

# High incidence and male predominance of transient form of isolated growth hormone deficiency in children. What is the optimal time for the therapy withdrawal and retesting?



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## INTRODUCTION

Normal growth hormone (GH) secretion after the attainment of final height (FH) is observed in most of GH-treated children with isolated GH deficiency (GHD), however it is still unclear when such normalization of GH secretion occurs. It is recommended to reassess GH secretion after the attainment of near-FH<sup>1</sup>, however there are data showing that normalization of GH secretion in children with isolated idiopathic GHD may occur in mid-puberty<sup>2,3</sup> or even earlier<sup>4</sup>.

## AIM

The aim of the study was to assess the incidence of transient GHD in retesting with respect to pediatric criteria in patients with isolated GHD diagnosed in childhood, depending on the moment of GH therapy withdrawal (before of after the attainment of near-FH).

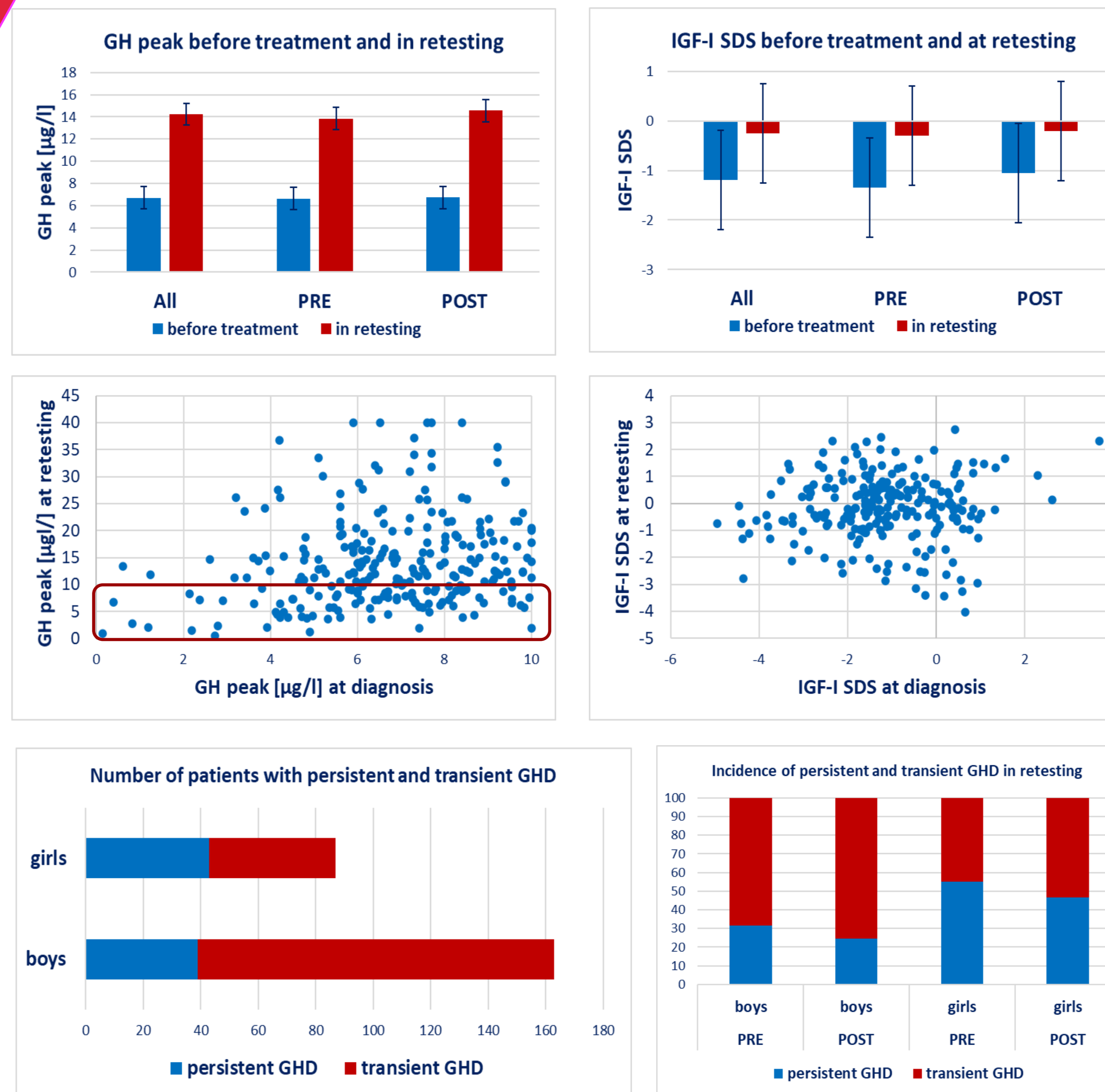
## RESULTS

Significant increase ( $p < 0.001$ ) of both GH peak in retesting and IGF-I SDS at retesting with respect to pre-treatment values was found for all the patients, as well as in PRE and POST Group.

Only 1/3 of the patients fulfilled the pediatric criteria of GHD in retesting.

There was also only a weak correlation between pre- and post-treatment values of GH peaks ( $r = 0.195$ ,  $p < 0.05$ ) and no correlation between pre- and post-treatment IGF-I SDS ( $r = 0.106$ ;  $p > 0.05$ ).

Male predominance (66.54%) among treated patients was observed, in both PRE and POST Group (77.03 vs. 58.27%, respectively). Transient GHD was diagnosed significantly more frequently ( $p = 0.0008$ ) in boys than in girls, while there was no significant difference in the incidence of transient GHD between Groups PRE and POST ( $p = 0.57$ ).



Group	All retested	PRE	POST
N° of patients (boys/girls)	260 (173/87)	121 (92/29)	139 (81/58)
GH peak [μg/l] before treatment	6.69±2.04	6.63±2.13	6.73±1.97
GH peak [μg/l] in retesting	14.23±8.42	13.85±8.99	14.55±7.91
IGF-I SDS before treatment	-1.19±1.48	-1.35±1.46	-1.06±1.50
IGF-I SDS at retesting	-0.25±1.38	-0.30±1.40	-0.21±1.36
Increase of height SDS during treatment	1.80±0.85	2.09±0.75	1.55±0.85
Patients with transient GHD (boys/girls)	168 (124/44)	76 (63/13)	92 (61/31)
<b>Incidence of transient GHD</b>	<b>64.62%</b>	<b>62.81%</b>	<b>66.19%</b>
Incidence of transient GHD in boys	71.68%	68.48%	75.31%
Incidence of transient GHD in girls	50.57%	44.83%	53.45%

Special attention should be paid to 19 non-responders (9 boys, 10 girls) including 7 ones with no height SDS increase and 12 with an increase by less than 0.5 SD. Only 2 of them were qualified to PRE group, while the remaining 17 were qualified to POST Group (i.e. continued ineffective treatment after the attainment of FH). None of the non-responders had GH peak  $< 3.0 \mu\text{g/l}$  (severe GHD) in retesting, while 14 of them had GH peak  $> 10.0 \mu\text{g/l}$ . Patients with severe GHD in retesting (9 cases in PRE, 1 in POST Group) are candidates for continuation of GH therapy in adulthood.

## PATIENTS

260 children with isolated GHD (height SDS  $< -2.0$ , GH peak in 2 stimulation tests  $< 10.0 \mu\text{g/l}$ ), who completed GH therapy before (Group PRE) or after (Group POST) the attainment of near-FH (bone age)  $> 16$  years in boys,  $> 14$  years in girls, height velocity  $< 2.5 \text{ cm/year}$ ) and have performed retesting: insulin tolerance test (ITT) followed by 2<sup>nd</sup> pharmacological test in case of GH peak  $< 10.0 \mu\text{g/l}$  in ITT; GH peak  $> 10.0 \mu\text{g/l}$  in retesting was diagnostic for transient GHD.

## STATISTICS

All continuous variables were expressed as mean±SDS. Values of pre-treatment height SDS, and of FH SDS were calculated according to Polish reference charts of Palczewska & Niedźwiecka<sup>5</sup>; IGF-I values were expressed as IGF-I SDS for age and sex, according to the formula proposed by Blum<sup>6</sup> and reference data for the used laboratory method<sup>7</sup>. For assessment of differences in proportion of males and females in particular groups Fisher exact test was used. As pre-treatment characteristics did not follow normal distribution in at least one Group (verified by Shapiro-Wilk test), Mann-Whitney U test was selected for comparisons of continuous variables between the Groups, while Wilcoxon test for comparisons of two consecutive measurements in the same Group. All correlations were assessed by non-parametric Spearman's method.

## CONCLUSIONS

**In most of patients diagnosed in childhood with isolated GHD normalization of GH secretion with respect to pediatric criteria occurs before the attainment of near-FH. Earlier retesting of GH secretion could help to avoid overtreatment of the patients with transient GHD.**

**Overrepresentation of boys and higher incidence of transient GHD in them suggests the possibility of overdiagnosing GHD in boys.**

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