Do insulin like growth factors also influence growth in children with congenital hypothyroidism: a cohort analysis

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BACKGROUND
• Thyroid & GH- insulin like growth factors (IGF) axis together are critical for somatic & skeletal growth. Hypothyroidism & derangement in this axis leads to profound growth retardation & delayed skeletal maturation.
• Limited studies suggest that thyroxine directly regulate IGF-1 independent of GH.

OBJECTIVE
To evaluate levels of insulin like growth factors (IGF) in children with congenital hypothyroidism and their role on growth parameters.

MATERIALS AND METHODS
➢ Approved by ethical committee of institute and consent taken
➢ Study design- Cross sectional
➢ Thirteen children with congenital hypothyroidism 1month- 15 years old recruited. Those with underlying GH deficiency and/or deranged liver functions were excluded.
➢ Height, weight, weight for height or body mass index recorded & interpreted on WHO growth charts for <5 year old & on New IAP growth charts for ≥5 years.
➢ Estimation of thyroid profile done by electro-chemiluminiscence and IGF-1, IGF binding protein-3 (IGFBP-3) by enzyme linked immunoassay (ELISA).

RESULTS
• Mean age of diagnosis- 1.65 ± 1.62 years with a range of 25 days to 4 years.
• Mean age of recruitment in the study- 7.76 ± 3.6 years
• Mean weight- 21.46 ± 9.41 kgs (-0.58SD), only 4/13 (30.7%) were underweight
• Mean height- 112.68 ± 22.11 cms (-2.15SD), 7/13 (53.8%) were stunted
• BMI (kg/m²)- 16.15 ± 2.43 (+0.26SD)- 11/13 (84.6%) had normal BMI
• Significant positive correlation observed between serum TSH and BMI (r= 0.538, p= 0.004)
• No significant correlation between TSH & height (r=0.07, p>0.05)

BIOCHEMICAL PARAMETERS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
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<tbody>
<tr>
<td>TSH (0.7-6.4 μIU/ml)</td>
<td>12.91±18.05</td>
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<tr>
<td>T4 (4.6-12 μg/dl)</td>
<td>5.36±4.72</td>
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<tr>
<td>T3 (2.3-4.2 pg/ml)</td>
<td>2.73±1.48</td>
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<td>IGF 1 (ng/ml)</td>
<td>103.34±81.38*</td>
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<tr>
<td>IGF3 (ng/ml)</td>
<td>2260.6±1594.2*</td>
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*Mean IGF-1 and IGFBP-3 was significantly low (<0.05) as compared to healthy reference population.

CORRELATION OF THYROID PROFILE WITH INSULIN LIKE GROWTH FACTORS:

- TSH & IGF-1
  \( r = -0.35, p>0.05 \)
- T3 & IGF-1
  \( r = 0.66, p<0.014 \)
- T4 & IGF-1
  \( r = 0.56, p<0.045 \)

Hence significant correlation observed between T3, T4 and insulin like growth factors.

On plotting ROC curve: IGF-1 cut off value of 93.2 ng/ml has a sensitivity of 85.7 % and specificity of 66.7% in predicting stunting (height <-2SD) in our cohort study (AUC=0.679)

REFERENCES
1. Inuikai T et al. Horm Metab Res,1999
5. Parandura A et al J Pediatr Endocrinol Metab. 2003

CONCLUSION:
➢ 53.8% children were stunted with overall mean height of the cohort at -2.1SD. Though their mean TSH was only mildly increased with normal serum T3, T4.
➢ Mean IGF-1, IGFBP-3 were significantly low as compared to age & sex matched normal population.
➢ Children with stunting had low levels of serum insulin like growth factors.
➢ Growth retardation observed seems to be attributed significantly to reduced levels of insulin like growth factors.

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