Objective

To assess the incidence of CH in Lombardia region and the percentage of patients identified by the 2nd NBS. To describe the clinical features and evolution of CH patients detected by the 2nd NBS.

Methods

The 1st NBS (cut-off blood-TSH>10mU/L) was performed at 2–5 days in all neonates born in Lombardia region. The 2nd NBS (cut-off blood-TSH>5mU/L) was performed in selected cases: prematurity, weight<2000g, malformations/syndromes, admission in NICU, twins, steroid treatment, maternal thyroid disease, borderline 1st NBS and associated risk factors.

Clinical data at diagnosis and reevaluation of patients detected by the 2nd NBS (period 2007-2014) and followed-up at a single tertiary centre for pediatric endocrinology were collected. At 2–3 years, patients with gland in situ (GIS) underwent reevaluation and were classified as permanent CH (s-TSH>10 mU/L), persistent hyperthyrotropinemia (HT) (s-TSH 5–10 mU/L), and transient CH (s-TSH<5 mU/L).

Results

Incidence of CH

767,157 neonates born in Lombardia between 2007-2014

842 patients affected by CH (1:911), detected by the NBS

273 patients detected by the 2nd NBS (32.4% of CH)

101 patients followed-up at San Raffaele Hospital (96 GIS, 5 dysgenesis)

Clinical features

Prematurity

- Preterm: 39%
- At term: 61%

Malformations

- No malformations: 84%
- 16%

Type of malformation

- Heart: 22%
- Genito-urinary tract: 6%
- Skin: 28%
- Digestive tract: 28%
- Central nervous system: 11%
- Hands / feet: 5%

CH severity at diagnosis

- Severe CH: 21%
- Moderate CH: 13%
- Mild CH: 40%
- Normal FT4: 26%

Patients with thyroid dysgenesis

<table>
<thead>
<tr>
<th>1st... 2nd b-TSH</th>
<th>Sieric TSH and FT4 at diagnosis</th>
<th>Age at start of therapy</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 6,83...8,93 mU/L</td>
<td>TSH 22,9 mU/L FT4 1,1 ng/dl</td>
<td>26 days</td>
<td>Thyroid ectopy</td>
</tr>
<tr>
<td>2 8,27..37,24 mU/L</td>
<td>TSH 110 mU/L FT4 0,43 ng/dl</td>
<td>20 days</td>
<td>Thyroid hemiagenesis</td>
</tr>
<tr>
<td>3 9,33...13,36 mU/L</td>
<td>TSH 18,2 mU/L FT4 1,1 ng/dl</td>
<td>31 days</td>
<td>Dysmorphic thyroid tissue</td>
</tr>
<tr>
<td>4 4,10..17,25 mU/L</td>
<td>TSH 138,5 mU/L FT4 1,09 ng/dl</td>
<td>29 days</td>
<td>Thyroid hemiagenesis</td>
</tr>
<tr>
<td>5 5,33...5,16 mU/L</td>
<td>TSH 22,9 mU/L FT4 1 ng/dl</td>
<td>28 days</td>
<td>Thyroid hemiagenesis</td>
</tr>
</tbody>
</table>

Diagnostic reevaluation of patients with GIS

- Permanent CH: 15%
- Persistent HT: 30%
- Transient CH: 55%

Genetic analysis

- 96 patients with GIS
- 23 genetic analysis
- 12 patients showed pathogenetic variants:
  - 9 patients: DUOX2
  - 2 patients: TSHR
  - 1 patient: PAX8

Conclusions

- Between 2007 and 2014 the incidence of CH confirmed at birth in Lombardia region was 1:911 (permanent and transient).
- In the absence of the 2nd NBS the incidence would have been 1:1348; 32.4% of patients were detected by the 2nd NBS.
- In our cohort, preterm infants were 39%, indicating that other risk factors can contribute to delayed TSH elevation.
- The frequency of malformations was higher than expected.
- Although the majority of patients identified by the 2nd NBS had transient CH and HT, the 2nd NBS allowed the identification of severe cases of CH, cases of thyroid dysgenesis, and cases of CH caused by genetic variants.