

# Clinical characteristics of children with congenital combined growth hormone deficiency without associated syndrome in Belgium



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## Introduction

Combined growth hormone (GH) deficiency (CGHD) refers to a rare heterogeneous group of conditions in which there is a deficiency of growth hormone and one or more other pituitary hormones (1,2). Congenital CGHD can be idiopathic, associated with structural pituitary abnormalities, such as pituitary interruption syndrome (PSIS), or be part of a more complex brain developmental disorder or syndrome (3,4).

Despite the fact that PSIS is a frequent finding in children with CGHD, clinical data are still limited and the height gain in response to GH treatment has not been evaluated in comparison with CGDH with a normal stalk.

We want to report the clinical and hormonal findings and evaluate the short term height gain in response to GH in Belgian children with congenital non-syndromic form of CGHD presenting with and without PSIS at MRI.

## Methods

This retrospective study includes 59 children with a congenital form of CGHD, who were started on GH treatment between January 1996 and December 2011, were recruited from the national GH database. MRI, hormonal and growth data in the first year of GH therapy were evaluated. The patients were divided into two groups: one with and the other without stalk abnormalities (PSIS versus normal pituitary stalk (NPS)).

## Results

GENERAL FEATURES	Total (n = 59)	PSIS (n = 36)	NPS (n=23)
Male/female	38/21	25/11	13/10
Family History	4	1	3
Height mother, cm (n = 55)	163.8 (8.6)	165.3 (8.5)	161.4 (8.3)
Height father, cm (n = 55)	176.9 (8.6)	178 (8.4)	175.2 (8.9)
Gestational age Weeks (n=57)	38.7 (2.9)	38.2 (3.9)	39.0 (2.0)
Birth weight, kg	3.0 (0.7)	3.0 (0.8)	3.0 (0.5)
Birth weight, SDS	-0.6 (1.0)	-0.4 (1.0)	-0.9 (1.0)
Birth length, kg	48.9 (3.1)	49.0 (3.6)	48.7 (2.5)
Birth length, SDS	-0.4 (1.0)	-0.3 (1.0)	-0.6 (1.1)
Micropenis, n	13 (22%)	9 (25%)	4 (17%)
Prolonged neonatal jaundice, n	3 (5%)	3 (8%)	0 (%)
Hypoglycaemia, n	20 (34%)	14 (39%)	6 (26%)
Age start GH therapy, years	6.1 (4.3)	6.7 (4.6)	5.3 (3.9)
Height start GH therapy, cm	97.8 (24.8)	99.1 (24.4)	95.8 (25.7)
Height start GH therapy, SDS	-3.4 (1.4)	-3.7 (1.4)	-2.9 (1.3)
Age at latest consultation, years	13.7 (5.3)	14.8 (5.0)	12.0 (5.4)

Table 1. General and Clinical Features; Data are expressed as mean (SD) unless indicated otherwise; SDS = standard deviation score;

HORMONAL STATUS	Total (n = 59)	PSIS (n= 36)	NPS (n=23)
GH peak median (ng/ml)	1.55	1.6	1.5
TSH deficiency, n	54 (92%)	35 (97%)	19 (83%)
ACTH deficiency, n	39 (66%)	28 (78%)*	12 (52%)*
LH/FSH deficiency, n	28 (47%)	20 (55%)*	8 (35%)*
PRL deficiency, n	2 (3%)	1 (3%)	1 (4%)
Hyperprolactinaemia, n	4 (7%)	4 (11%)	0
Diabetes insipidus, n	4 (7%)	2 (6%)	2 (9%)

Table 2. Hormonal status : median GH peak after stimulation test and different other pituitary hormone deficiencies at latest follow up (\*p< 0.05)

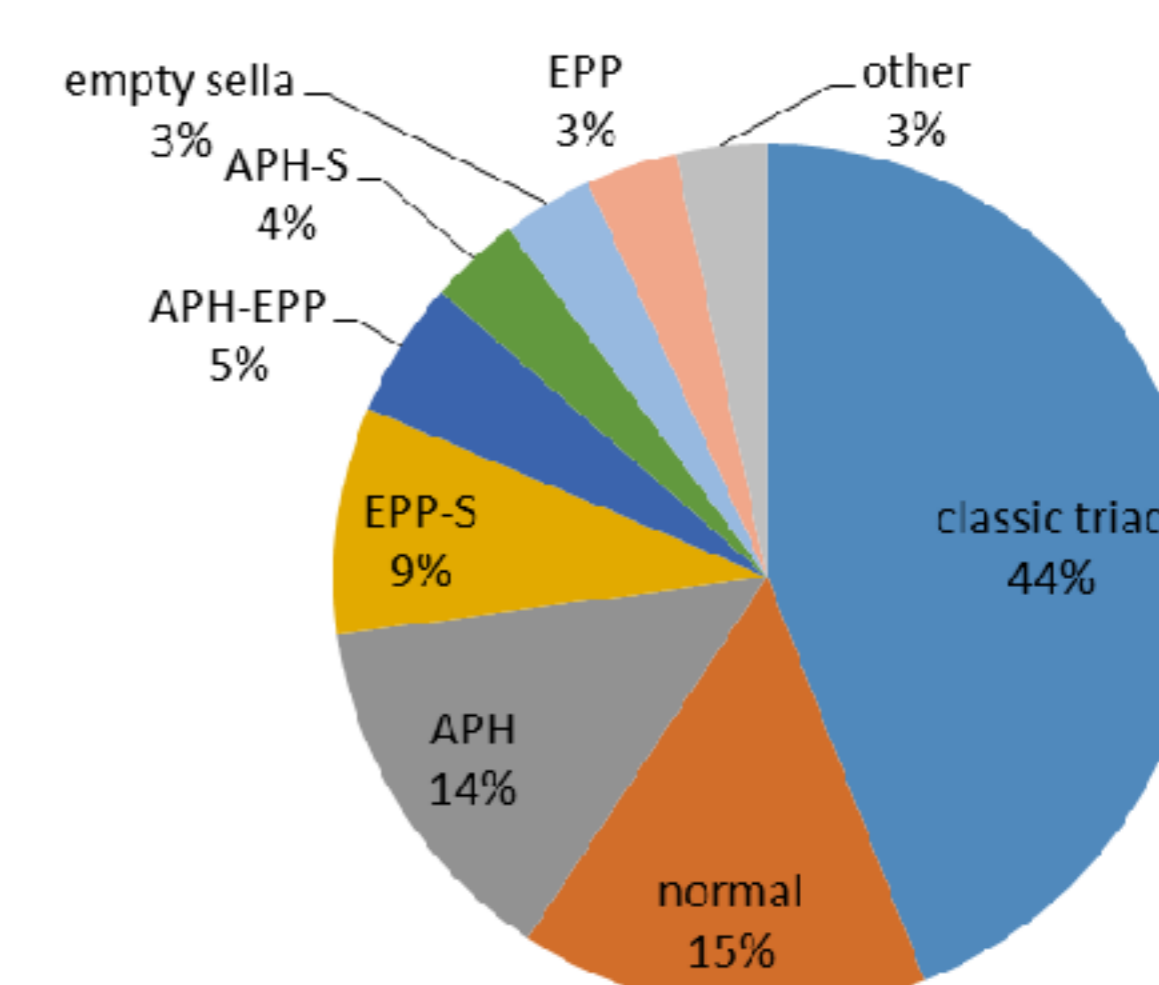
36 of the 59 patients, whose general features are listed in Table 1, were diagnosed with PSIS. Anterior pituitary hypoplasia was present in 86% of PSIS patients and in 48% of the patients with a NPS, while an ectopic posterior pituitary was seen in respectively 86% and 13%. MRI data are summarized in Fig 1.

At the start of GH treatment, 28% of PSIS patients had 1 deficiency, 19% 2 deficiencies, 47 % 3 deficiencies and 6% 4 deficiencies. For the NPS patients, 18% of patients had 1 deficiency, 61% 2 deficiencies, 17% 3 deficiencies and 4 % 4 deficiencies. During GH therapy 75% of PSIS patients developed additional pituitary hormone deficiencies, compared to 48 % of NPS patients (Fig. 2).

Pituitary hormone deficiencies at the latest follow up are represented in Table 2. PSIS patients have significantly more frequent ACTH deficiency and LH/FSH deficiency.

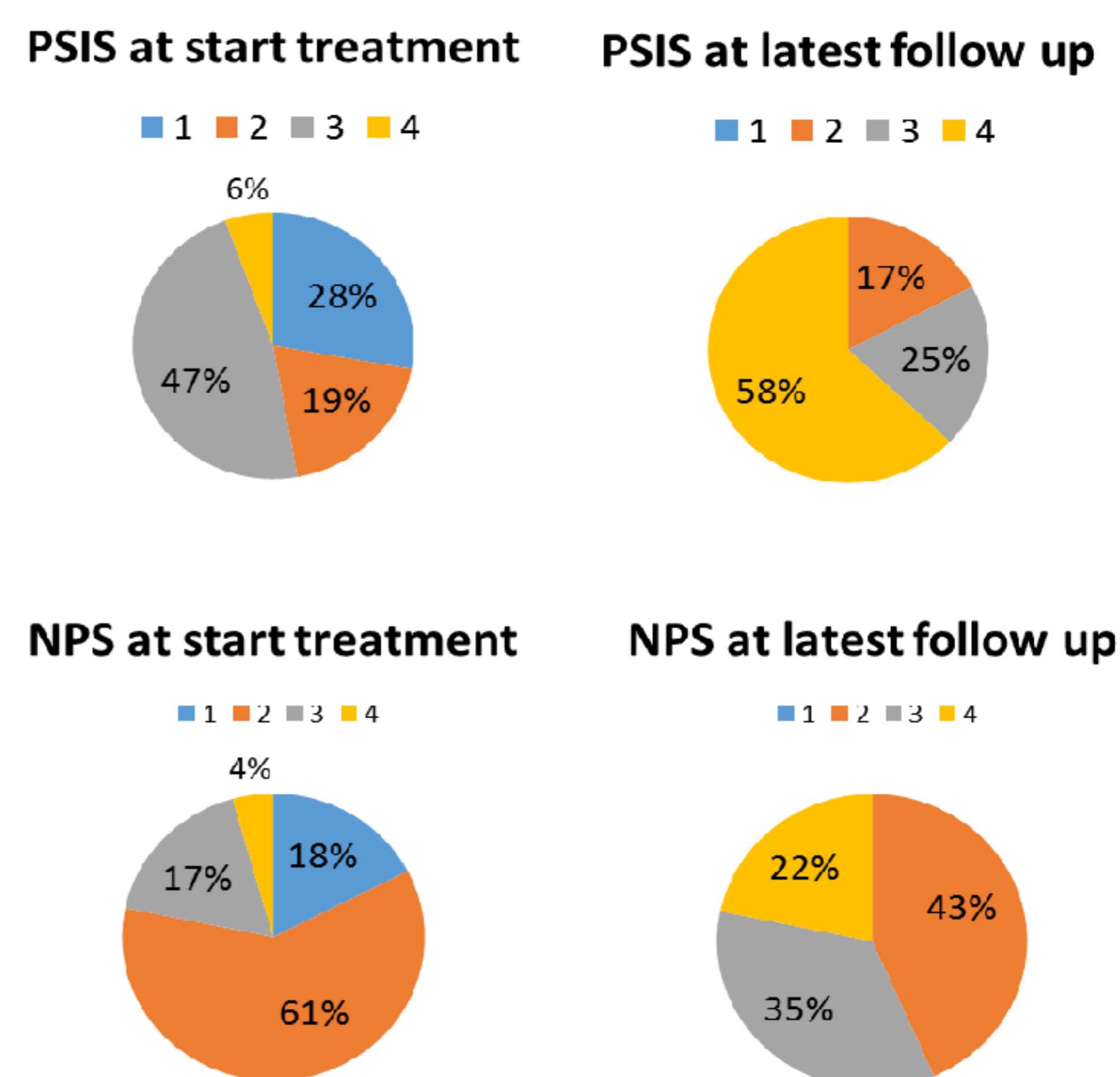
The mean height gain after 1 year of GH therapy was similar in both groups, respectively 11.6 cm (4.2 cm; range 5.7 – 29.4 cm) in PSIS patients and 11.1 cm (5.8 cm, range 1.5 – 29.8 cm) in NPS patients

Figure 1 MRI data



EPP = ectopic posterior pituitary; APH = anterior pituitary hypoplasia; S = stalk involvement; Classic triad = combination of small AP, EPP and invisible or interrupted pituitary stalk.

Figure 2 Number of pituitary hormone deficiencies



## Conclusion

PSIS is found in the majority of non-syndromic CGHD children. Compared to NPS patients, these patients have a higher probability of abnormal pituitary morphology on MRI, a higher number of pituitary hormone deficiencies at start of GH treatment and a higher risk of developing more pituitary hormone deficiencies during follow up, whereas the severity of the GH deficiency and height gain after 1 year of GH treatment are similar.

## References

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