and body mass index (BMI); well-nourished (BMI > 18), mildly-malnourished (BMI = 15-18) and moderately-malnourished (BMI < 15). In well-nourished children, IGF-I levels increased significantly ($P = 0.02$) with pubertal development, where girls at Tanner 5 had significantly higher ($P = 0.03$) IGF-I levels than the boys. Whilst there was no change in fasting GH levels with nutritional status, IGF-I levels of prepubertal boys and girls decreased significantly with BMI ($P < 0.001$ and $P = 0.01$ respectively). Hence, measurement of IGF-I levels is a sensitive biochemical index in the assessment of mild and moderate form of malnutrition in prepubertal children.

Introduction

Growth hormone (GH) mediates its growth-promoting effect via a group of peptides known as somatomedin-C or insulin-like growth factor-I (IGF-I)¹. Generally, short stature is caused by the lack of GH², although in Laron-type dwarfism, it is due to IGF-I deficiency³. Growth retardation also occurs in children with protein-energy malnutrition (PEM), where IGF-I levels were found to be low^{1,4,5} and GH were reported to be elevated^{4,6-8}. Compared to other biological markers such as albumin and transferrin, IGF-I was reported to be very sensitive to changes in nutritional status and was recommended as a potential biological marker in the assessment of chronic malnutrition such as kwashiorkor and marasmus^{5,9-12}. However, as such severe conditions are rarely seen in Malaysia, we undertook this study to evaluate the sensitivity of IGF-I and GH measurements in less severe forms of malnutrition, and to assess their usefulness as biochemical indicators of nutritional status.

Patients and methods

A total of 255 children (163 males and 92 females, age 6-17 years) from three rural villages were studied. Their pubertal development was determined by the method of Tanner, whereby 143 children were prepubertal (scrotum/breast stage 1) and 112 had already achieved puberty (Tanner stages 2 to 5). These children were also grouped into three groups according to their body mass index (BMI); well-nourished (BMI > 18), mildly-malnourished (BMI = 15-18) and moderately-malnourished (BMI < 15) (Table 1). Informed consent was obtained from all subjects and their parents.

After an overnight fast, 5 ml of blood was obtained by venepuncture, 2.5 ml being immediately transferred into an EDTA tube and the remainder allowed to clot in a plain tube. All plasmas and sera were separated immediately and stored frozen at -20°C until assayed.

Plasma IGF-I levels were measured by SM-C RIA kit from Nichols Institute, San Juan, Capistrana, CA, USA. Intra-assay coefficient of variations (CVs) at concentrations of 0.5, 0.82 and 1.24 U/ml were 12.0, 9.0 and 7.4% respectively, whilst the respective inter-assay CVs were 12.2, 10.0 and 8%.

Serum samples were assayed for GH using our own in-house enzyme-linked immunoabsorbent assay¹³. Intra- and inter-assay CVs at concentrations of 3.4-55.7 mIU/l were all within 10%. GH reference standard used was I.S. 80/505 and minimal detectable concentration of the assay was 0.4 mIU/l. As far as possible, samples within each group were assayed in a single assay.

Statistical analysis

Differences between groups were analysed by non-parametric Kruskal-Wallis and Wilcoxon Rank Sum tests. A P value of ≤ 0.05 was regarded as significant.

Results

Plasma IGF-I levels in 74 normal, well-nourished children (BMI > 18) (35 males and 39 females) at different Tanner stages are shown in Fig 1. IGF-I levels

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Table 1. Characteristics of the children in the study.

Children	Total	Pubertal development					
		Prepubertal			Pubertal		
		BMI<15	BMI 15-18	BMI>18	BMI<15	BMI 14-18	BMI>18
Boy	163	51	24	13	10	43	22
Girl	92	33	16	6	0	4	33
Together	255	84	40	19	10	47	55

increased significantly ($P = 0.02$) with pubertal development. Sex-difference in IGF-I levels was observed only at Tanner stage 5. Girls in this group had significantly higher ($P = 0.03$) IGF-I levels than the boys (Fig 1).

Changes in nutritional status (based on BMI) were found to influence only the IGF-I levels of the prepubertal group (Fig 2). Plasma IGF-I levels decreased significantly in the mildly and moderately-malnourished boys and girls ($P < 0.001$ and $P = 0.01$ respectively). Median IGF-I levels of the moderately-malnourished boys and girls (0.5 and 0.78 U/ml respectively) were significantly lower ($P = 0.004$ and $P = 0.03$ respectively) than the respective sex-matched well-nourished group (1.1 and 1.8 U/ml respectively) (Fig 2). On the other hand, there was no significant difference in fasting GH levels between the well-nourished, mildly- and moderately-malnourished prepubertal children (Fig 3) or pubertal boys (Fig 4). We were however, unable to draw any conclusion on the fasting GH levels of the pubertal girls, as there were insufficient data in the mildly- and moderately-malnourished groups ($n = 4$ and $n = 0$ respectively) (Fig 4).

Discussion

The pubertal increase in IGF-I levels of normal children seen in this study is comparable to that reported by others¹⁴⁻¹⁶. Similarly to the report by Ruland et al.¹⁶, who found that girls age 6-14 years had higher IGF-I levels than boys, we found that sex-difference was most significant at Tanner 5 ($P = 0.03$). We suggest that this was due to the influence of oestrogens^{17,18}.

The various alterations in hormonal levels seen in severe malnutrition are believed to be part of the endocrine adaptive processes to conserve energy and protein metabolism in adverse conditions^{19,20}. In this study, plasma IGF-I levels in prepubertal children were found to decrease significantly with BMI. This finding is comparable to that observed by others^{4,8}. In contrast to previous reports,^{4,6-8} we found that there was no significant difference in fasting GH levels between the well-nourished, mildly and moderately malnourished children. This is probably due to the less severe form of malnutrition of our subjects, compared to other studies^{4,7,8} where the children were suffering from marasmus and kwashiorkor.

Hence, in agreement with several previous studies,^{5,9,11,12} we have showed that measurement of IGF-I concentrations is indeed sensitive to slight changes in nutritional status and thus is a better biochemical index than GH in the assessment of growth retardation due to malnutrition.

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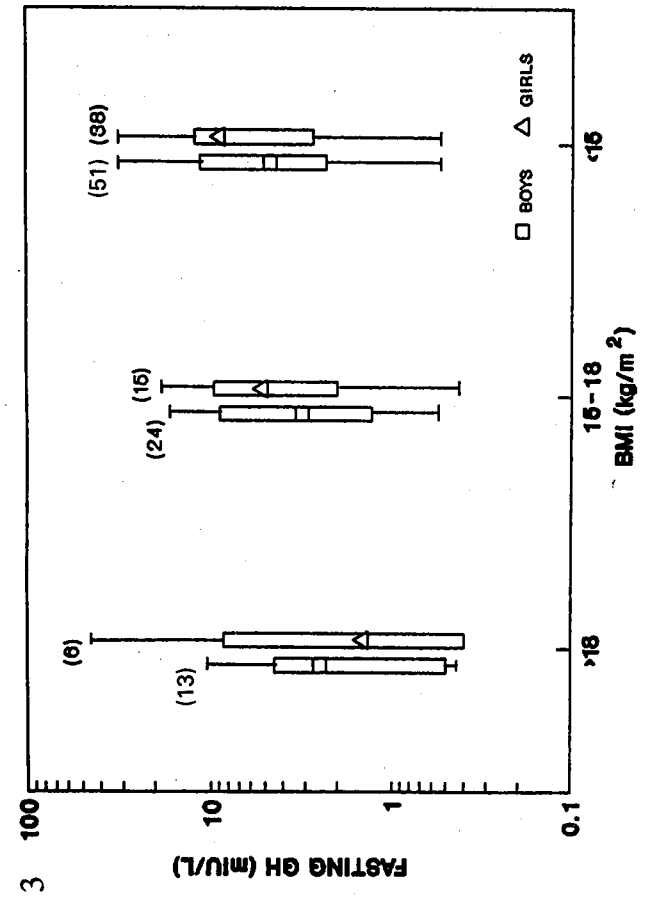
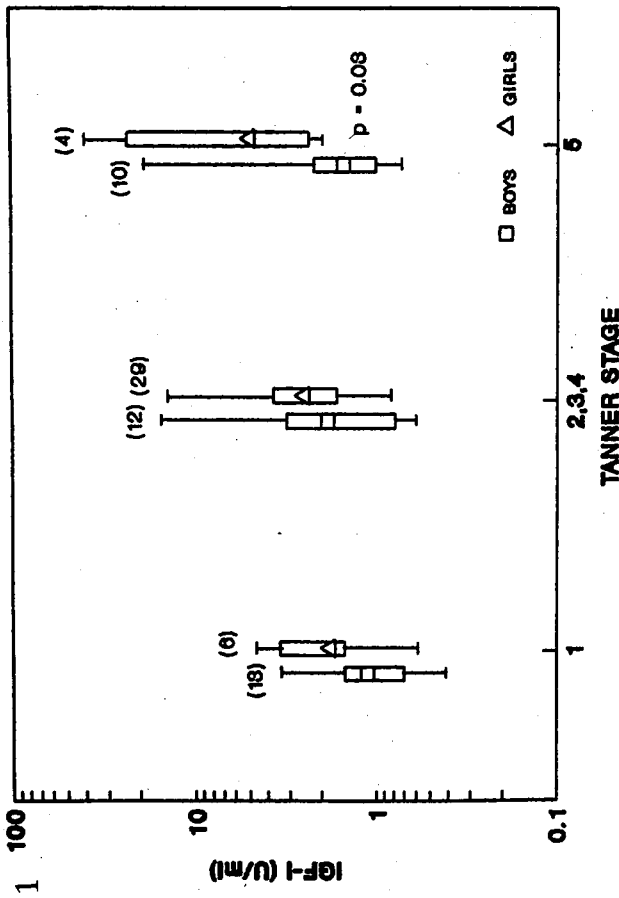
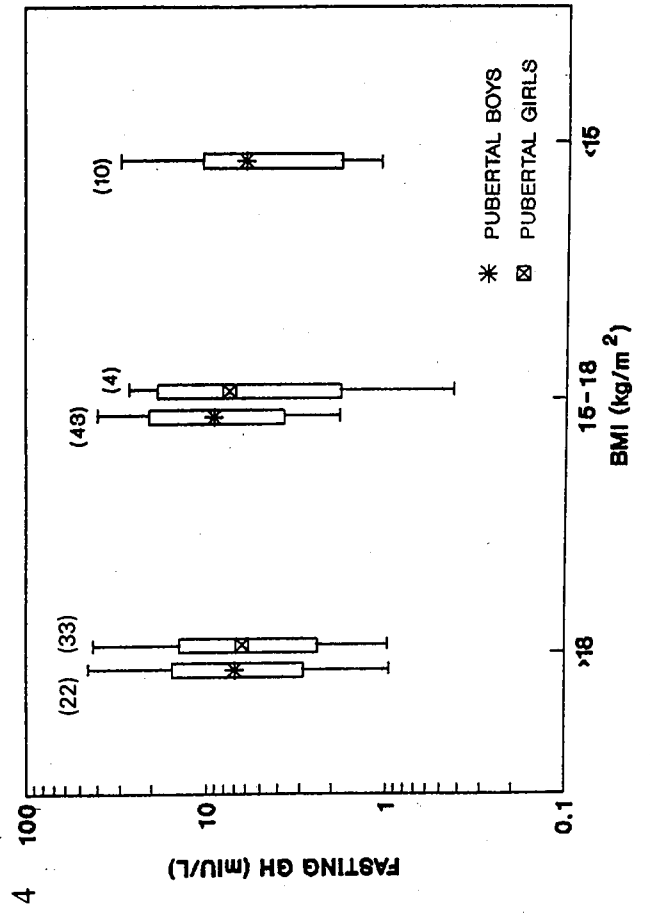
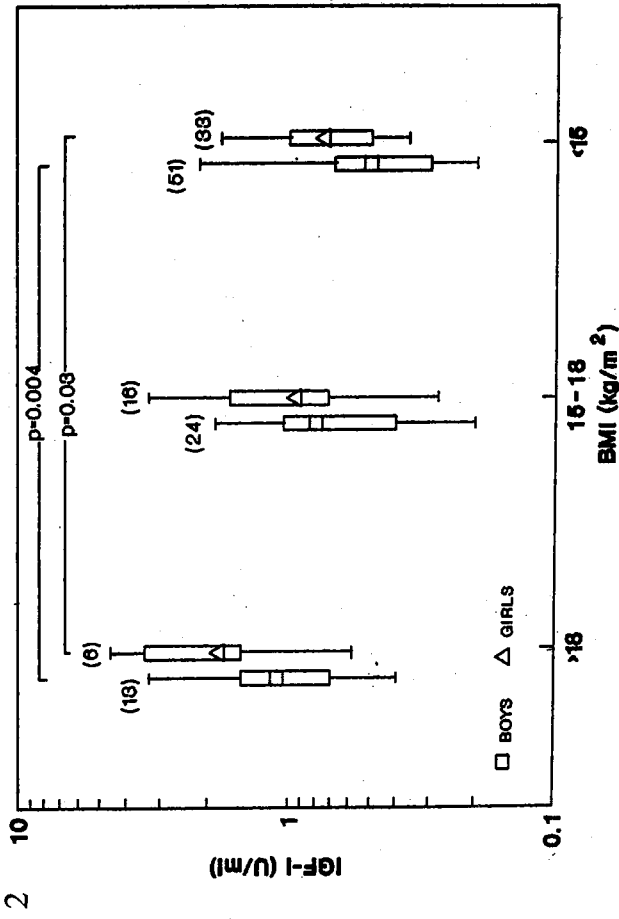
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Fig. 1. Plasma insulin-like growth factor-I (IGF-I) of normal boys and girls at different Tanner stages. 95% confidence limits and interquartile ranges are represented by vertical columns and bars respectively. Numbers above bars represent number of children studied.

Fig. 2. Plasma insulin-like growth factor-I (IGF-I) of prepubertal boys and girls at different nutritional status.

Fig. 3. Fasting growth hormone of prepubertal boys and girls of different nutritional status.

Fig. 4. Fasting growth hormone of pubertal boys and girls of different nutritional status.



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ARAS FAKTOR PERTUMBUHAN MENYERUPAI INSULIN I (IGF-I) DAN HORMON PERTUMBUHAN BERPUASA PADA KANAK-KANAK YANG MENGALAMI KEKURANGAN GIZI YANG RENDAH DAN SEDERHANA

Aras faktor pertumbuhan menyerupai insulin I (IGF-I) dan hormon pertumbuhan berpuasa dihitung pada 273 orang kanak-kanak (186 orang kanak-kanak lelaki dan 87 orang kanak-kanak perempuan, yang berusia sekitar 6-17 tahun) dari pelbagai peringkat pubertas dan indeks massa tubuh (BMI); tanpa kekurangan gizi (BMI > 18), kekurangan gizi yang rendah (BMI = 15-18) dan kekurangan gizi yang sederhana (BMI < 15). Pada kanak-kanak yang tidak mengalami kekurangan gizi, aras IGF-I meningkat secara signifikan ($P=0.02$) bersama peringkat pubertas, yang mana kanak-kanak perempuan pada Tanner 5 mempunyai aras IGF-I yang signifikan lebih ketara dari kanak-kanak lelaki ($P=0.03$). Sungguhpun tiada perubahan aras hormon pertumbuhan berbanding status gizi, paras IGF-I pada kanak-kanak lelaki dan perempuan prepubertas menurun secara signifikan bersama-sama BMI (masing-masing $P<0.001$ dan $P=0.01$). Oleh itu, perhitungan aras IGF-I merupakan indeks biokimia yang sensitif untuk menilai kekurangan gizi yang rendah dan sederhana pada kanak-kanak prapubertas.

摘要

輕度和中等度營養不良兒童的胰島素樣生長因子 I 和空腹生長激素水平

作者測定了 273 位不同青春發育期和體重指數 (BMI) 兒童 (186 位男童和 87 位女童, 年齡在 6-17 歲) 的胰島素樣生長因子 I (IGF-I) 和空腹生長激素水平。他把體重指數 > 18 定為營養良好, 體重指數 = 15-18 為輕度營養不良和體重指數 < 15 為中等度營養不良。營養良好兒童, 其 IGF-I 水平隨青春發育而明顯地增加 ($P=0.02$), 而女童在 Tanner 5 時, 其 IGF-I 水平明顯較男童為高。但空腹生長激素水平並沒有隨着營養狀況而改變, 男童在青春前期, 其 IGF-I 水平隨着體重指數而明顯下降 (分別為 $P<0.001$ $P=0.01$), 因此作者認為, 對青春前期兒童, 測定 IGF-I 水平是一個評估輕度和中等度營養不良的敏感生化指標。