Prospective evaluation of autoimmune and non-autoimmune subclinical hypothyroidism in a large cohort of children and adolescents with Down Syndrome

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OBJECTIVES

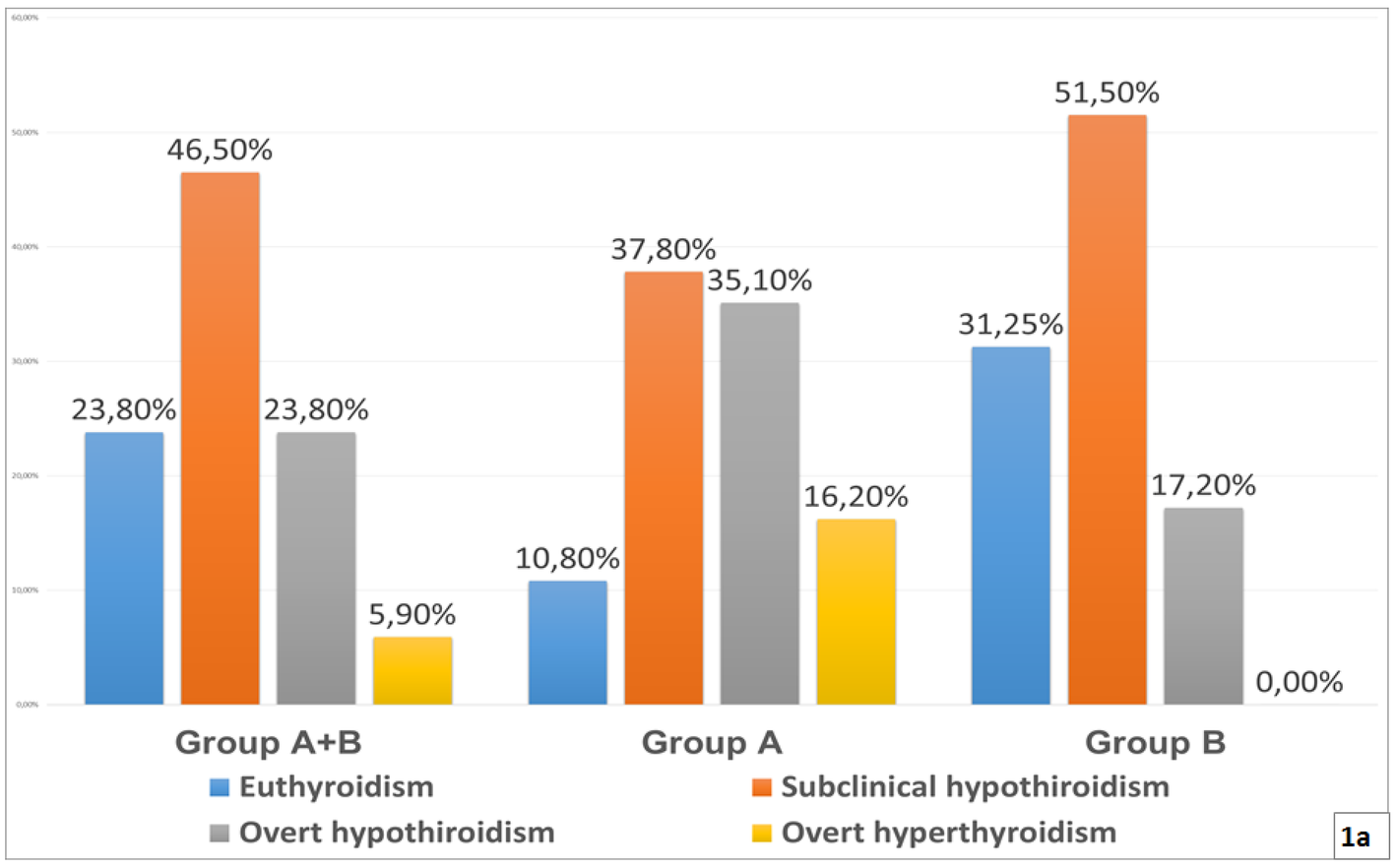
Subclinical hypothyroidism (SH) is the most common thyroid abnormality in Down Syndrome (DS) children (25-60%); its etiology remains still not completely clarified. Aim of this prospective multicenter study was to evaluate prevalence and natural course of autoimmune and non-autoimmune SH in a large cohort of DS children and adolescents.

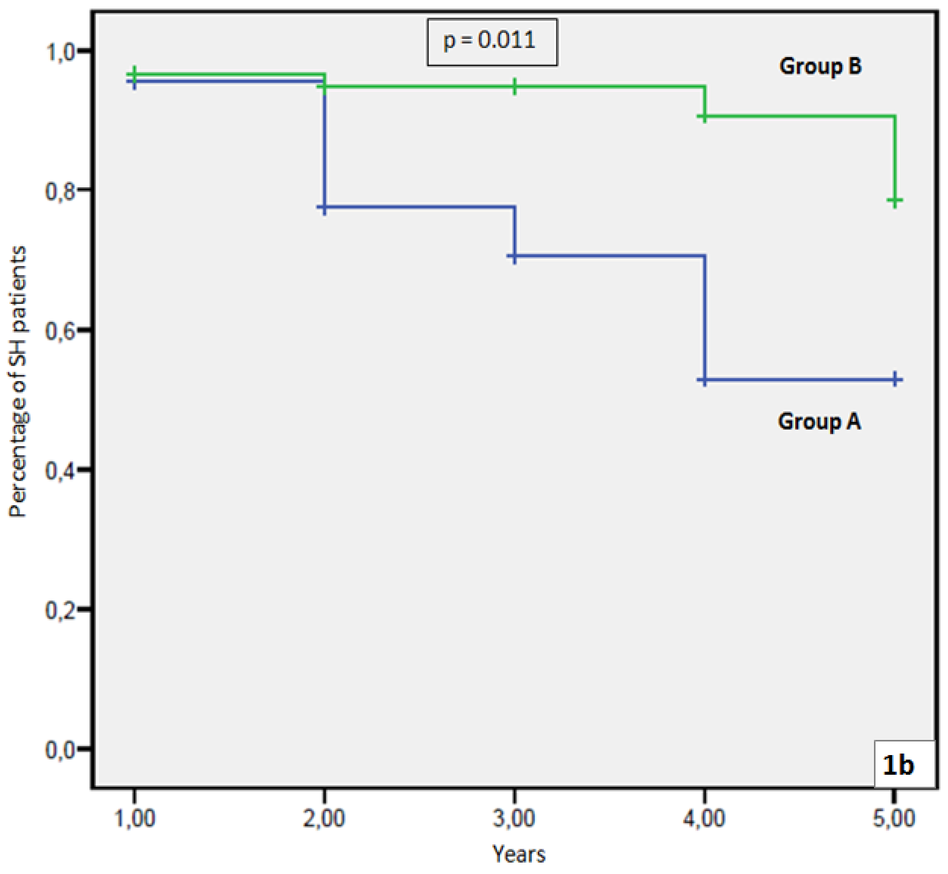
METHODS

The study population included 101 DS patients with SH (TSH 5-10 mIU/L; FT4 12–22 pmol/L), aged 2-17 years at SH diagnosis. DS children with congenital hypothyroidism or early onset isolated hyperthyrotropinemia were excluded. Annual monitoring of TSH, FT4, BMI and height was performed for 5 years. Thyroglobulin autoantibodies (TGAbs) and thyroid-peroxidase autoantibodies (TPOAbs) were tested at diagnosis and at the end of follow-up.

RESULTS

- **37/101 (36.6%)** patients displayed autoantibodies positivity (**group A**); the remaining **64 (63.4%)** were classified **as non-autoimmune SH** (group B), (p=0.0001).
- Group A was characterized by higher median age at SH diagnosis and by more frequent family history of thyroid disease (6.6 vs 4.7 years, p=0.001; 32.4% vs 7.8%, p=0.001 respectively), whereas congenital heart defects were more common in group B (65.6% vs 43.2%, p=0.028).
- Gender, median BMI (SDS), height (SDS), FT4 and TSH were similar between the two groups.
- At the end of follow-up: 35.1% of **group A** patients developed an **overt hypothyroidism** (OH) vs 17.2% of group B (p=0.041); 31.25% of **group B** vs 10.8% of group A became biochemically **euthyroid** (p=0.02); 37.8% of group A vs 51.5% of group B maintained, over time, SH condition (p=0.183). Overt hyperthyroidism was only observed in group A (16.2%, p=0.004).
  Logistic regression suggested autoimmunity (OR=3.2) and baseline TSH values (OR=1.13) as predictive factors of evolution from SH to OH.





Outcome of subclinical hypothyroidism at the end of 5-year follow-up (**figure 1a**); Kaplan-Meier curves showing that the progression from subclnical hypothyroidism to overt hypothyroidism was significantly more frequent in group A than in group B (**figure 1b**).

CONCLUSIONS

- In DS children, **non-autoimmune SH** showed higher prevalence and earlier onset.
- The risk of thyroid function deterioration over time, from SH to OH, seems to be influenced by **autoimmune etiology** and **higher baseline TSH values.**