Subclinical Hypothyroidism is Associated with Low IGF-I Levels and Decreased Growth Velocity

Helena Bellini, Lea M. Maciel, Rodrigo J. Custodio, Soraia L.S. Milani, Mariana S. Paula, Sonir R.R. Antonini, Raphael D.R. Liberator Jr., Carlos E. Martinelli Jr. Departments of Pediatrics and Medicine, Ribeirão Preto Medical School-USP, Ribeirão Preto-SP, Brazil. (cemart@fmrp.usp.br)

Background
- Subclinical hypothyroidism (SH) is defined as normal thyroxine levels in the presence of TSH concentrations between 5 and 10 mU/ml.
- Thyroxine seems to regulate IGF-I levels via modulating GH sensitivity.
- However, the role of GH on IGF-I secretion is not so strong in the early years of life, and
- The impact of SH on IGF system and growth of infants remains unknown.

AIM
To evaluate serum IGF-I, IGFBP-3 concentrations and growth velocity (GV) of infants with SH.

Subjects and Methods

Subjects
- 98 children up to 36 months of age were recalled due to a TSH > 5 mU/ml in the neonatal screening test.
- They were divided in two age-groups:
  - Group I (0 – 4 months)
  - Group II (4.1 – 36 months).
- These groups were further split into subgroups according to the TSH level observed during follow-up:
  - Group IA (n=14) and IIA (n=49): TSH ≤ 5 mU/ml,
  - Group IB (n=5) and IIB (n=16): 5< TSH ≤ 10 mU/ml
  - Group IC (n=4) and IIC (n=10): TSH > 10 mU/ml.

Design and Assay
GV-SDS was calculated based on the previous 3 months of follow-up.
IGF-I and IGFBP-3 were determined in the same blood sample as TSH (Immulite 2000, Siemens)

Statistical Analysis
Data were compared by t-test, Mann-Whitney and Fisher tests using the GraphPad Prism 6.0 (GraphPad Software Inc., San Diego, CA).

P ≤ 0.05 was assumed as statistically significant

Results
- IGF-I levels were higher in Group IIA than in IIB and IIC (median: 66; 37 and 30 ng/ml, respectively) (P=0.005) (Figure 1).
- Similar results were observed for GV-SDS (mean ± SEM) with higher values in IIA (0.74 ± 0.3) than in IIB (~0.78 ± 0.4) and IIC (~0.5 ± 0.5) (P=0.03) (Figure 1).
- These findings were even more significant when Group IIA was compared to IIB+IIC (IGF-I: 66 vs. 36 ng/ml, P=0.001) (GV: 0.74 ± 0.3 vs. ~0.67±0.3, P=0.004).
- No difference was found on IGFBP-3 levels comparing groups IA, IIB and IIC.
- No difference was observed comparing group IA, IB, and IC regarding IGF-I, IGFBP-3 levels or GV, even when group IA was compared to combined IB+IC (Figure 2).

Conclusion:
- Reduced serum IGF-I levels and GV were observed in children aged 4–36 months with SH. This was not found earlier in life.
- These findings may reflect a direct action of thyroid hormones on IGF-I secretion rather than a modulation of GH action, as no changes were found on IGFBP-3 levels.
- The real impact on height would demand a longer period of observation.