CONGENITAL HYPOTHYROIDISM: THE USE OF A TSH CUT-OFF LIMIT OF 6 mIU/L IN SCREENING PROGRAMS LEADS TO THE DIAGNOSIS OF MILD BUT, IN MOST CASES, PERMANENT FORMS OF HYPOTHYROIDISM.

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Background knowledge

Since the initiation of neonatal screening programs for Congenital Hypothyroidism (CH) in the 1970's, a gradual decrease of TSH cut-off limits has been observed worldwide. Nevertheless, lack of universal consensus has led to wide variation of cut-off limits and LT4-initiation criteria applied in screening programs even within the same country.

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 in Greece. Over the last 35 years, more than **3,690,000 neonates** have been screened. The program has followed the TSH cut-off lowering-trend, observed worldwide, from the initial 35 to 6 mIU/L. Nevertheless, TSH levels above the cut-off limit is not the diagnostic criterion for CH but initiates monitoring and follow-up. **Importantly, more than 50% of CH patients are followed by the same Endocrine Department**.

Objective and hypotheses

To assess the effect of using a TSH cut-off limit of 6 mIU/L in Guthrie cards and determine whether the use of such low cut-off limits is justified.

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Patients and Methods

The data of CH neonates born in 2009 were reviewed. At study initiation, all children were at least **6 years old** and therefore characterization of CH as permanent or transient could be considered accurate. Long-term hormonal, clinical and ultrasonographic data were recorded and evaluated.

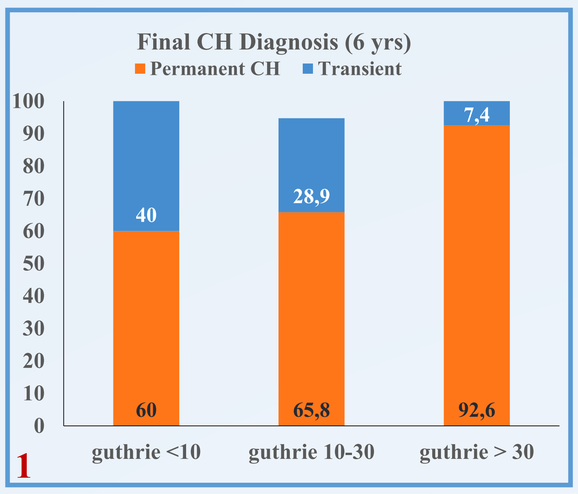
Results

From a total of 120.852 newborns screened for CH in 2009, LT4 treatment was initiated in 324 (~1 in 14.4 recalled due to TSH levels above the cut-off limit). Long-term data from **210 CH patients** were available for analysis and are herein presented (**Table 1**). We emphasize that 91.4% of patients with TSH between 6 -10 mIU/L in the Guthrie card, started LT4 treatment according to the latest ESPE criteria (~1 in 20 recalled).

Patients were divided into **three groups** according to the Guthrie card's TSH value: **<10, 10-30 and >30 mIU/L** (69%, 18% and 13% of total, respectively). CH proved transient in 40% (girls 35.2% and boys 42.9%) in the <10 mIU/L group, 28.9% (girls 41.2% and boys 19%) in the 10-30 mIU/L group and 7.4% (girls 0% and boys 18.2%) in the >30 mIU/L group (**Figure 1 and 2**). Likelihood of permanent CH in Preterm Neonates with respect to initially diagnosed patients is depicted in **Figure 3**. Likelihood of permanent CH in patients with TSH in the Guthrie card <10mIU/L with respect to wks of gestation (Full-term and Preterm newborns) and mode of conception (Natural and IVF,) are depicted in **Figures 4** and **5**, respectively.

Group	Guthrie <10 mIU/L	Guthrie 10 - 30 mIU/L	Guthrie >30 mIU/L
N (%)	145 (69 %)	38 (18 %)	27 (13 %)
Preterm Neonates	28,3 %	11,1 %	10,3 %
Dysgenesis	2,7 %	8,3 %	62,9 %
ESPE Criteria	91,4 %	91,3 %	100 %
Permanent CH	60 %	71,1 %	92,6 %

Table 1: CH patients born in 2009 and diagnosed through the Greek CH Screening Program. Newborns with TSH levels above the cut-off limit are followed until proven normal or diagnosed with CH. Patients herein presented were divided in three groups according to the Guthrie card's TSH value: <10, 10-30 and >30 mIU/L. Percent of patients diagnosed according to the latest ESPE criteria is depicted for each group. Characterization of CH as permanent or transient occurred at age 6 yrs and percent of permanent CH was calculated with respect to patients initially diagnosed.



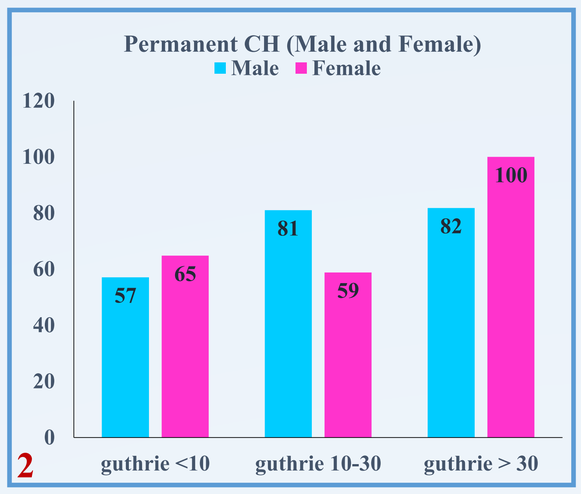


Figure 1: Transient and permanent CH as percent of total. Patients were divided into 3 groups according to the Guthrie card's TSH value: <10, 10-30 and >30 mIU/L and their status was assessed at age 6 years (i.e., transient or permanent CH). **Figure 2:** Permanent CH in male and female patients as percent of total initially diagnosed.

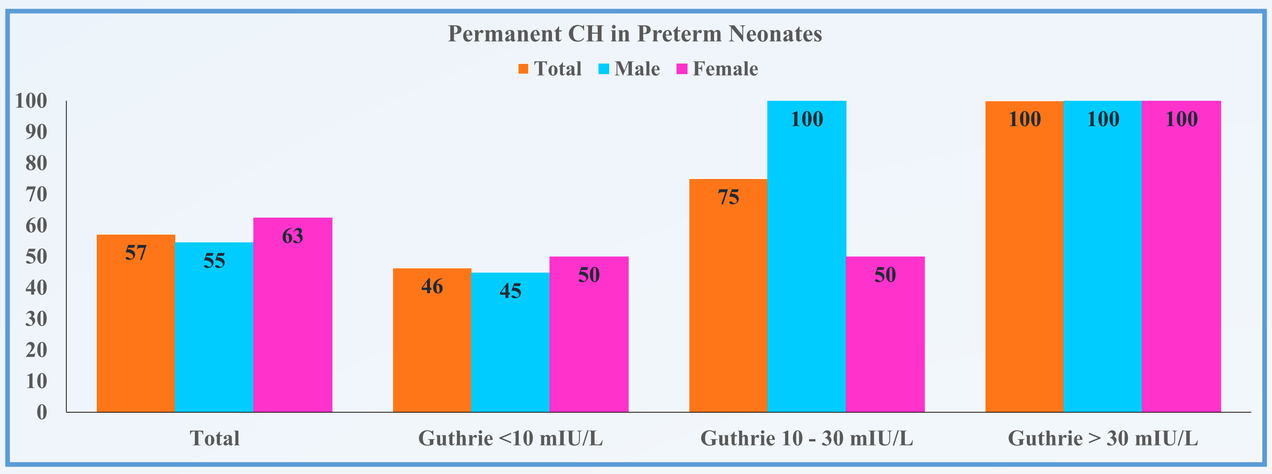
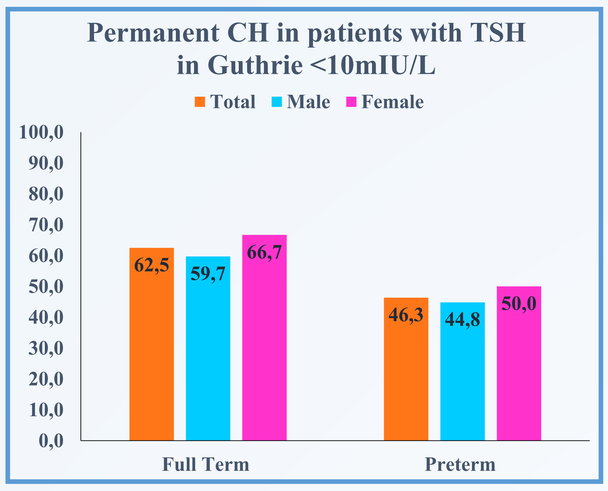


Figure 3: Permanent CH in preterm neonates as percent of patients initially diagnosed (in total, males and females). Patients were divided into 3 groups according to the Guthrie card's TSH value: <10, 10-30 and >30 mIU/L and their status was assessed at age 6 years (i.e., transient or permanent CH).



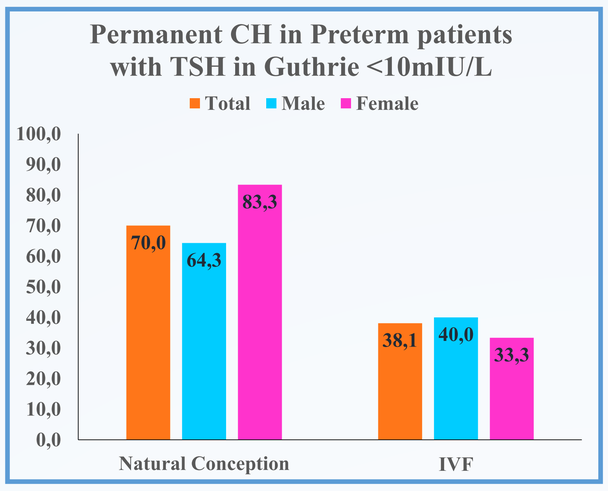


Figure 4: CH patients with TSH in the Guthrie card <10 mIU/L were divided into two groups (Full-term and Preterm Neonates) and percent of permanent CH is depicted in total, males and females compared to patients initially diagnosed.

Figure 5: Preterm CH patients with TSH in the Guthrie card <10 mIU/L were further sub-divided according to mode of conception (Natural or IVF) and percent of permanent CH is depicted in total, males and females compared to patients initially diagnosed (wks of gestation do not differ between groups).

Conclusions

Use of a TSH cut-off limit of 6 mIU/L in the CH screening program identifies milder but nevertheless mostly permanent CH cases. If a TSH cut-off limit >10 mIU/L in Guthrie cards were used, a substantial number of patients who fulfill the ESPE criteria for LT4-initiation would not have been uncovered (~60% of total in our CH group, ~60% of which proved permanent). Hence, the use of such low cut-off limits followed by proper monitoring of suspected CH cases proves valuable with respect to the diagnosis and treatment of CH.

Acknowledgments

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