The role of early thyroid imaging in infants with congenital hypothyroidism

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Introduction

Congenital hypothyroidism (CH), occurs in 1:3000 to 1:4000 newborns. Most of the cases are sporadic caused by thyroid dysgenesis or dyshormonogenesis and typically require lifetime therapy. However, some of the children diagnosed with CH will have a transient form of the disease. Most of newborns with CH are detected by the routine newborn screening programs and treatment is promptly initiated following confirmatory measurements of serum thyroid stimulating (TSH) and free T4 (FT4) levels. Imaging of the thyroid gland is considered to be essential in determining the underlying etiology of CH. Radioisotope scintigraphy and ultrasonography are the most widespread and readily available imaging modalities. Both are not perfect and have diagnostic pitfalls as well as clinical drawbacks. Despite these limitations and the fact that imaging of the gland does not influence the treatment decision or initial dose, it is universally recommended at diagnosis as it may distinguish between permanent and transient CH.

Objectives

- **To assess the role of early thyroid imaging in the diagnosis and management of CH.**
- **To detect early clinical and laboratory factors that will enable a more selective approach for thyroid imaging**

Methods

Design
Retrospective study

Setting
Institute for Endocrinology and Diabetes, Schneider Children's Medical Center of Israel (SCMCI)

Patients
- **Diagnosed with CH at SCMCI between the years 2000-2012**
- **Born at term**
- **Followed for at least 3 years**
- **Underwent thyroid imaging**

Excluded from the study
- **Patients with major congenital malformation or genetic abnormalities**
- **Treatment with medications that may interfere with thyroid functions**

Data collected
- **Pregnancy and perinatal history; maternal hypothyroidism or treatment with L-thyroxin during pregnancy**
- **Anthropometric measurements obtained at diagnosis, 1, 3, 6, 9,12 and 24 months**
- **L-thyroxin treatment dose calculated as mcg/kg/day obtained at diagnosis, 1, 3, 6, 9,12 and 24 months**

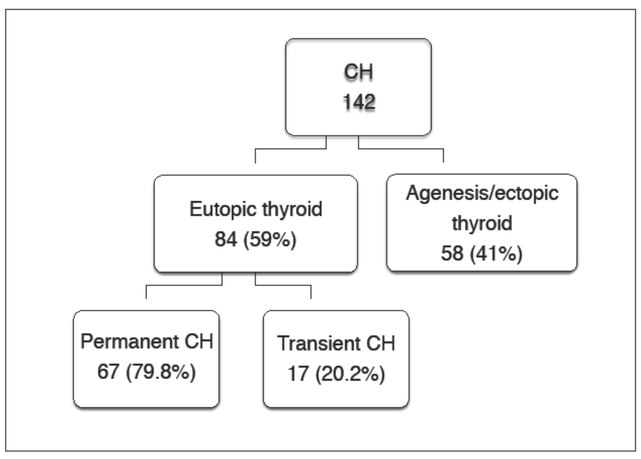
Imaging studies (thyroid scan and/or thyroid sonography) findings:
- **Normal sized and positioned gland with normal radioisotope uptake**
- **Normal gland with increased radioisotope uptake**
- **Agenesis of gland**
- **Ectopic gland**
- **Hypoplastic gland**

Infants were categorized into 3 groups:
- **Thyroid dysgenesis - infants with agenesis/ectopic thyroid and permanent CH**
- **Eutopic-permanent - infants with normal sized or hypoplastic thyroid gland and permanent CH**
- **Eutopic-transient - infants with normal sized or hypoplastic thyroid gland and transient CH.**

Statistical analysis
Data are expressed as mean ± SD, or as percentages. The two-tailed $\chi 2$ test and Fisher exact test were used to compare categorical variables. The t-test was used to compare numerical variables. Continuous variables were compared using ANOVA. A multivariate forward stepwise logistic regression model was used to detect variables predicting the overall outcome at diagnosis and through disease progression. The efficiency of each of the parameters detected to serve as a biomarker was determined using the receiver operating characteristic (ROC) analysis with 95% confidence interval. The optimal cut-offs of each parameter were calculated using the Youden index . For all tests a P value <0.05 was considered significant

Results

The study cohort



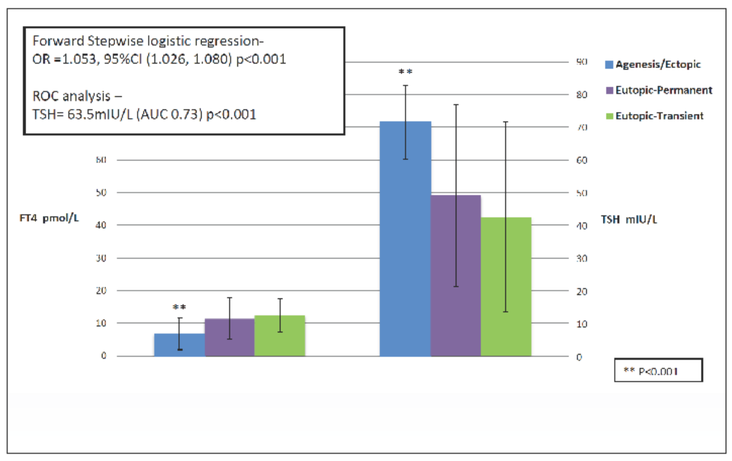
Overall transient 17/142-11.9%

Average age of L-thyroxine treatment discontinuation (years)-2.3±1.5

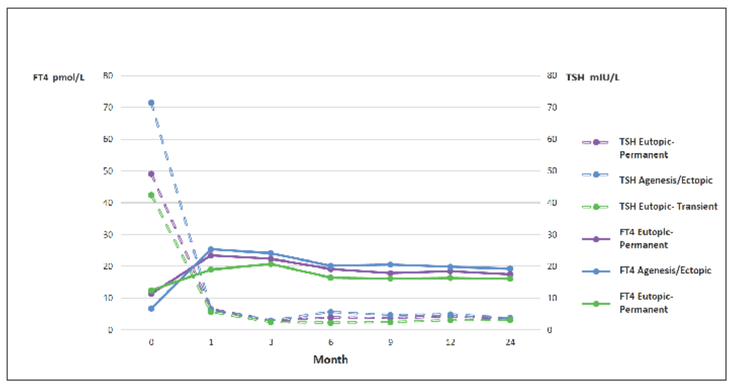
Clinical and perinatal characteristics of the study cohort

	Thyroid dysgenesis N=58	Eutopic Permanent N=67	Eutopic Transient N=17	P
Gender				
Male, n (%)	15 (25.8)	31 (46.3)	10 (58.8)	0.015
Pregnancy				
Singleton, n (%)	54 (93.1)	64 (95.5)	15 (88.2)	0.193
Twin/triplets, n (%)	1 (1.7)	3 (4.5)	2 (11.8)	
Uncomplicated, n (%)	54 (93.1)	55 (82.1)	14 (82.4)	0.17
High-risk pregnancy, n (%)	4 (6.9)	12 (17.9)	3 (17.6)	
Birth parameters				
Birth weight, kg mean±SD	3.3±0.5	3.0±0.6	2.9±0.6	0.1
AGA, n (%)	54 (93.1)	62 (92.5)	16 (94.1)	
SGA, n (%)	1 (1.7)	2 (3.0)	1 (5.9)	0.796
LGA, n (%)	3 (5.2)	3 (4.5)	0 (0.0)	
Perinatal history				
Normal, n (%)	52 (89.7)	53 (79.1)	13 (76.5)	0.358
Complicated, n (%)	6 (10.3)	14 (20.9)	4 (23.5)	
Maternal hypothyroidism, n(%)	4 (6.9)	13 (19.4)	3 (17.6)	0.869
At diagnosis				
Age, days median (IQR)	10 (7,19)	13(9,17)	10 (7,19)	0.730
Weight, kg mean±SD	3.48±0.62	3.25±0.63	3.24±0.48	0.926

TSH & FT4 at diagnosis

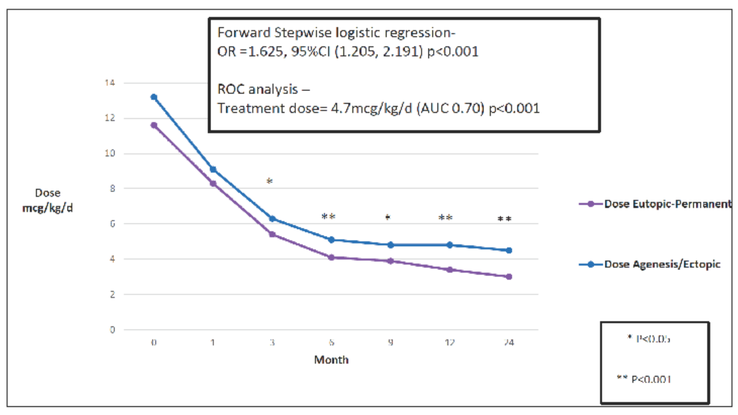


TSH & FT4 levels during follow-up

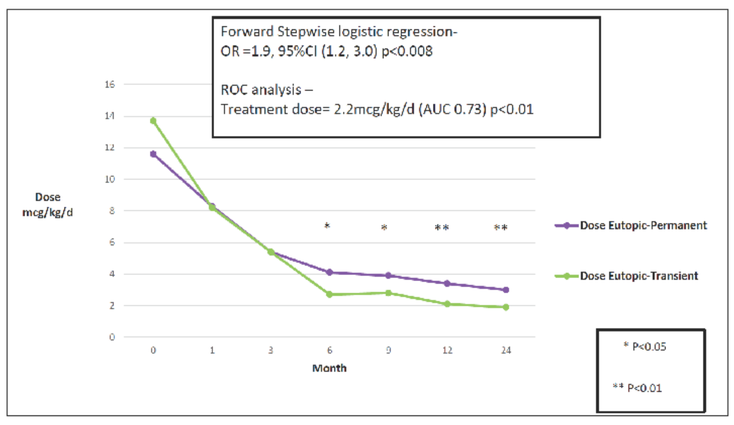


Results

LT4 dose Eutopic-Permanent vs. Agenesis/Ectopic



LT4 dose Eutopic-Permanent vs. Eutopic-Transient



Summary & Conclusions

Transient and permanent CH are distinct in TSH levels at diagnosis and thyroxin requirements throughout follow-up.

Early thyroid imaging does not distinguish between permanent and transient CH.

Imaging can be postponed and preformed according to clinical judgment or needs.

A more selective approach for early thyroid imaging in CH is suggested.

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