Establishment of reference ranges for thyrotropin, thyroxine, free thyroxine, triiodothyronine and T-uptake in neonates and infants
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Background: Pediatric healthcare is critically dependent on the availability of accurate and precise reference intervals to allow appropriate clinical interpretation.

Objective and hypotheses: To obtain reference intervals for TSH, T4, FT4, T3 and T-Uptake in a pediatric population from Córdoba, Argentina.

Methods: Serum samples of 807 healthy neonates and infants (age range 2 to 365 days) were analyzed using electrochemiluminescent immunoassay (cobas e601).

Results: No significant differences were observed between the sexes. The percentile 2.5th, 50th and 97.5th were calculated for all reference groups. The TSH, T4, FT4, T3 and T-Uptake levels are shown in Table 1.

<table>
<thead>
<tr>
<th>TSH (uIU/mL)</th>
<th>T4 (ug/dL)</th>
<th>FT4 (ng/dL)</th>
<th>T3 (ng/dL)</th>
<th>T-Uptake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days</td>
<td>n</td>
<td>2.5th - 50th</td>
<td>2.5th - 97.5th</td>
<td>2.5th - 50th</td>
</tr>
<tr>
<td>2-14</td>
<td>77</td>
<td>0.80 - 5.29</td>
<td>7.4 - 19.1</td>
<td>1.3 - 2.9</td>
</tr>
<tr>
<td>15-29</td>
<td>58</td>
<td>1.15 - 7.61</td>
<td>7.3 - 16.4</td>
<td>1.1 - 2.0</td>
</tr>
<tr>
<td>30-88</td>
<td>419</td>
<td>0.85 - 7.79</td>
<td>7.3 - 17.7</td>
<td>1.0 - 2.1</td>
</tr>
<tr>
<td>90-366</td>
<td>213</td>
<td>0.80 - 7.77</td>
<td>7.1 - 17.0</td>
<td>0.9 - 2.1</td>
</tr>
</tbody>
</table>

Conclusions: We report pediatric reference intervals for TSH, T4, FT4, T3 and T-Uptake. It should assist pediatricians in interpreting these hormonal results more accurately and thereby lead to improve diagnosis of childhood thyroid diseases. Our results reveal that physiological behavior of TSH, T4 and FT4 levels is similar in the first 4 age groups, showing a tendency to decrease at one year of life, whereas T3 values are slightly higher than in the neonatal period and remain high. This behavior can be the result of different mechanisms, including an increased tissue activity of type I deiodinase and the “reset” of the hypothalamic hypothalamic “set point” for the control of TSH.

Familial non-autoimmune hyperthyroidism: activating mutation of thyrotropin receptor gene discovered after three generations of a family
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Background: Familial Non-autoimmune hyperthyroidism (FNAH) is a rare aetiology for congenital hyperthyroidism due to activating mutation of thyrotropin receptor (TSHR). Recommended treatment is total ablation of thyroid tissue by total thyroidectomy followed by radiodine administration.

Objective and hypotheses: To describe a family with three generations of members affected by this condition. Index case was a Chinese girl who had been having hyperthyroidism since seven years old and was treated as Graves’ disease. Her course of illness was prolonged and difficult to be controlled with anti-thyroid medication. Her mother also suffered from hyperthyroidism and had undergone two thyroid surgeries. The patient delivered a newborn girl at the age of twenty, who was hyperthyroid since birth and remained so by fifteen months old. Thyroid receptor antibody was found to be negative for the patient and her daughter, and subsequently their blood samples were sent to investigate for mutation in TSHR gene.

Methods: DNA were isolated from peripheral blood lymphocytes and all TSHR coding exons were amplified, purified and sent for direct DNA sequencing.

Results: The index case and her daughter were heterozygous for p.L629F (TGT→TCT) activating mutation in TSHR gene.

Conclusions: Diagnosis of FNAH can sometimes be as difficult as similar familial predisposition can also be found in autoimmune hyperthyroidism. Genetic confirmation is important to predict outcome and provide most appropriate treatment.

Clinical utility of thyroid scans in mild neonatal hyperthyrotoeinemia
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Background: Mild neonatal hyperthyrotoeinemia (MNH) is characterized by an abnormal newborn screen (NBS), followed by mildly elevated TSH and normal FT4 on confirmatory tests. The literature on MNH is sparse, and no studies have assessed the prognostic value of thyroid scintigraphy in infants with MNH.

Objective and hypotheses: To evaluate the utility of information provided by thyroid scintigraphy for management of infants with MNH.

Methods: Retrospective study of infants with MNH between 2000-2011. MNH was defined as abnormal NBS followed by TSH between 5-30 mIU/L and normal FT4 on confirmatory scans. We assessed the clinical course of infants with MNH according the etiology determined by Te-99m scan. Scan data and clinical course of infants with classic congenital hyperthyroidism (CH) were analyzed in parallel.

Results: We identified 69 infants (52% boys) with MNH and 164 infants (34% boys) with classic CH. Te-99m scan results were divided into four subgroups as follows: no uptake in 7% of MNH vs 24% of classic CH (p<0.01), decreased uptake/normal uptake in 39% vs 46% (p=NS), increased uptake in 35% vs 26% (p=NS), and normal uptake in 70% vs 4% of infants (p<0.01). Among the MNH patients, neither NBS TSH, confirmatory TSH and FT4, mean LT-4 treatment doses, number of dose escalations, nor post-treatment FT4 and TSH differed among the 4 Te-99m subgroups. In contrast, the clinical features in classic CH differed, as expected, among the subgroups. Among MNH infants, who reached 3 years of age, trial-off treatment was successful in 6 of 11 (55%) with no difference in success rates among the Te-99m subgroups.

Conclusions: Clinical data did not differ among Te-99m-defined etiologies in MNH, and scintigraphy did not predict success of trials off therapy. The clinical utility of information provided by Te-99m scan during the evaluation of MNH is low; therefore, obtaining these scans in MNH infants may not be an effective use of healthcare resources.

Familial papillary thyroid carcinoma: description of 4 paediatric cases
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Introduction: Familial papillary thyroid carcinoma (FPTC) represents 5% of all Papillary Thyroid Carcinomas and is clinically defined by 2 or more first degree relatives with the tumor, without components of any genetic syndrome. Its inheritance is autosomal dominant with incomplete penetrance.

Objective: To describe 4 index cases, their clinical features and variable expressivity.

Cases:
1. Girl with autoimmune thyroiditis, FPTC in maternal family: 1 cousin, 1 aunt and grandfather. At 10y was diagnosed with focal PTC. No local, vascular or lymph node invasion. No recurrence at 1 year follow up.
2. Healthy girl, mother with PTC; at 13y was diagnosed with bilateral PTC, diffuse sclerotic variety. She had local, vascular and lymph node invasion. The cancer recurred in 9 months of follow up.
3. Girl with autoimmune thyroiditis. 2 cousins (mother’s family) with PTC. At 13y was diagnosed with multinodular PTC with local invasion. 4 years of follow up, without recurrence.