

Immunogenicity of recombinant growth hormone and relationship its growth-promoting effect in the children with short stature

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INTRODUCTION

Although there are many well-known components that affect the growth response to recombinant growth hormone (rGH), its effect on total height gain is still not fully predictable. Current knowledge on the relationship between growth response to rGH and its immunogenicity is limited

AIM

The aim of the study was to reveal its relationship with the antibody formation against rGH and growth-promoting effect.

METHOD

Study involving 193 children treated with rGH therapy,
 • 111 of whom diagnosed with growth hormone deficiency (GHD),
 • 37 idiopathic short stature (ISS), and
 • 45 short stature due to non-endocrine disorders.

The number of the participants according to treatment years was as follows:
 24, 34, 46, 39, 21, 29 children;
 at onset, first, second, third, 4th, and ≥5th years on treatment.

GH antibody (GH-Ab) and total IgE assays were studied from 193 and 97 participants, respectively

The presence of GH-Ab and their association with growth response to rGH were evaluated in three groups.

RESULTS

•Seropositivities for GH-Ab and total IgE were detected in 103 (53.3%) and 25 (25.7%), respectively.

•The number of GH-Ab positive patients was higher in the ISS group (67.5%) (p=0.013).

•In 15 of 24 (62.5%) patients whose test was studied, GH-Ab seropositivity was detected before treatment

•In all three groups, first-year height velocity was found to be lower in GH-Ab-positive patients than in GH-Ab negative patients

•(GHD; 8.62±2.97 vs. 10.91±3.63, I

•SS; 5.63±0.11 vs. 8.30±1.79,

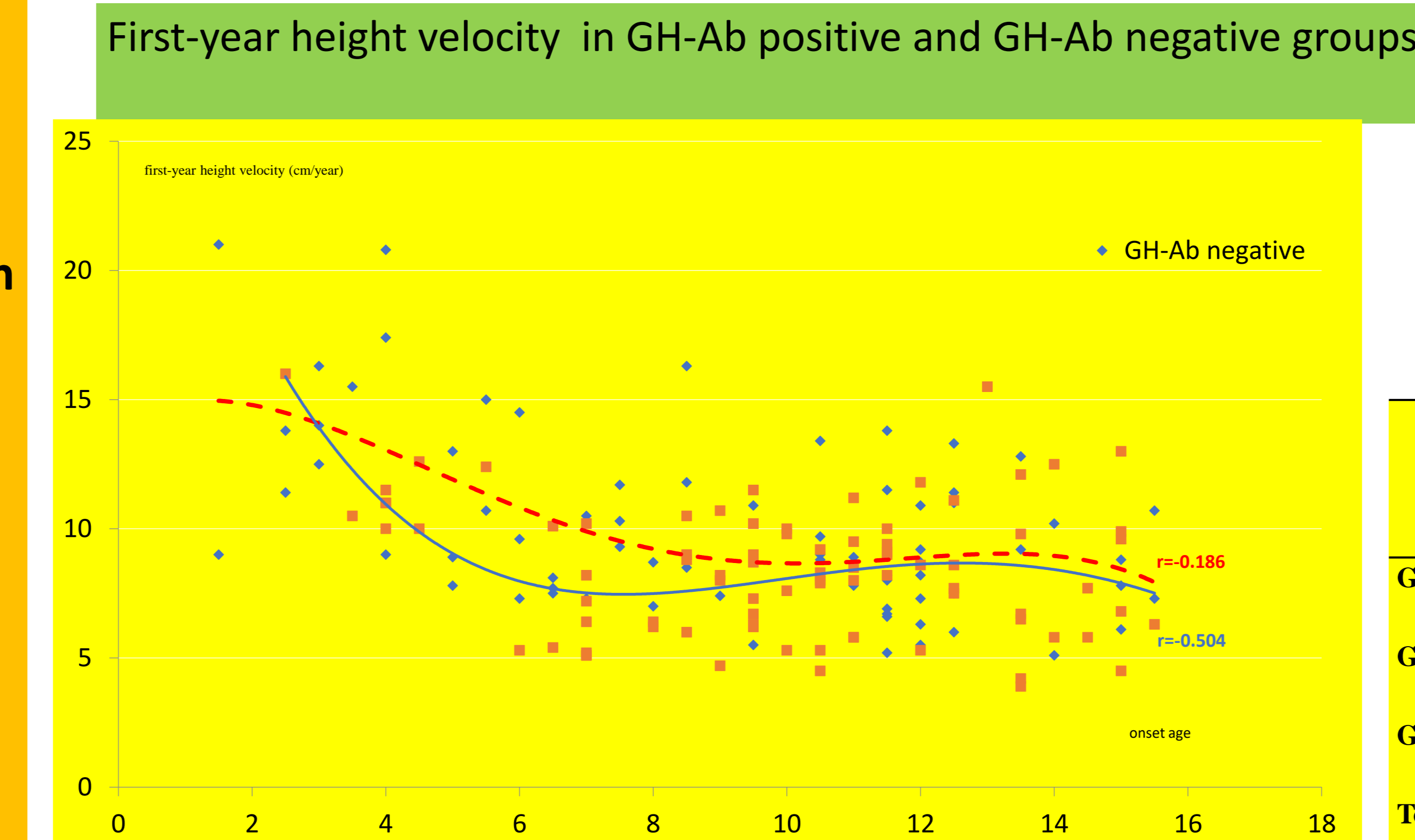
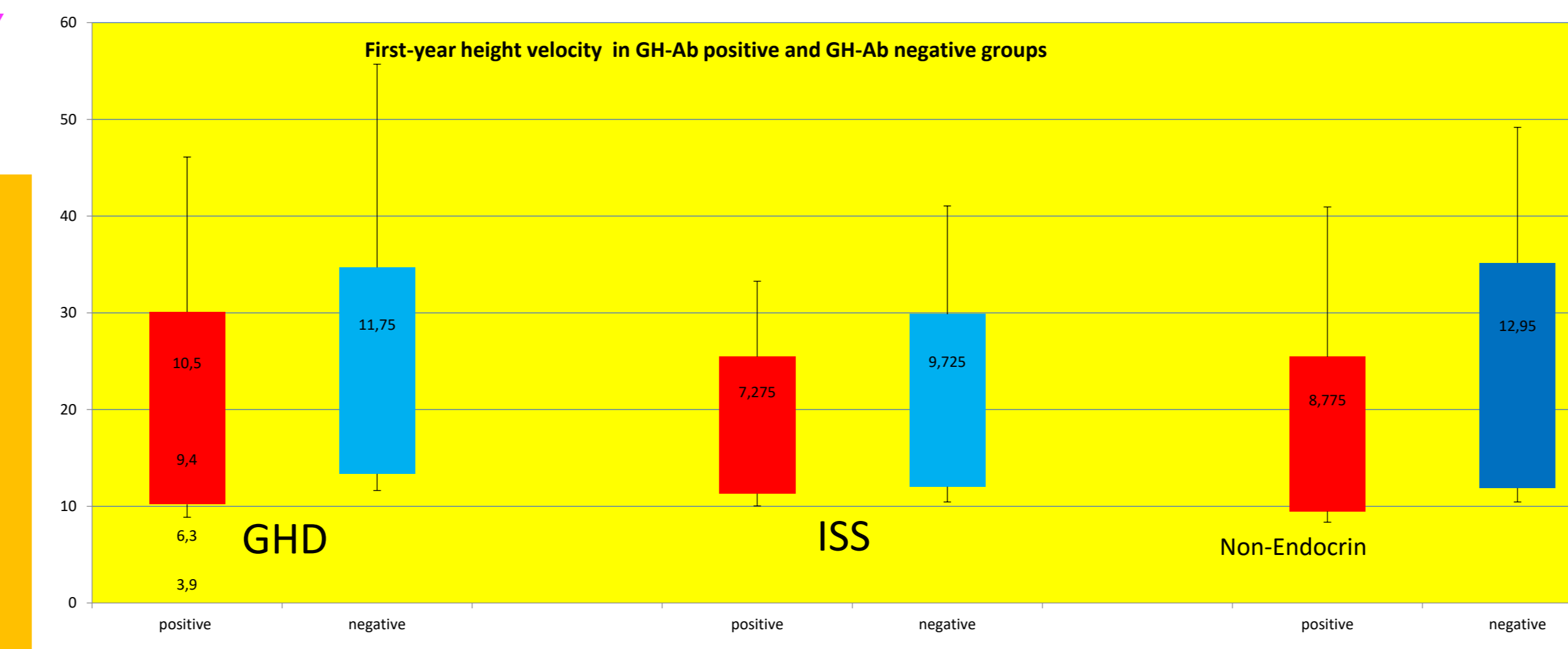
•non-endocrine; 7.75±1.26 vs. 10.12±2.26 cm/year;

first-year height velocity was found to be lower in IgE positive patients (7.01±3.25 vs. 8.93±2.16; p = 0.032).

CONCLUSIONS

•This study showed that GH-Ab formation is common in children with short stature, especially those with ISS, before and during rGH treatment, and also GH-Ab positivity is associated with lower first-year height velocity.

• It also indicates that GH-Abs both could play a role in the etiology of GH-related short stature and that immunogenicity against rGH could have an impact on first-year height velocity.



Comparison of growth-related variables in GH-Ab positive and GH-Ab negative patients

	GHD* (n=111)			ISS (n=37)			NON-ENDOCRIN (n=45)			TOTAL (n=193)			p
	Total N	Positive (n)	%	Total N	Positive (n)	%	Total N	Positive (n)	%	Total N	Positive (n)	%	
Total GH-Ab positivity	111	52	46.8	37	25	67.5	45	26	57.7	193	103	53.3	0.013*
Positivity time													
At onset	14	7	50	3	3	100	7	5	71.4	24	15	62.5	0.868
3 rd month	3	0	0	2	0	0	2	0	0	7	0	0	0.709
6 th month	6	4	66.6	0	0	0	1	1	100	7	5	71.4	0.262
First year	14	8	57.1	1	0	0	5	3	60	20	11	55	0.645
Second year	25	9	36	7	5	71.4	14	6	42.8	46	20	43.4	0.774
Third year	21	11	52.3	13	8	61.5	5	4	80	39	23	58.9	0.301
Fourth year	9	3	33.3	7	5	71.4	5	5	100	21	13	62	0.657
Fiveth and up	19	10	52.6	4	4	100	6	2	33.3	29	16	55	0.743
IgE positivity	38	9	23.7	25	8	32	26	8	30.7	97	25	25.7	0.905

means: SDS: standart deviation score. *GHD: growth hormone deficiency: idiopathic, organic, isolated, multiple. GH-Ab: growth hormone antibody. ISS: idiopathic short stature. Non-endocrin: due to systemic disorders, skeletal dysplasia or Turner syndrome. IGF-1: insulin growth factor-1. IgE: immunoglobulin E. p is significant at <0.05. ANOVA was used to compare between groups.

Comparison of growth-related variables in total IgE positive and IgE negative patients

	IgE positive (n=27)	IgE negative (n=70)	p
GH-Ab (pg/mL)	3453±1861	3287±1992	0.700
GH-Ab positivity (n)	24	59	0.563
Growth velocity (first year)	7.01±3.25	8.93±2.16	0.032*
Total height gain (cm)	19.51±12.45	20.35±14.91	0.606
Total year of treatment	3.24±1.86	3.16±1.59	0.866

means: SDS: standart deviation score. GH-Ab: growth hormone antibody. IGF: insulin growth factor. IgE: immunoglobulin E. p is significant at <0.05. ANOVA and Chi-square tests were used to compare between groups.

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