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Table 1a. Clinical and hormonal characteristics of the children

	SGA Group	GHD Group	PWS Group
Clinical data			
Number of children:	20	61	11
Age (years)	12.27 ± 3.50 (5.9 – 18.9)	12.02 ± 4.09 (1.4 – 18.9)	10.88 ± 5.23 (1.4 – 16.4)
Boys/girls	15/5	41/20	6/5
Weight (SDS)	-0.71 ± 2.52	0.83 ± 2.46	0.83 ± 2.46
Height (SDS)	-1.46 ± 0.87	-0.97 ± 1.16	-0.76 ± 1.53
BMI (SDS)	0.57 ± 2.44	0.58 ± 1.88	1.51 ± 1.86
Biological data			
IGF1/IGFBP3 ratio before rGH	0.14 ± 0.04	0.07 ± 0.01	0.12 ± 0.02
IGF1/IGFBP3 ratio after rGH	0.19 ± 0.07	0.20 ± 0.08	0.19 ± 0.09

Table 1b. Change in IGF1/IGFBP3 molar ratio in control children with age and pubertal stage

Samples, *n*	23	18	15	16	18
Puberty stage				P1	P2-P5
Age (years)	0 - 4	≥ 4 - 8	≥ 8 - 10	9 - 13	11 - 17
Mean IGF1/IGFBP3 molar ratio	0.10	0.12	0.14	0.16	0.27
Standard deviation	0.05	0.03	0.03	0.05	0.06
Range	0.03 – 0.24	0.08 – 0.18	0.10 – 0.21	0.10 – 0.20	0.19 – 0.39

Table 2. Clinical and metabolic characteristics of children on rGH with molar ratios higher or lower than the normal range

	Low Ratio (*n*=41)	Normal Ratio (*n*=33)	High Ratio (*n*=18)	ANOVA		Post hoc ANOVA *P* Values		
				F - Value	*P* Value	Low vs. Normal	Low vs. High	Normal vs. High
Ratio (Post rGH)	0.12 ± 0.02	0.24 ± 0.03	0.32 ± 0.02	467.56	<0.0001	< 0.0001	< 0.0001	< 0.0001
Age (years)	9.92 ± 4.77	12.61 ± 2.85	14.19 ± 2.01	10.00	0.0001	0.0051	0.0004	0.0379
BMI (SDS)	0.41 ± 1.63	0.31 ± 1.01	0.18 ± 1.30	0.16	0.84	0.7661	0.6139	0.7267
Height (SDS)	-0.85 ± 1.10	-0.95 ± 1.41	-1.38 ± 0.99	1.19	0.30	0.7228	0.0933	0.2828
Dose of rGH (µg/kg/ day)	24.99 ± 9.46	28.33 ± 9.82	39.67 ± 17.20	8.82	0.0003	0.1989	0.0002	0.0153
Insulin (mIU/l)	5.47 ± 3.30	5.85 ± 3.15	9.77 ± 4.17	7.25	0.0017	0.7450	0.0011	0.0125
HbA1c (%)	5.33 ± 0.36	5.07 ± 0.28	5.40 ± 0.34	1.87	0.17	0.0976	0.7801	0.1334
Fasting glycemia (mmol/l)	4.72 ± 1.30	4.77 ± 0.25	4.80 ± 0.29	0.03	0.96	0.8974	0.8152	0.7744
Total cholesterol (mmol/l)	4.00 ± 0.64	4.18 ± 1.13	3.60 ± 0.59	1.57	0.22	0.6327	0.1188	0.1296
HDL-cholesterol (mmol/l)	1.63 ± 0.38	1.66 ± 0.56	1.46 ± 0.17	0.65	0.52	0.9131	0.2256	0.3279

8

LDL-cholesterol (mmol/l)	1.96 ± 0.49	2.06 ± 0.75	1.9 ± 0.47	0.19	0.82	0.6973	0.7734	0.5844
Triglycerides (mmol/l)	0.61 ± 0.29	0.73 ± 0.38	0.77 ± 0.30	0.92	0.40	0.3828	0.1715	0.7808

9

Figure 1. Distribution of IGF1/IGFBP3 ratio in the three groups before (a) and after (b) rGH treatment.
SGA: small for gestational age; GHD: growth hormone deficiency; PWS Prader Willi Syndrome
Rectangles represent values between +1 and -1 SDS and bars represent SDS values.
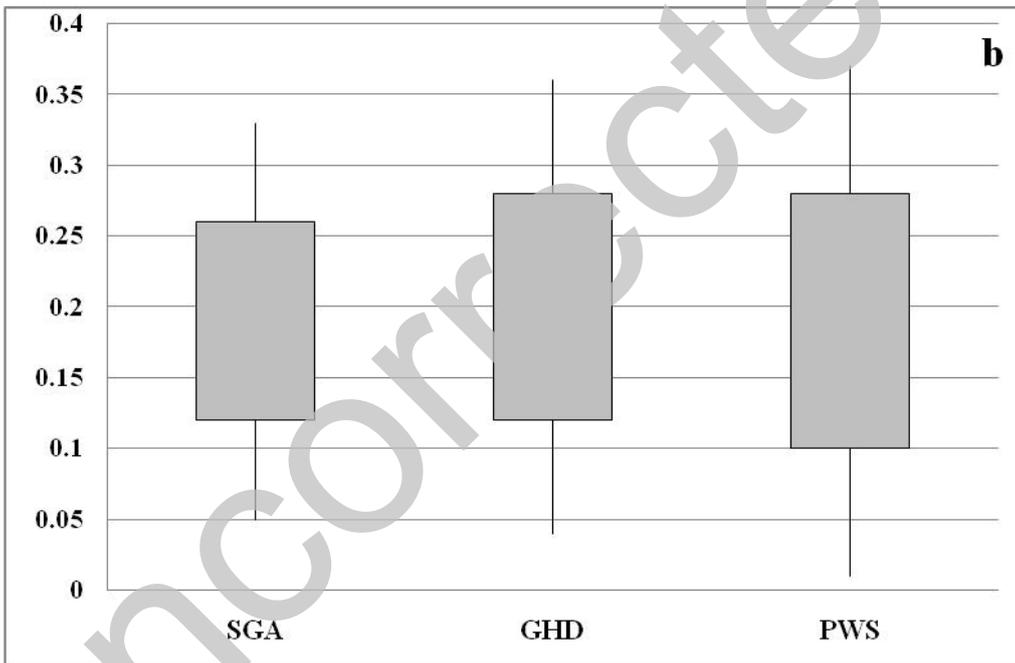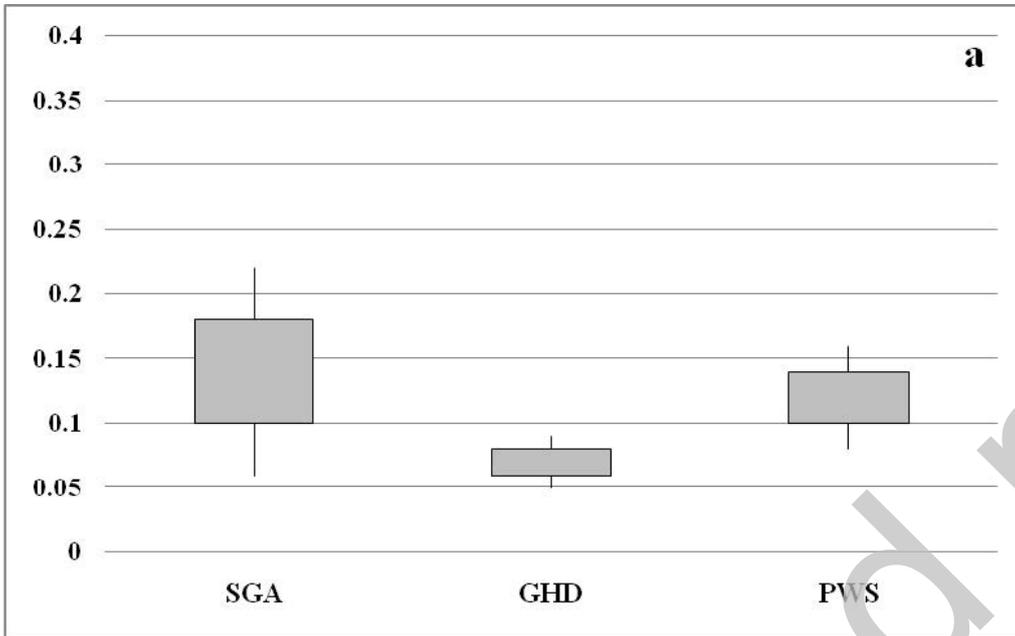
Figure 2. Distribution of IGF1 concentration (a) and IGF1/IGFBP3 molar ratio (b), in SGA children during GH treatment. The IGF 1values have been distributed according to the SDS intervals established by Bidlingmaier et al (10).
In the group SGA group, 2 children had IGF1 concentrations > + 2SDS, but IGF1/IGFBP3 molar ratios in the normal range (arrows).
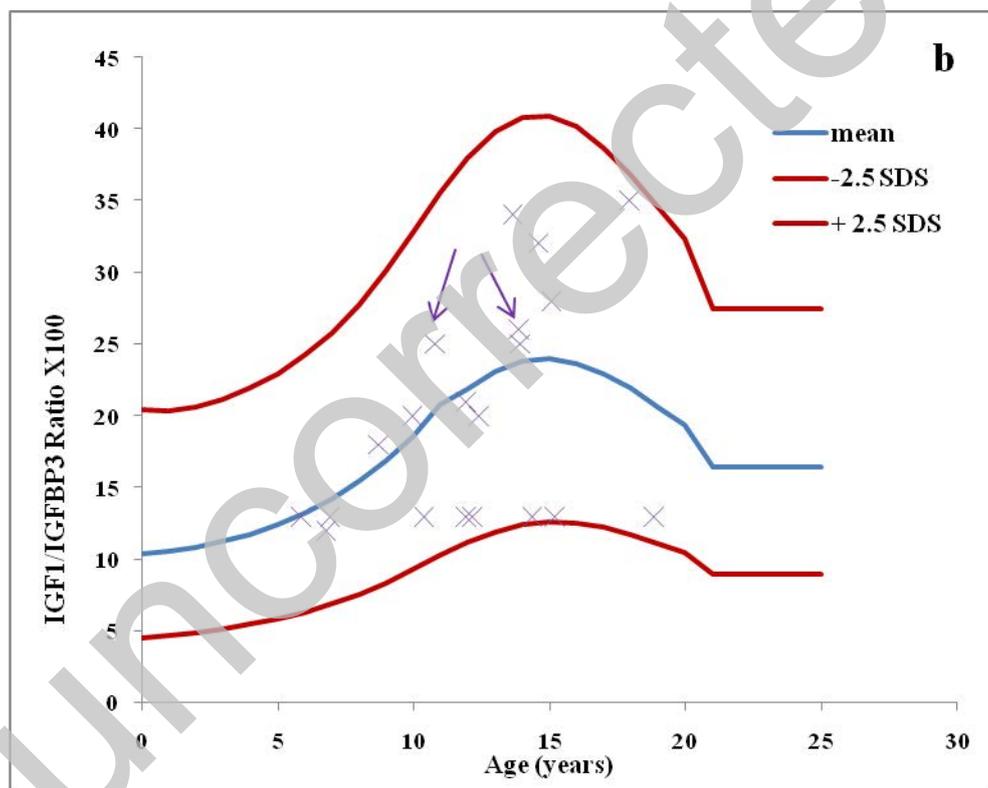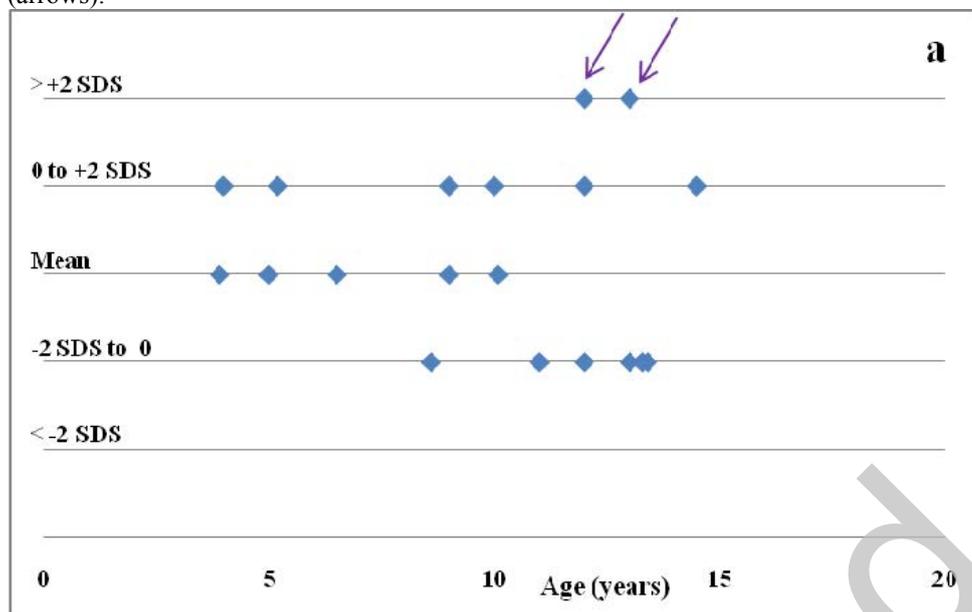
Figure 3. Distribution of IGF1 (a) and IGF1/IGFBP3 molar ratio (b), in children with GHD during GH treatment.
In the group GHD group, 8 children had IGF1 concentrations > + 2SDS (circled cases), but IGF1/IGFBP3 molar ratios in the reference range. Conversely, one five-year-old child had an IGF1 concentrations in the reference range but a very high molar ratio due to a very low IGFBP3 concentration (<-2SDS; arrow).
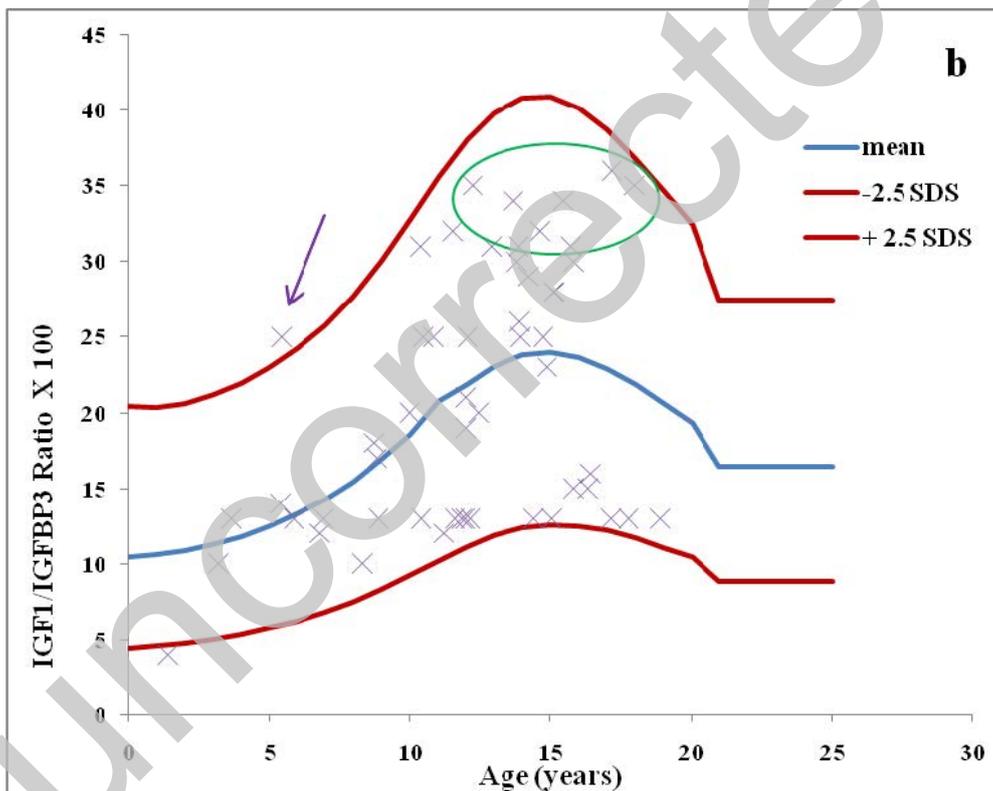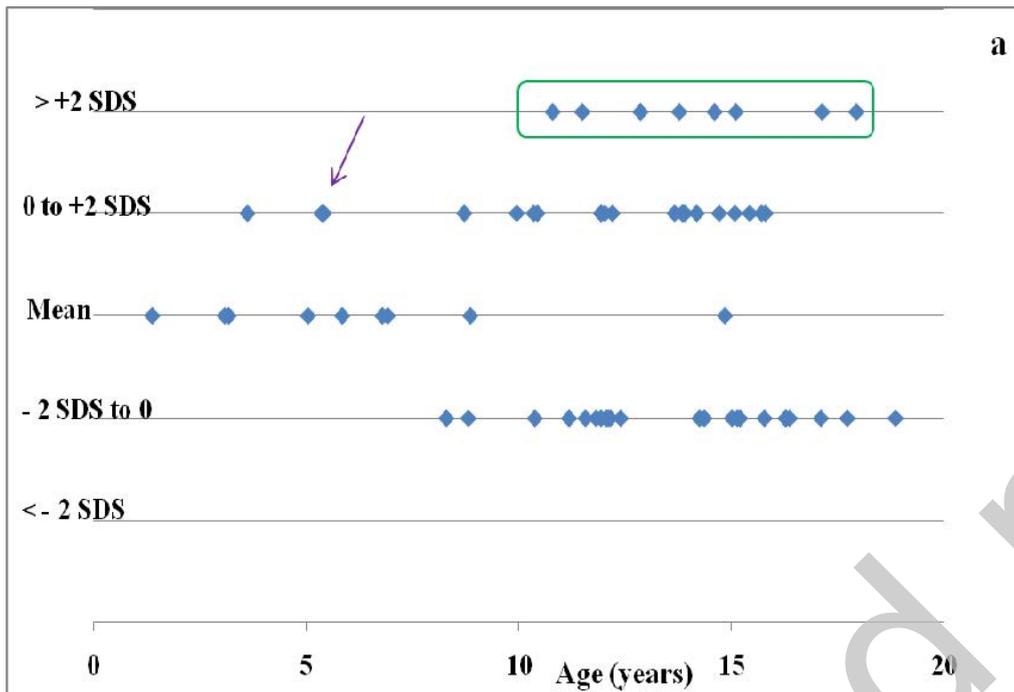
Figure 4. Distribution of IGF1 (a) and IGF1/IGFBP3 molar ratio (b), in children with PWS during GH treatment.
In the PWS group, 3 children had discrepancies between serum IGF1 levels (expressed in SDS) and IGF1/IGFBP3 molar ratio. 1st case (arrow 1): 1.4-year-old child with PWS and an IGF1 concentration in the normal range (expressed in SDS) but a low molar ratio (due to very high IGFBP3 concentration > + 2SDS). 2nd case (arrow 2): 5.4-year-old child with PWS and an IGF1 concentration in the normal range (expressed in SDS) but a high IGF1/IGFBP3 molar ratio (due to low IGFBP3 concentration). 3rd case (arrow 3): 11.4-year-old child with a high IGF1 concentration (expressed in SDS) and an IGF1/IGFBP3 molar ratio in the reference range (IGFBP3 concentration towards the upper end of the reference range).