

## Association between IGF-1 (Insulin-like Growth Factor) SD levels in children with Growth Hormone Deficiency(GHD) with and without pituitary morphological abnormalities.

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### BACKGROUND

IGF-1 levels are low in patients with GHD(4). Patients with morphological abnormalities in pituitary were associated with lower IGF-1(9). The diagnostic use of IGF-1 in children suspected of GHD is based on the assumption that a single determination of this parameter reflects the integrated 24-hour GH secretion. The aim of this study was to evaluate the value of IGF-1 according Standard Deviation(SD) at the diagnosis in patients with GHD and correlate with the presence or not of pituitary morphological abnormalities.

### METHOD

The study was carried out at a Pediatric Endocrinology Ambulatory and used a sample of 125 patients diagnosed with GHD(1993-2015). It was analyzed the IGF-1 Standard Deviation(SD) value at diagnosis and correlated with the presence, or not, of pituitary morphological abnormalities. The samples were categorized in IGF-1 level below 0SD to -2SD and below -2SD. The variables analyzed were sex, H-SDS and chronological age at the diagnosis. The medical imaging exams used for pituitary analysis were Magnetic Resonance Imaging (MRI) and/or Computed Tomography (CT-Scan) when available. This study was approved by the University ethics committee.

### RESULTS

In a sample of 125 patients, 70 male(56%), and 91(72.8%) were IGF-1 <0 SD, and 23 of them <-2SD. Pituitary abnormalities were found in 39(31.2%), in 30 patients IGF-1 <0SD. There is no difference between IGF-1 SD and morphological pituitary changes, when considering level of IGF-1 values <0 SD to -2SD. Although when analyzed IGF-1 value <-2SD (23 patients) the number of patients with morphological pituitary abnormalities were significantly higher than the patients without pituitary abnormalities( $p < 0.05$ )(12/39). (Table 1).

In 34 patients whose IGF-1 was >0SD, nine presented morphological abnormalities. Hypoplasia pituitary was the most frequent alteration found in 27 patients, seven with ectopic neurohypophysis and two with empty sella. The relation between H-SDS and chronological age at the beginning of treatment according to IGF-1 <0SD and <-2SD did not indicate significant difference between the group with and without pituitary abnormalities(-1.76 x -1.52,  $p = 0.53$ ).

**Table 1 – IGF-1 association with image exam**

	Without morphological abnormalities (n=86)	With morphological abnormalities (n=39)	Total (n=125)	p
IGF-1( $\sigma < 0$ )	61 (70.9%) [50(59.3%)]	30 (76.9%) [18 (46.1%)]	91 (72.8%)	0.4854
IGF-1 ( $\sigma < -2$ )	11(12.7%)	12 (30.7%)	23 (18.4%)	0.0162

I – p: Chi-square test,  $p < 0.05$  statistically significant.  
II –  $\sigma$ : Standard deviation

**Table 2 – Comparison of age and H-SDS at the beginning of treatment in patients with and without pituitary abnormalities according IGF-1 0 to -2SD (91patients) and IGF-1 < -2SD (23patients).**

Variable	Without morphological abnormalities (61patients)			With morphological abnormalities			T-test	M-W test
	n	Amplitude	Median $\pm$ SD	n	Amplitude	Median $\pm$ SD	p	p
IGF-1 $\sigma < 0$								
Age at the beginning of treatment	61	(3.6 – 14.6)	( <b>9.8</b> $\pm$ 2.45)	30	(3.5 - 14)	( <b>9.93</b> $\pm$ 2.87)	0.82	0.60
H-SDS	61	(-4.8 – 0.1)	( <b>-1.76</b> $\pm$ 1.02)	27(III)	(-4.9 – 4.6)	( <b>-1.52</b> $\pm$ 1.84)	0.53	0.72
IGF-1 $\sigma < -2$								
Age at the beginning of treatment	11	(8.3 – 14.1)	( <b>11.27</b> $\pm$ 2)	12	(4.1 - 14)	( <b>9.94</b> $\pm$ 3.4)	0.27	0,40
H-SDS	11	(-4.8 - -0.9)	( <b>-2.59</b> $\pm$ 1.21)	12	(-4.9 – 2.6)	( <b>-2.14</b> $\pm$ 1.84)	0.49	0.71

I – p: p value of Student 's t test (parametric test) and Man-Whitney test (non parametric test).  $p < 0,05$ , statistically significant  
II –  $\sigma$ : standard deviation  
III – In 3 patients was not reported height

### DISCUSSION

The diagnosis of IGF-1 deficiency is probable when average IGF-1 values are <-2 SD for chronological age. Values between -2SD and -1 SD are considered reduced and they indicated a probable IGF-1 deficiency or GHD. The level of IGF-1 could be correlated with abnormalities in pituitary gland.

In this sample all patients had GHD, 31.2% presented pituitary abnormalities. When IGF-1 was <-2SD were found a significant amount patients with pituitary abnormalities.

Pituitary hypoplasia was the most prevalent abnormality, followed by ectopic neurohypophysis and empty sella, as described in the literature. When the IGF-1 were <-2 SD, it's necessary to think that the patient could have morphological pituitary changes.

H-SDS at beginning of treatment was not a good parameter to show if the patient has or not pituitary abnormalities.

In relation to chronological age in patients with IGF-1 < -2 it was found that patients without pituitary morphological changes were older than patients with pituitary morphological changes. Even though this difference was not statistically significant, it is assumed that patients with pituitary morphological changes seek for treatment earlier than patients without morphological changes in pituitary.

### CONCLUSION

According this study in patients with GHD, when IGF-1 were <-2 SD this were a good parameter to indicate the presence of pituitary abnormalities.

### REFERENCES

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