# IGF-1 serum concentrations and growth in children with Congenital Leptin Deficiency (CLD) before and after replacement therapy with Metreleptin

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## Summary

Most studies show that obese children have normal or increased IGF-1 levels, and it is known that IGF-1 levels decrease under caloric restriction (1). Interestingly, in **8 children** with **congenital leptin deficiency** we found that :

- **IGF-1 serum** levels were **low at baseline** and **increased** during **12 months Metreleptin** substitution despite reduced caloric intake and significant weight loss. IGFBP3 SDS and IGF-1/IGFBP3 ratio SDS also showed an increase under Metreleptin substitution.
- **Height SDS** after **12 months of Metreleptin** substitution was **increased** in **4/5** children **(2-12 yrs).** This age range is the period in which IGF-1 plays a major role in growth.

**Our findings support the hypothesis that leptin, as a signal of the energy status, promotes IGF-1 production and growth in children.**

## Background and Objective

**Leptin** is a key signal of the **body´s energy status** and exhibits pleiotropic effects:

- **Congenital Leptin Deficiency** (CLD) *in humans* results in intense hyperphagia and early-onset severe obesity, along with multiple metabolic, hormonal and immunological abnormalities (2).
- *In vitro* and *animal model* studies suggest that leptin promotes **linear growth** (3).

With the aim to investigate the possible **effect of leptin on growth in humans**, we evaluated **IGF-1** serum levels and **growth before** and **after** 12 months of **leptin replacement** therapy in **children** with **CLD.**

## Patients and Methods

Our **case-series** contains n=8 patients (6 males) with CLD due to defective leptin production (n=5) or bioinactive leptin (n=3). We retrospectively analyzed data regarding:

- **BMI SDS** (4)
- **Height SDS** (5)
- **IGF-1 SDS** (6)
- **IGFBP3 SDS, IGF-1/IGFBP3 molar ratio SDS** (7)

before and after 12 months of leptin replacement therapy (0.024mg/kg Metreleptin LBW/day; Aegerion Pharmaceuticals GmbH).

## Results

**Patients characteristics:**
- N= 8 (6 males)
- Range of age at T0= 0.9-14.8 yrs

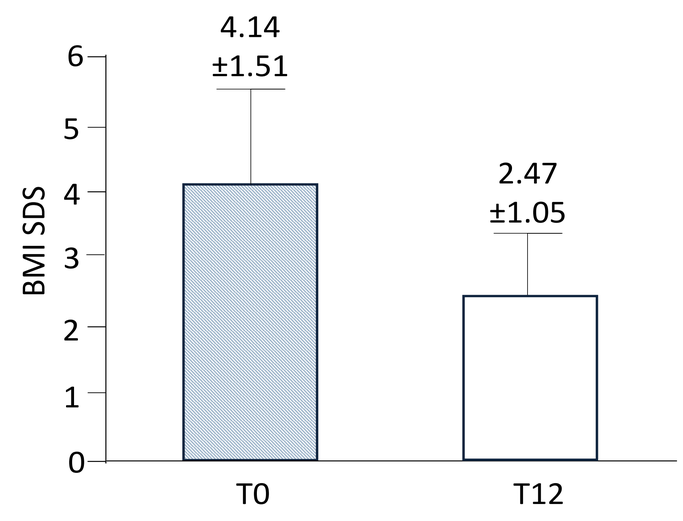


**Fig. 1**: Mean **BMI SDS** before (T0) and after 12 months (T12) of leptin replacement therapy.

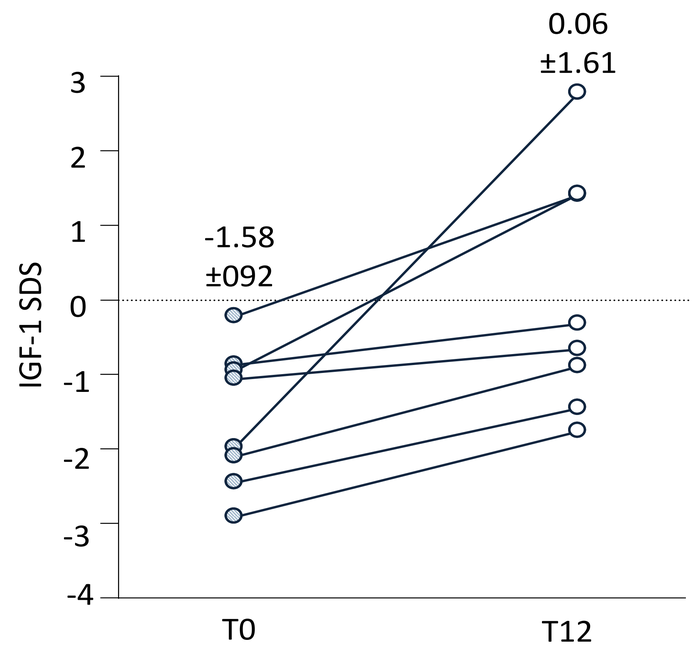


**Fig. 2**: **IGF-1 SDS** before (T0) and after 12 months (T12) of leptin replacement therapy.

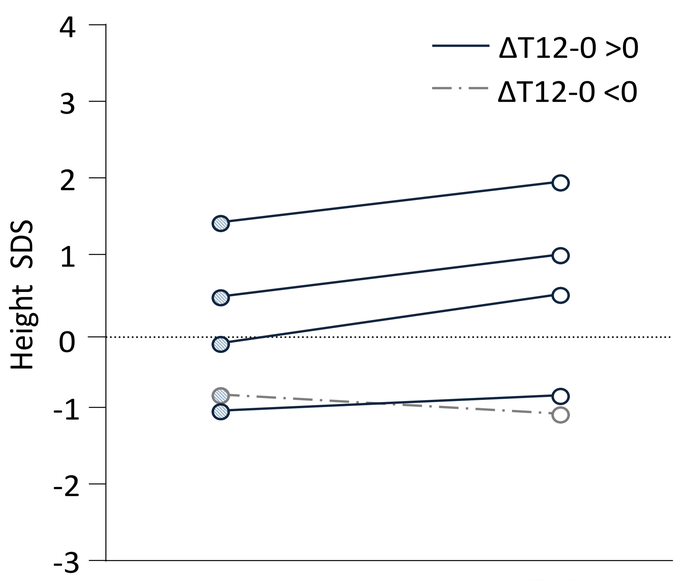


**Fig. 3**: **Height SDS** before (T0) and after 12 months (T12) of leptin replacement therapy in children of *age 2-12 years.*

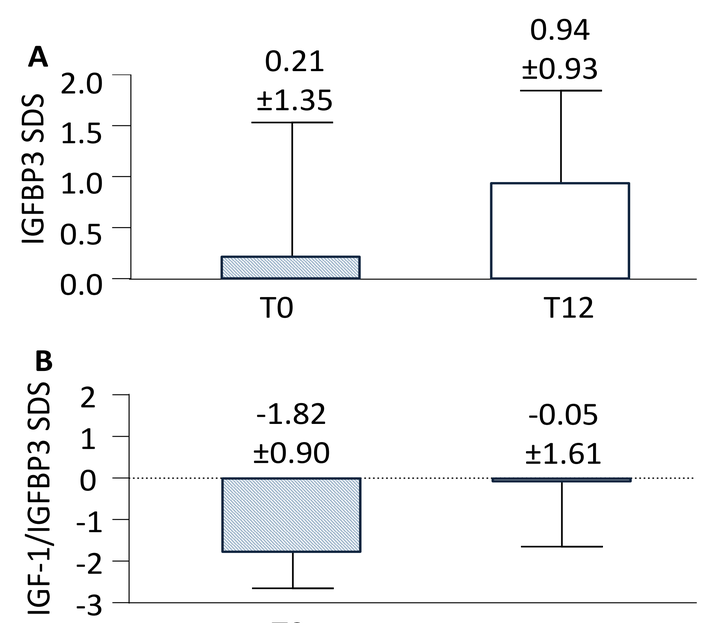


**Fig. 4**: Mean **IGFBP3 SDS** (A) and mean **IGF-1/IGFBP3 molar ratio SDS** (B) before (T0) and after 12 months (T12) of leptin replacement therapy.

## Contact

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