Transient *vs.* Permanent Congenital Hypothyroidism: The Use of Baseline Characteristics and Long-term Data can help formulate a Practical Prognostic Algorithm

Giogli V[1,2], Kanaka-Gantenbein C[1,3], Chouliaras G[3], Arditi JD[3], Gika A[1], Iliadi A[1], Platis D[1], Kyritsi EM[3], Karkalousos PL[2], Karikas GA[2], Mengreli C[1], Chrousos GP[3], Girginoudis P[1], Voutetakis A[1,3]

[1] Department of Biochemistry, Institute of Child Health, [2] Department of Medical Laboratories, Technological and Educational Institute of Athens
[3] Division of Endocrinology, Metabolism and Diabetes, 1st Department of Pediatrics, "Aghia Sophia" Children's Hospital, Athens University School of Medicine

Background knowledge

Implementation of neonatal screening programs for Congenital Hypothyroidism (CH) has reduced related nosologies and has eradicated CH-associated mental impairment. With the decrease of the TSH cut-off limits employed in order to avoid false negative results, milder cases of CH are diagnosed. Obviously, in a number of patients, especially among milder CH cases, thyroid dysfunction is transient. The diagnosis of transient *vs.* permanent CH is established in time. No specific prognostic factors have been introduced allowing prediction of the outcome.

The **National Greek Neonatal CH screening program** was initiated in 1980 and is carried out by a **single laboratory** that receives and tests the Guthrie cards from all the maternity hospitals. The program initially covered the Athens Metropolitan area but quickly expanded and covered the entire country. Over the last 35 years, more than **3,690,000 neonates** have been screened.

Objective and hypothesis

To identify the baseline characteristics as well as the clinical and biochemical data acquired through follow up that influence the outcome in neonates with CH. To formulate an algorithm that estimates the probability of transient CH in a given neonate based on specific data.

Patients and Methods

Data from the medical records of children diagnosed with CH by the Greek neonatal CH screening program were analysed retrospectively. Patients were diagnosed during the last 35 years using variable TSH cutoff limits ranging from 30 to 6 mIU/ml. Laboratory, clinical and ultrasonographic data were recorded and evaluated.

Results and Discussion

A total of **968** children with CH were included in our study (525 males and 443 females, ratio 1.17:1). Overall, in 27% of patients (30% in males and 27% in females) CH was transient (**Table 1** and **Figure1**).

TSH values at diagnosis: 49% of patients had an initial TSH <10 mIU/L, 29% between 10-40 mIU/L and 21% >40 mIU/L. The probability for transient CH with respect to TSH values at diagnosis is shown in **Figure 2**.

Gestational age: 9% of patients were born <32 wks, 29% between 32-37 wks and 62% born >37 wks. The probability for transient CH with respect to weeks of gestation is shown in **Figure 3**.

Thyroid ultrasonography: imaging data were available for analysis in 623 patients. Diagnoses were categorized as normal, ambiguous (low normal size of thyroid with respect to age, prominent heterogeneity etc) or as anatomical defect (absence, ectopy etc). In 65% of patients the thyroid gland was considered as normal, in 12% ultrasonographic data were categorized as ambiguous and in 24% anatomical defects were apparent. The probability for transient CH with respect to ultrasonographic data is shown in **Figure 4**.

A **prognostic algorithm** leading to probability of CH being transient was formed based on baseline and long-term data of 290 premature and 502 full term non-syndromic CH patients (**Figure 5**).

	Group		Females		Males	
Total	968		443		525	
Start >6 months	86		43		43	
Long term data unavailable	67		24		43	
Characterization impossible	52		24		28	
Syndromes	18		7		11	
Thyroid anatomical defect	146		100		46	
LT4 dose increase	244		90		154	
LT4 stop unsuccessful	152		73		79	
LT4 stop successful	203		82		121	
Permanent CH	542	**73%**	263	76%	279	70%
Transient CH	203	**27%**	82	**24%**	121	**30%**
Total	745		345		400	

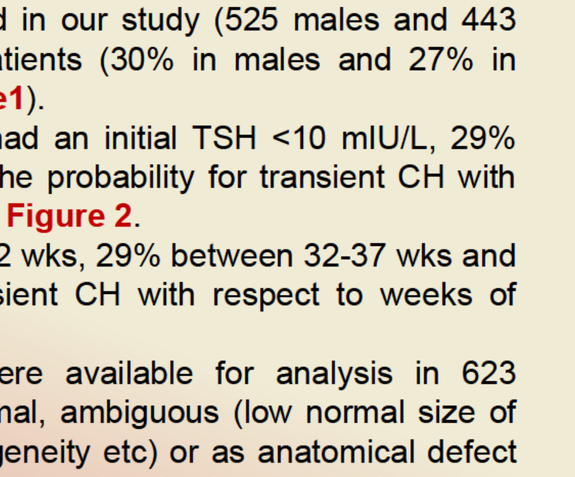

Table 1: CH patients that were included in the study. The overall percent of **transient CH** was 27% (males: 30%, females: 24%)

Figure 1: Demographic data of CH patients: A marginal male predominance is observed (boys to girls ratio 1.17:1). Overall, 14% were born after IVF, 38% were born prematurely, 32% with a low birth weight, and 18% were multitons.

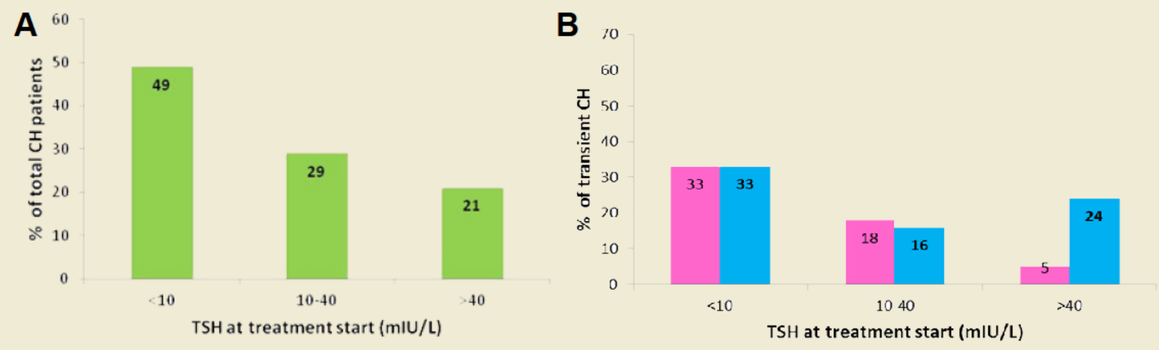

Figure 2: (A) The distribution of CH neonates (males and females) according to TSH values at diagnosis (data depicted as percent of total number of patients): 49% of patients had an initial TSH <10 mIU/L, 29% between 10-40 mIU/L and 21% >40 mIU/L. **(B)** Transient CH (shown as percent within each TSH subgroup) in female (pink) and male (blue) CH neonates with respect to TSH values at diagnosis. The probability of CH to be transient is inversely related to the initial TSH values in females whereas in males seems independent.

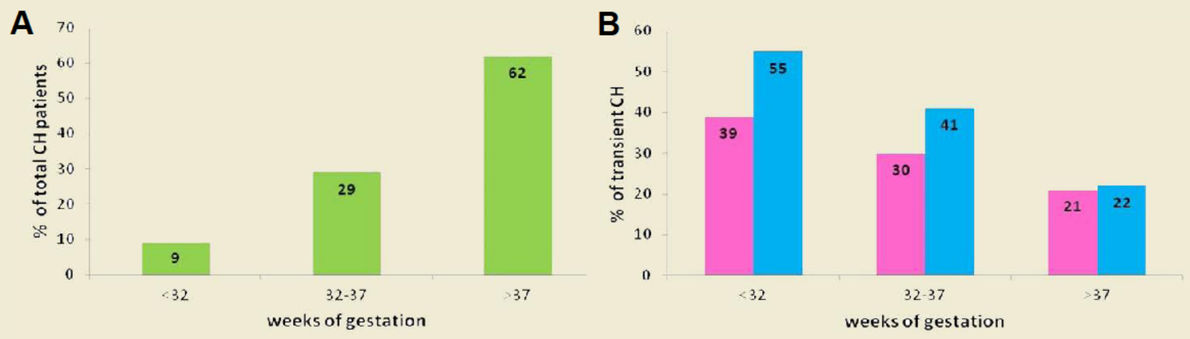

Figure 3: (A) The distribution of CH neonates according to gestational age (in weeks, data depicted as percent of total number of patients): 9% of patients were born <32 wks, 29% between 32-37 wks and 62% born >37 wks. **(B)** Transient CH (shown as percent within each gestational age subgroup) in female (pink) and male (blue) CH neonates with respect to weeks of gestation.

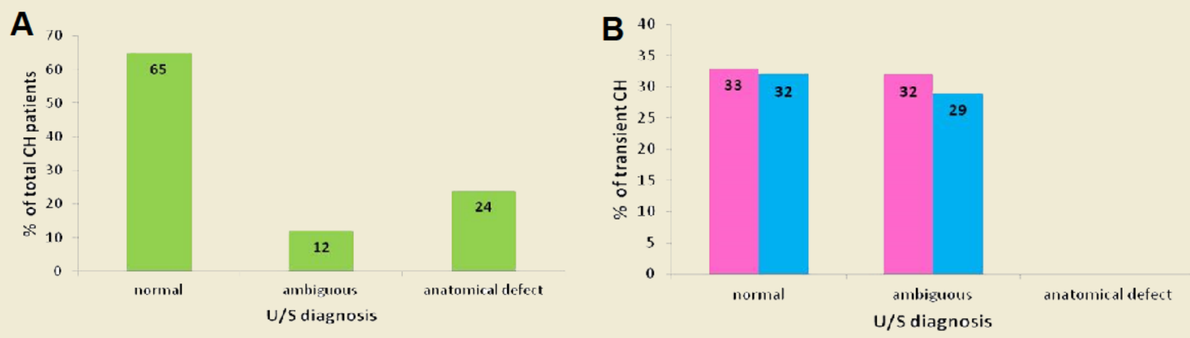

Figure 4: (A) The distribution of CH neonates according to ultrasonographic (U/S) diagnosis (data depicted as percent of total number of patients): in 65% of patients the thyroid gland was considered as normal, in 12% ultrasonographic data were categorized as ambiguous and in 24% anatomical defects were apparent **(B)** Transient CH (shown as percent within each U/S subgroup) of female (pink) and male (blue) CH neonates with respect to weeks of gestation.

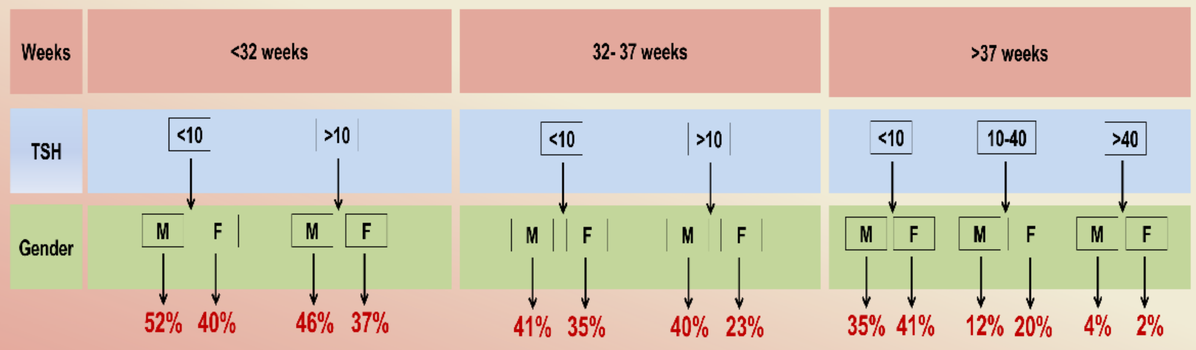

Figure 5: Prognostic algorithm leading to probability of CH being transient (in red) for premature (<32 and 32-37 wks of gestation) and full-term neonates. Algorithm was formed based on baseline and long-term data of 290 premature and 502 full term non-syndromic CH patients and takes into account gender (males and females) and initial TSH levels (grouped as <10, >10, 10-40 or >40 mIU/L, as appropriate). All premature neonates that started LT4 substitution therapy due to low FT4 values have transient CH.

Conclusions

The use of baseline characteristics and long-term data (e.g. gestational age, initial TSH value,ultrasonographic data, gender etc) can help formulate a practical algorithm calculating the probability of CH being transient.

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Thyroid.

Vassiliki Giogli

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