GROWTH HORMONE DEFICIENCY PERSISTENCE DURING THE TRANSITION PERIOD BETWEEN CHILDHOOD AND ADULTHOOD IN PATIENTS WITH CHILDHOOD ONSET GROWTH HORMONE DEFICIENCY TREATED WITH rhGH – PRELIMINARY DATA

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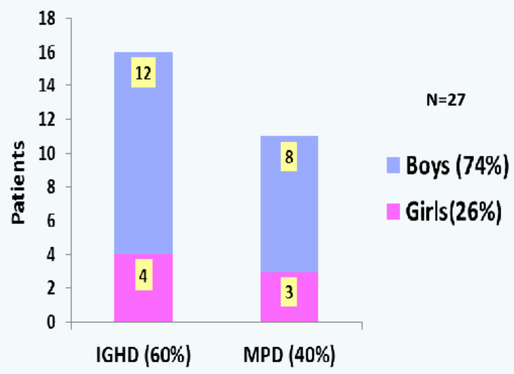
Background: Transition = a period from mild – to late teens until 6-7 years after achievement of final height.More than two thirds of teenagers with childhood-onset GH defficiency (CO-GHD) documented normal GH response when retested at final height; possible causes for the normal response to GH stimulation tests in the transition period are: 1) transient GHD in childhood; 2) lack of reproducibility of GH stimulation tests; 3) sex steroid- mediated maturational changes in hypothalamic control of GH secretion during puberty.

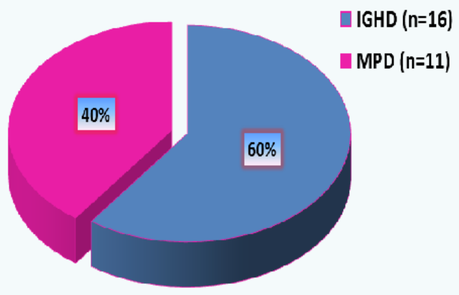
Objective :to identify potential predictors for persistent GHD after reaching final height under rhGH with a particular accent on children with isolated GHD (IGHD).

Methods: Prospective study started last year- reevaluation CO-GHD in the transition period; cohort of 27 CO-GHD patient who received rhHG and reached final height; cohort has 20 boys (74%) and 7 girls aged 14-20 years, the mean duration of therapy = 7.06 years (3 to 12.4 years); average time to cessation of therapy = 1.63 years (0.3 to 5.4 years); anthropometric parameters (Height Z score, BMI, target height (TH)) were analyzed; Retest –GH in insulin tolerance test (ITT) , adenohipofizare functions, IGF1 levels.The main outcome measures were sensitivity, specificity, positive and negative predictive values (PPV,NPV) of clinical and hormonal factors for persistent GHD (GHD-P) defined as peak GH < 5 ng/ml.

Results :

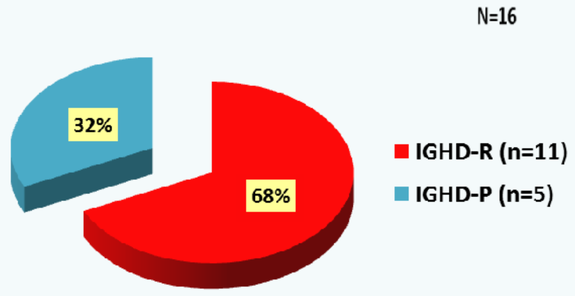
Cohort features





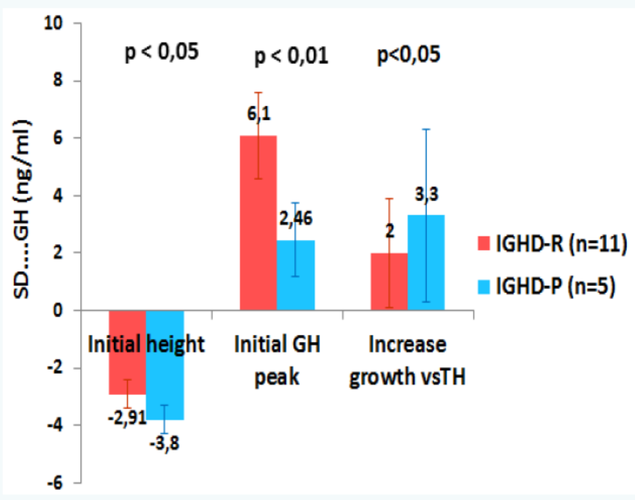
60% of patients are isolated GHD, 40% are multiple pituitary deficiency (MPD); boys accounted for 74% of all patients

Characteristics of patients with isolated GHD (IGHD)



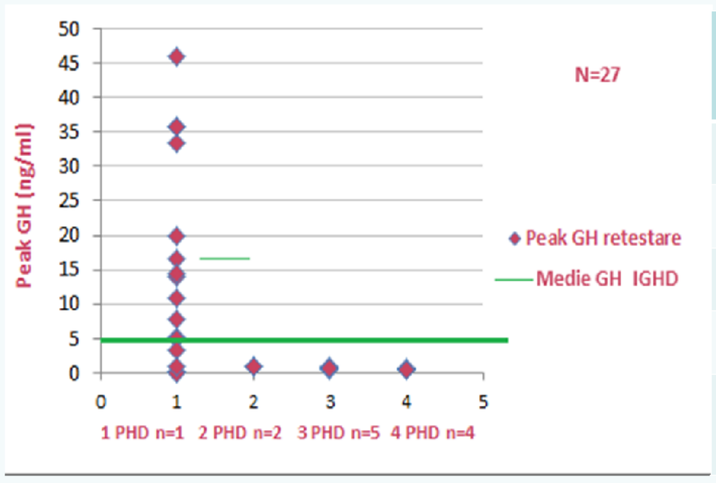
32% of IGHD are persistent GHD (IGHD-P) (peak GH in ITT< 5ng/ml) and 68% are reversible IGHD (IGHD-R) (peak GH in ITT > 5 ng/ml

Parameters at baseline that differ significantly - between the 2 groups of patients IGHD



Patients with IGHD-P had a significantly initial growth retardation,a significantly lower initial GH response in ITT and significantly better recovery for growth retardation than IGHD-R patients

Predictive value for persistent GH deficiency -association with other pituitary deficits



Pituitary Hormone Deficiencies >1	
PPV	100%
PNV	68,75%
Specificity	100%
Sensitivity	68,75%
Diagnostic efficiency	81,5%

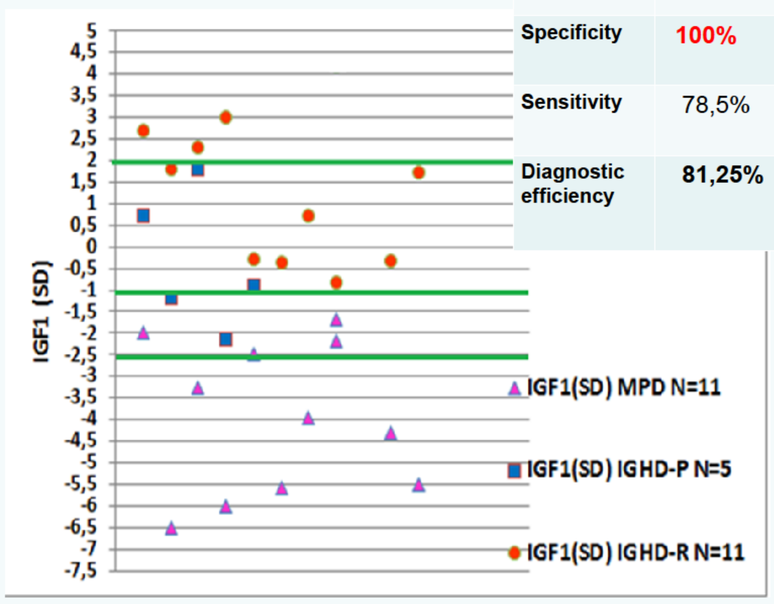
Presence of **≥1** additional pituitary hormone deficiency predict 100% persistent GHD status at reevaluation

Factors predicting the persistence of GHD after final height achievement

	cut-off value	PPV	PNV	Specificity	Sensitivity	Diagnostic Efficiency
-association with other pituitary deficits	≥1	100%	68,75%	100%	68,75%	81,5%
Initial level of peak GH in ITT	≤ 3 ng/ml	100%	91,66%	100%	80%	93,75%
Growth recovery vs TH with treatment	≥ 3SD	100%	84,6%	100%	80%	87,5%
Initial height Z score	≤ -3,5 SD	66%	90%	82%	80%	81,25%
Chronological age at treatment initiation	≤ 5 ani	66%	77%	90%	40%	75%

Cut-off values of IGF1 (SD) for differentiating patients with persistent GHD on reevaluation

	IGF1 (SD) ≥ - 1 (IGHD-R vs IGHD-Persistent)	IGF1 (SD) ≥ - 1,5 (IGHD-P vs MPD)	IGF1 (SD) ≤ - 2,5 (MPD)
PPV	100%	80%	100%
PNV	40%	100%	73%
Specificity	100%	91,6	100%
Sensitivity	78,5%	100%	63%
Diagnostic efficiency	81,25%	93%	81%



CONCLUSIONS

- In transition - GH-IGF1 status reassessment is required to detect cases requiring further treatment with rhGH- replacement doses;
- Approximately one third of IGHD patients - have persistent GH deficiency after final height achievement;
- GH peak in ITT value ≤ 3 ng / ml at initial diagnosis – 100% positive predictive value -status of persistent IGHD;
- IGF1 value <-1.5 SD at reevaluation requires retesting all pituitary axes given that the combination of additional pituitary deficiency can occur gradually;
- IGF1 ≤ - 2.5 SD at reevaluation - oriented the diagnosis of MPD with 100% specificity in selecting the cases that do not require dynamic tests

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