10.4274/jcrpe.galenos.2025.2024-9-18

Research article

Attitudes Towards the Management of Congenital Hypothyroidism in Türkiye: National Survey Study

Sagsak E et al. Survey: Attitudes Towards the Management of Congenital Hypothyroidism

Elif Sagsak[1], Aydilek Dagdeviren Cakır[2], Yavuz Ozer[3], Gul Yesiltepe Mutlu[4], Bahar Ozcabi[5], Cengiz Kara[6], Thyroid Research Group[7]
[1]University of Yeditepe Faculty of Medicine, Division of Pediatric Endocrinology, Istanbul, Türkiye
[2]University of Health Sciences, Şişli Hamidiye Etfal Health Practices and Research Centre, Division of Pediatric Endocrinology, Istanbul, Türkiye.
[3]Health Science University Zeynep Kamil Maternity and Children's Diseases Training and Research Hospital, Division of Pediatric Endocrinology, Istanbul, Türkiye
[4]Koç University Faculty of Medicine, Division of Pediatrics Endocrinology, Istanbul, Türkiye.
[5]Acibadem Atasehir Hospital, Division of Pediatric Endocrinology, Istanbul, Türkiye.
[6]Istinye University Faculty of Medicine, Department of Pediatric Endocrinology, Istanbul, Türkiye
[7]Turkish Pediatric Endocrinology and Diabetes Society, Thyroid Research Group, Türkiye

What is already known on this topic?
In 2021, an international consensus guideline on congenital hypothyroidism was published by the European Society for Pediatric Endocrinology and the European Society for Endocrinology. The consensus guideline provides strong evidence-based recommendations for diagnosis and treatment. However, in cases with insufficient evidence, it asserts weak recommendations based on expert opinion. For this reason, there may be differences in attitude among physicians.

What does this study add?
Physicians may have different attitudes toward the management of congenital hypothyroidism. Working conditions and professional experience can affect these attitudes. Approaches may even vary from country to country, depending on differences in local conditions. The data obtained from this survey may pave the way for such a consensus that could serve as a model for Türkiye and similar countries.

Abstract
Objective: This study was conducted to assess the perspectives of pediatric endocrinologists in Türkiye on the management of congenital hypothyroidism (CH) and to analyze the potential impact of work environment and professional experience on different attitudes.
Methods: The members of the Turkish Society for Pediatric Endocrinology and Diabetes were invited to participate in an online survey. An evaluation was made by obtaining survey responses from 95 (19%) of 502 members.
Results: Participants' mean age was 42.0±9.6 years, 46.3% of them were working in a university hospital, and 48.6% had >7 years of work experience. When the participants were asked about their approach to a 1–3-week-old neonate whose serum TSH concentration was 6–20 mU/L with a serum-free T4 (FT4) concentration within the age-specific reference interval, 97.7% of the participants preferred to monitor without medication. Only 24% of physicians consider starting treatment immediately if the serum TSH concentration is 20-40 mU/l with a normal FT4 level. While 5.3% of participants preferred dual imaging (ultrasound and scintigraphy), 90.5% requested only thyroid ultrasound for etiological investigation. When considering the discontinuation of levothyroxine in patients with a normal thyroid gland and a low LT4 dose, 28.4% of the participants stated that treatment should be stopped at the earliest at the age of 3 years, 16.8% at 2 years, 5.3% at 1 year, 16.8% at 6 months, and 32.6% at any time if the TSH levels remain low despite the low dosage. Physicians with over 7 years of experience can discontinue medication if TSH is low, even with a lower dose, more frequently than those with less experience (p=0.011). There were no significant differences in the approach of the physicians between employees at university hospitals and other health institutions,
Conclusion: Although the attitudes of pediatric endocrinologists working in Türkiye towards the management of CH are generally consistent with the recommendations of international guidelines, their approaches to the treatment for isolated neonatal TSH elevation, thyroid imaging preferences and time to discontinue treatment differ significantly. These different attitudes, which are almost similar among all subgroups by experience and work setting, reflect the differences in local conditions in Türkiye and underline the need for a national consensus on the management of CH.
Keywords: attitude in management, questionnaire, Congenital hypothyroidism, Turkish Society for Pediatric Endocrinology and Diabetes

Presented in: The study was presented as an oral presentation at the National Pediatric Endocrinology and Diabetes Congress on 03.04.2024.

Elif Sagsak MD, Yeditepe University School of Medicine/ Istanbul/ Türkiye
elif.sagsak@yeditepe.edu.tr
0000-0001-7121-1575
11.10.2024
25.01.2025

Epub: 31.01.2025

Cite this article as: Sagsak E, Dagdeviren Cakır A, Ozer Y, Yesiltepe Mutlu G, Ozcabi B, Kara C, Thyroid Research Group. Attitudes Towards the Management of Congenital Hypothyroidism in Türkiye: National Survey Study. J Clin Res Pediatr Endocrinol. [Epub Ahead of Print]

Conflict of interest: None declared

Introduction
Congenital hypothyroidism (CH) is defined as thyroid hormone deficiency present at birth (1). Newborn screening programs (NSP) enabled early diagnosis before the onset of clinical symptoms, based on biochemical measurement of thyroid stimulating hormone (TSH) and thyroxin (T4). Since CH is one of the most common preventable causes of intellectual disability worldwide, prompt diagnosis and treatment are critical to optimizing long-term outcomes (2). In 2021, an international consensus guideline on CH was published by the European

Society for Pediatric Endocrinology and the European Society for Endocrinology, to update the practice guidelines for the diagnosis and management of CH (3). The consensus guideline provides strong evidence-based recommendations for diagnosis and treatment. However, in cases with insufficient evidence, it asserts weak recommendations based on expert opinion. For this reason, there may be differences in attitude among physicians. In addition, alternative approaches may be needed in countries such as Türkiye, where transient neonatal hyperthyrotropinemia and hypothyroidism are more common due to perinatal iodine deficiency or overload (4-7).
This study aimed to determine the attitudes of pediatric endocrinologists in Türkiye regarding the management of CH and to examine the effects of work environment and professional experience on differences in attitudes. To our knowledge, this is the first study to delineate physicians' attitudes toward CH management. We believe that the results obtained from this study can contribute to the development of a national consensus on the management of CH.

Methods

The survey was created by six members of the Thyroid Working Group of the Turkish Society for Pediatric Endocrinology and Diabetes (TSPED). It was in Google Forms based on the updated consensus guideline recommendations. The survey link consisting of 24 questions was sent to 502 members of TSPED via e-mail. While the initial four questions inquired about personal data, the subsequent questions assessed the practices of pediatric endocrinologists in diagnosing, treating, and monitoring CH. The entire survey is available as an online supplement (supplementary 1).
Descriptive statistics of the data included mean, standard deviation, median and range, frequency, and rate values. The chi-square test was used to compare qualitative independent data between subgroups formed based on professional experience (less than or more than 7 years of work) or place of work (university hospital or other). When test conditions were not met, the Fischer test was used. Statistical analyses were performed using the SPSS 28.0 software version.3
The study protocol was approved by the local ethics committee of the University of Health Sciences Şişli Hamidiye Etfal Training and Research Hospital Health Application and Research Center (4459-09/07/2024).

Results

Out of the 502 members questioned, 95 (19%) submitted valid surveys. Participants' characteristics are shown in Table 1. Participants' mean age was 42.0 ± 9.6 years ranging from 30 to 74 years old, and 48.6% of them had been working in the field of pediatric endocrinology for >7 years. In the survey, 44 out of 95 doctors (46.3%) are employed at a university hospital, while the others work in different settings (Table 1).
Table 2 shows the responses regarding treatment approaches for newborns with elevated TSH and normal serum-free T4 (FT4) levels. When the participants were asked about their approach to a 1-3 week-old neonate whose serum TSH concentration is 6–20 mU/L with FT4 concentration within the age-specific reference interval, most of the participants (94.7%) preferred monitoring without medication and retesting 1 to 2 weeks later to re-evaluate the need for treatment. When the serum TSH concentration is between 20-40 mU/l, only 24% of physicians consider starting treatment immediately. In addition, 42% reported that they decided on treatment according to the FT4 level, while the remaining 28% stated that they followed these babies without any intervention. In the survey, when asked about the approach to a baby with TSH between 6-20 mU/l for 3-4 weeks, the responses regarding treatment and monitoring were similar, but the frequency of decisions based on thyroid imaging has significantly increased (Table 2).
When asked about their approach to initiating levothyroxine (LT4) dose, 18% of physicians preferred to start treatment with 10-15 µg/kg per day for each case, while 25% favored starting treatment with 5-15 µg/kg per day based on FT4 level. Additionally, 57% preferred starting treatment with 5-15 µg/kg based on FT4 level and etiology. While 52.6% of physicians always prefer the brand, 47.4% do not care whether it is brand or generic. When asked about the approach to LT4-LT3 (liothyronine) combination therapy, 20% of the participants reported that they never used it; 80% reported that they could use it in cases with persistent TSH elevation. A 10% subgroup stated that LT4-LT3 treatment could also be used in cases of thyroid agenesis. When evaluating treatment response, 57% of the participants stated that the appropriate sample collection time for FT4 measurement was before taking LT4, while for 43% of the participants, at least 4 hours after taking LT4 was sufficient.
Attitudes towards determining the etiology of CH and possible associated problems are given in Table 3. In the etiological investigation of CH, 90.5% (n: 86) of the participants preferred thyroid ultrasound (US) alone, 5.3% (n: 5) preferred dual imaging (the combination of US and scintigraphy), while 4.2% (n: 4) stated that they did not want routine imaging. No one requested scintigraphy alone for thyroid imaging. When the radioactive element used in scintigraphy was questioned, technetium-99m and iodine-123 were reported as 45% and 18%, respectively. However, 37% of physicians were not aware of which isotope was used. Lack of knowledge about the substance used in scintigraphy was higher in those with less than 7 years of experience (51.7%) than in those with more experience (14.3%) ($p<0.05$). This was one of the rare differences between the two subgroups (Figure 1). The most frequently requested tests (always/often) for the etiological evaluation of CH after thyroid US (96%) were thyroglobulin (71%), thyroid antibodies (42%), and urinary iodine levels (33%). In addition, 42% of physicians occasionally want to take knee X-rays to evaluate possible developmental effects of CH, while 58% never request it (Table 3). Only 4.2% of physicians request both echocardiography (ECHO) and abdominal US for all cases of CH, while 60-63% prefer these imaging studies only in the presence of dysmorphic findings on physical examination. Additionally, 22-29% of physicians state that abdominal US and ECHO are needed only in cases with thyroid dysgenesis (Table 3).
While 55% of the participants want genetic testing for patients with CH, 45% do not. Participants most commonly request genetic tests for patients with the common accompanying anomalies or syndromic features (42%), those confirmed to have permanent CH (23.2%), and those found to have persistently high TSH (21%).
Fifty-three percent of physicians believe that the screening program should also cover central hypothyroidism cases, while 38% are undecided. The question 'In which patient group would you consider post-screening strategy?' was mostly responded as premature babies (91%) by participants. Other respondents, in order of frequency, are sick babies (87.4%), infants with clinical suspicion of hypothyroidism (76.8%), low birthweight infants (72.6%), Down syndrome (48.4%), babies with congenital anomalies (40%) and twins (37.9%).
When asked about physicians' approach to the timing of trial off therapy in patients with a normal thyroid gland and a low LT4 dose (<3 µg/kg/day), 28.4% of the participants stated that treatment should be stopped at the earliest at the age of 3 years, 16.8% at 2 years, 5.3% at 1 year, 16.8% at 6 months, and 32.6% at any time if the TSH levels remain low despite the low dosage. Physicians with over 7 years of experience can discontinue medication if TSH is low, even with a lower dose, more frequently than those with less experience ($p<0.05$) (Figure 2). No significant difference was found when comparing other survey responses between groups with a working duration of ≤7 years and >7 years. Also, no significant difference was found between the survey responses of participants working in university hospitals and other healthcare institutions.

Discussion

The field of CH currently has a wealth of excellent guidelines and expert opinions. While these guidelines encompass various aspects of CH, clinicians may face challenges in evaluating the quality of evidence for specific issues related to CH (8). Physicians may have different attitudes toward the management of CH. Working conditions and professional experience can affect these attitudes. Approaches may even vary from country to country, depending on differences in local conditions. Therefore, there is a need to establish a national consensus on routine practices for CH. The data obtained from this survey may pave the way for such a consensus that could serve as a model for Türkiye and similar countries.
Current consensus guidelines recommend starting treatment if venous TSH is above 20 mU/l even if the FT4 level is normal (3, 9, 10). This is an arbitrary threshold for treatment decisions and is based on expert opinion due to the lack of sufficient evidence. Despite the consensus

recommendation, when the survey questions asked about TSH elevations of 20-40 mU/l in the first 3 weeks of life, only 24% of responding physicians stated that they would immediately start treatment in this case. In addition, 42% of the participants reported that they would take into account the FT4 level (in the lower or upper half of the reference range) for the treatment decision, and 28% would prefer follow-up without treatment. These responses show us that most pediatric endocrinologists in Türkiye do not prefer to start treatment when serum TSH elevation is at a moderate level (20-40 mU/l). Likewise, if serum TSH is mildly elevated (6-20 mU/l), almost no one starts treatment.

In fact, the definition and management of neonatal hyperthyrotropinemia (NHT) is unclear (11-13). NHT can be defined as an increase in serum TSH concentrations between 6 and 20 mU/L with normal FT4 concentrations in newborns (3, 10, 13). This description overlaps with the definition of subclinical (compensated) hypothyroidism (SCH) in childhood (14, 15). The term SCH implies that elevated TSH secretion occurs to compensate for insufficient hormone production due to an impairment in the hypothalamic-pituitary-thyroid (HPT) axis and that this condition must be treated. However, TSH elevation can occur outside the HPT feedback loop, for example in response to stress, such as the neonatal TSH surge after birth. This increased TSH concentration at birth usually returns to normal within 24-48 hours. However, in some newborns, recovery from elevated TSH concentrations may take longer, possibly due to delayed HPT axis maturation (16). This transient NHT state, usually accompanied by high FT4 levels, does not require treatment. Indeed, transient NHT are most commonly caused by maternal iodine deficiency and/or perinatal iodine exposure (13). Of course, iodine deficiency or excess increases TSH secretion by impairing T4 production, but it is usually a temporary condition that resolves itself within a few days or weeks. LT4 treatment is not necessary unless the serum FT4 levels fall below normal limits, indicating true hypothyroidism. In Türkiye, mild iodine deficiency is still an ongoing problem in pregnant women and nursing mothers (4, 5, 17-23). Perinatal iodine exposure is also common due to the use of iodine-containing antiseptics during delivery (5). In addition, the use of a TSH cutoff as low as 5.5 mU/l whole blood in the national NSP has led to more frequent detection of false positives and transient NHT cases (7). Therefore, pediatric endocrinologists working in Türkiye are familiar with iodine problems in their environments and frequently encounter cases of iodine-related transient NHT. It seems that this experience of physicians is reflected in the high rate of "follow-up without treatment" responses in the survey. These responses also suggest that each country should determine its own TSH threshold values for treatment decisions in accordance with regional conditions. Otherwise, transferring guideline recommendations directly to daily practice may lead to unnecessary treatments, long-term follow-ups, and increased workload and costs.

Attitudes towards NHT lasting longer than 21 days varied among participants, with only 23% of participants reporting a preference for starting treatment immediately. As in the current consensus (3), physicians' treatment decisions are based on FT4 level, TSH trend, or further investigations, especially thyroid imaging.

Although scintigraphy is the most accurate diagnostic test for determining the etiology of CH, this study showed that pediatric endocrinologists in Türkiye did not prefer scintigraphy or dual imaging. The preference for less invasive and faster-yielding tests in the diagnosis of CH may lead doctors to prefer scintigraphy less frequently. However, there may be other explanations for the 90% preference for the US alone. In Türkiye, the incidence of CH at birth is as high as 1/650 (24), and more than half of the cases consist of transient hypothyroidism (6, 7). On the other hand, permanent CH occurs in 40-80% of the patients due to dyshormonogenesis, and this figure varies directly proportional to the frequency of consanguineous marriage in the study area (6, 7, 25). In iodine-replete countries where the incidence of CH is relatively low and about 80% of cases are due to thyroid dysgenesis (1, 2), scintigraphy may be the first-choice imaging modality as recommended by guidelines. Considering the high number of cases of transient NHT and CH, and permanent CH with gland in situ, exposing a large group of infants to radioactive isotopes for treatment decisions or etiological investigation would not be a reasonable approach for Türkiye (26). Thus, this perspective is reflected in the responses that the majority of physicians prefer only the US as a non-invasive imaging method.

After thyroid US, the most frequently requested tests were thyroglobulin, thyroid antibodies and urinary iodine concentrations, which is consistent with the high prevalence of transient hypothyroidism in Türkiye, and possible causes, such as iodine deficiency or overload and maternal blocking antibodies. On the other hand, knee X-rays are rarely requested, indicating that the physicians focus on the etiological investigation of CH rather than its intrauterine effects. In addition, the abdominal US and ECHO are occasionally demanded in special cases such as dysmorphism or thyroid dysgenesis, which shows that the pediatric endocrinologists in Türkiye work by considering the cost-benefit ratio of expensive examinations.

The treatment goal is to quickly achieve euthyroidism and then maintain it consistently. Normalization of serum TSH and FT4 levels within 2 weeks after starting therapy appears to improve cognitive outcomes. Undertreatment in the first years of life is linked to adverse neurodevelopmental outcomes (27, 28). However, it is also important to avoid overtreatment, which may also be harmful (29). In the survey, only one fifth of physicians chose directly a starting LT4 dose of 10–15 µg/kg/day, while the remaining majority preferred doses ranging from 5–15 µg/kg/day, depending on FT4 levels (very low to normal) and/or etiology (athyreosis or not). This attitude is consistent with guideline recommendations and reflects sensitivity to overtreatment and its potential deleterious effects on brain development.

The data indicating the preference for brand-name LT4 over its generic counterpart is inconclusive. However, taking personal experiences and expert opinions into account, the general agreement leans towards recommending the brand-name medication over the generic version (3). According to survey results, half of the participants indicated that it does not matter whether the molecule is original or not.

A subgroup of infants with CH displays variable degrees of thyroid hormone resistance with persistently elevated TSH levels despite high-normal or frankly elevated free T4 concentrations (30, 31). For these patients, adding LT3 to LT4 therapy can facilitate the normalization of TSH (32, 33). Indeed, 80% of the survey participants reported that they were able to use the LT4-LT3 combination in CH cases with persistent TSH elevation despite high-normal FT4 levels. Although this response does not mean that 80% of physicians routinely use LT3 treatment in cases of persistent TSH elevation, it does show that they are aware of this treatment option and may prefer it in some cases. Interestingly, 10% of physicians stated that they could also use LT3 in patients with thyroid agenesis. This response was attributed to the knowledge that central T4 resistance is more common in patients with thyroid dysgenesis (32).

Recent studies have shown that transient CH is very common among CH patients with gland in situ (7, 34). The consensus emphasizes that early treatment withdrawal to assess the necessity of further treatment can be considered and done from the age of 6 months onward, particularly in patients with a gland in situ, a negative first-degree family history of CH, or in those requiring a low LT4 dose (3). While 17% of physicians follow this recommendation, a larger group prefer to re-evaluate at any time if TSH is low despite low LT4 doses. The preference for early cessation of treatment is probably based on the physicians' observations that thyroid dysfunction due to iodine deficiency or excess resolves in a relatively short time. At this point, the difference in experience is striking, as more senior physicians are more likely to discontinue LT4 therapy whenever the possibility of overtreatment appears, regardless of guideline recommendations and therefore a time limit. In the entire survey, it was observed that professional experience did not cause any difference in attitudes towards CH management, except for the time of drug withdrawal. Similarly, work dynamics (employed in university hospitals and others) did not seem to affect the participants' responses.

In TSH-based neonatal screening programs, some groups of children, such as preterm or low birthweight and sick babies may not be able to generate an adequate TSH response in the first weeks of life. They pass their initial screening test but are at high risk for later development of mild CH (35, 36). Therefore, consensus strongly recommends re-screening for these groups. Moreover, in patients with Down's syndrome, measuring TSH at the end of the neonatal period is a strong recommendation (3, 10). While almost all of the survey participants stated that they re-screened preterm and sick babies, only less than half re-screened for Down's syndrome. The reason for this might be that since individuals with Down syndrome have frequent doctor visits, there is a higher likelihood of detecting high TSH levels during routine

appointments. On the other hand, approximately half of the participants reported re-screening babies with congenital anomalies, even though no recommendation in the consensus. Congenital hypothyroidism appears to be associated with an increased risk of congenital malformations. In one study of 1420 infants with congenital hypothyroidism, extrathyroidal congenital malformations had a prevalence of 8.4% (37). Thus, babies with congenital malformations can also be re-screened.

Although there are not many studies in the literature reporting physicians' attitudes toward congenital hypothyroidism, a survey study was published in England in 2009. A questionnaire survey of the British Society for Pediatric Endocrinology and Diabetes (BSPED) membership was undertaken to examine clinical practice in CH. Results were compared with published management guidelines from Europe and the UK. There were differences in preference for tablet or liquid preparation, method of tablet administration, time of seeing infant after notification, the interval between the initial-first follow-up visit, and initial LT4 dose (38). In a survey study conducted by Clelonko et al. in 2017 with 44 respondents, differences were found regarding imaging methods and the dose of LT4 (39).

This study has some limitations. The main limitation is the low response rate for the survey, which may limit the generalizability of the findings to the broader population of pediatric endocrinologists in Türkiye. Those who choose not to respond may differ significantly in the results. Another limitation is that, like all other survey studies, respondents may not accurately reflect actual behaviors, attitudes, or experiences.

Conclusion

Although the attitudes of pediatric endocrinologists working in Türkiye towards the management of CH are generally consistent with the recommendations of international guidelines, their approaches to the treatment for isolated neonatal TSH elevation, thyroid imaging preferences and time to discontinue treatment differ significantly. These different attitudes, which are almost similar among all subgroups by experience and work setting, reflect the differences in local conditions in Türkiye and underline the need for a national consensus on the management of CH.

References

1. Rastogi MV, LaFranchi SH. Congenital hypothyroidism. Orphanet J Rare Dis. 2010;5:17. doi: 10.1186/1750-1172-5-17.
2. Wassner AJ. Congenital Hypothyroidism. Clin Perinatol. 2018;45(1):1-18.
3. Van Trotsenburg P, Stoupa A, Léger J, Rohrer T, Peters C, Fugazzola L, Cassio A, Heinrichs C, Beauloye V, Pohlenz J, Rodien P, Coutant R, Szinnai G, Murray P, Bartés B, Luton D, Salerno M, de Sanctis L, Vigone M, Krude H, Persani L, Polak M. Congenital Hypothyroidism: A 2020-2021 Consensus Guidelines Update-An ENDO-European Reference Network Initiative Endorsed by the European Society for Pediatric Endocrinology and the European Society for Endocrinology. Thyroid. 2021;31(3):387-419.
4. Evliyaoğlu O, Kutlu A, Kara C, Atavci SG. Incidence of iodine deficiency in Turkish patients with congenital hypothyroidism. Pediatr Int. 2008;50(3):276-80.
5. Yaman AK, Demirel F, Ermiş B, Pişkin IE. Maternal and neonatal urinary iodine status and its effect on neonatal TSH levels in a mildly iodine-deficient area. J Clin Res Pediatr Endocrinol. 2013;5(2):90-4.
6. Kara C, Günindi F, Can Yılmaz G, Aydın M. Transient Congenital Hypothyroidism in Turkey: An Analysis on Frequency and Natural Course. J Clin Res Pediatr Endocrinol. 2016;8(2):170-9.
7. Özer Y, Anık A, Sayılı U, Tercan U, Deveci Sevim R, Güneş S, Buhur Pirimoğlu M, Elmaoğulları S, Dündar I, Ökdemir D, Besci Ö, Jalilova A, Çiçek D, Singin B, Ulu ŞE, Turan H, Albayrak S, Kocabey Sütçü Z, Eklioğlu BS, Eren E, Çetinkaya S, Savaş-Erdeve Ş, Esen I, Demir K, Darcan Ş, Hatipoğlu N, Parlak M, Dursun F, Şıklar Z, Berberoğlu M, Keskin M, Orbak Z, Tezel B, Yürüker E, Keskinkılıç B, Kara F, Erginöz E, Darendeliler F, Evliyaoğlu O. High frequency of transient congenital hypothyroidism among infants referred for suspected congenital hypothyroidism from the Turkish National screening program: thyroxine dose may guide the prediction of transients. J Endocrinol Invest. 2024 Mar 28. doi: 10.1007/s40618-024-02348-9.
8. Itonaga T, Hasegawa Y, Higuchi S, Satoh M, Sawada H, Shimura K, Takahashi I, Takubo N, Nagasaki K. Knowns and unknowns about congenital hypothyroidism: 2022 update. Clin Pediatr Endocrinol. 2023;32(1):11-25.
9. Léger J, Olivieri A, Donaldson M, Torresani T, Krude H, van Vliet G, Polak M, Butler G; ESPE-PES-SLEP-JSPE-APEG-APPES-ISPAE; Congenital Hypothyroidism Consensus Conference Group. European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. Horm Res Paediatr. 2014;81(2):80-103.
10. Rose SR, Wassner AJ, Wintergerst KA, Yayah-Jones NH, Hopkin RJ, Chuang J, Smith JR, Abell K, LaFranchi SH; Section on Endocrinology Executive Committee; Council on Genetics Executive Committee. Congenital Hypothyroidism: Screening and Management. Pediatrics. 2023;151(1):e2022060419.
11. Connelly KJ, LaFranchi SH. Detection of neonates with mild congenital hypothyroidism (primary) or isolated hyperthyrotropinemia: an increasingly common management dilemma. Expert Rev Endocrinol Metab. 2014;9(3):263-271.
12. Vigone MC, Capalbo D, Weber G, Salerno M. Mild Hypothyroidism in Childhood: Who, When, and How Should Be Treated? J Endocr Soc. 2018;2(9):1024-1039.
13. Chiesa AE, Tellechea ML. Update on Neonatal Isolated Hyperthyrotropinemia: A Systematic Review. Front Endocrinol (Lausanne). 2021;12:643307. doi: 10.3389/fendo.2021.643307.
14. Salerno M, Capalbo D, Cerbone M, De Luca F. Subclinical hypothyroidism in childhood - current knowledge and open issues. Nat Rev Endocrinol. 2016;12(12):734-746.
15. Lazarus J, Brown RS, Daumerie C, Hubalewska-Dydejczyk A, Negro R, Vaidya B. 2014 European thyroid association guidelines for the management of subclinical hypothyroidism in pregnancy and in children. Eur Thyroid J. 2014;3(2):76-94.
16. Fisher DA, Nelson JC, Carlton EI, Wilcox RB. Maturation of human hypothalamic-pituitary-thyroid function and control. Thyroid. 2000;10(3):229-34.
17. Kurtoglu S, Akcakus M, Kocaoglu C, Gunes T, Budak N, Atabek ME, Karakucuk I, Delange F. Iodine status remains critical in mother and infant in Central Anatolia (Kayseri) of Turkey. Eur J Nutr. 2004;43(5):297-303.
18. Kut A, Gursoy A, Senbayram S, Bayraktar N, Budakoğlu II, Akgün HS. Iodine intake is still inadequate among pregnant women eight years after mandatory iodination of salt in Turkey. J Endocrinol Invest. 2010 Jul-Aug;33(7):461-4.
19. Oguz Kutlu A, Kara C. Iodine deficiency in pregnant women in the apparently iodine-sufficient capital city of Turkey. Clin Endocrinol (Oxf). 2012;77:615-620.
20. Egri M, Ercan C, Karaoglu L. Iodine deficiency in pregnant women in eastern Turkey (Malatya Province): 7 years after the introduction of mandatory table salt iodization. Public Health Nutr. 2009;12(6):849-52.
21. Celik H, Guldiken S, Celik O, Taymez F, Dagdeviren N, Tuğrul A. Iodine deficiency in pregnant women living in Western Turkey (Edirne). Acta Endocrinol (Buchar). 2016;12(1):14-18.
22. Oral E, Aydogan Mathyk B, Aydogan BI, Acıkgoz AS, Erenel H, Celik Acıoglu H, Anık Ilhan G, Dane B, Ozel A, Tandogan B, Cakar E, Isci H, Kayan B, Aslan H, Ekiz A, Sancak S, Celik A, Yoldemir T, Uzun O, Erdogan MF. Iodine status of pregnant women in a metropolitan city which proved to be an iodine-sufficient area. Is mandatory salt iodisation enough for pregnant women? Gynecol Endocrinol. 2016;32(3):188-92.
23. Vural M, Koc E, Evliyaoglu O, Acar HC, Aydin AF, Kucukgergin C, Apaydin G, Erginoz E, Babazade X, Sharifova S, Perk Y; Turkish Iodine Survey Group. Iodine status of Turkish pregnant women and their offspring: A national cross-sectional survey. J Trace Elem Med Biol. 2021;63:126664

24. Dilli D, Ozbaş S, Acıcan D, Yamak N, Ertek M, Dilmen U. Establishment and development of a national newborn screening programme for congenital hypothyroidism in Turkey. J Clin Res Pediatr Endocrinol. 2013;5(2):73-9.
25. Asena M, Demiral M, Unal E, Öcal M, Demirbilek H, Özbek MN. Validity of Six Month L-Thyroxine Dose for Differentiation of Transient or Permanent Congenital Hypothyroidism. J Clin Res Pediatr Endocrinol. 2020;12(3):275-280.
26. Özon A, Tekin N, Şıklar Z, Gülcan H, Kara C, Taştekin A, Demir K, Koç E, Evliyaoğlu O, Kurtoğlu S. Neonatal effects of thyroid diseases in pregnancy and approach to the infant with increased TSH: Turkish Neonatal and Pediatric Endocrinology and Diabetes Societies consensus report. Turk Pediatri Ars. 2018;53(Suppl 1):S209-S223.
27. Oerbeck B, Sundet K, Kase BF, Heyerdahl S. Congenital hypothyroidism: influence of disease severity and L-thyroxine treatment on intellectual, motor, and school-associated outcomes in young adults. Pediatrics. 2003;112(4):923-30.
28. Selva KA, Harper A, Downs A, Blasco PA, Lafranchi SH. Neurodevelopmental outcomes in congenital hypothyroidism: comparison of initial T4 dose and time to reach target T4 and TSH. J Pediatr. 2005;147(6):775-80.
29. Bongers-Schokking JJ, Resing WC, de Rijke YB, de Ridder MA, de Muinck Keizer-Schrama SM. Cognitive development in congenital hypothyroidism: is overtreatment a greater threat than undertreatment? J Clin Endocrinol Metab. 2013;98(11):4499-506.
30. Kara C, Ocal G, Berberoğlu M, Siklar Z, Adiyaman P. Persistently raised thyroid stimulating hormone in adequately treated congenital hypothyroidism on long-term follow-up. J Pediatr Endocrinol Metab. 2008;21(3):251-6.
31. Lacámara N, Lecumberri B, Barquiel B, Escribano A, González-Casado I, Álvarez-Escolá C, Aleixandre-Blanquer F, Morales F, Alfayate R, Bernal-Soriano MC, Miralles R, Yildirim Simsir I, Özgen AG, Bernal J, Berbel P, Moreno JC. Identification of Resistance to Exogenous Thyroxine in Humans. Thyroid. 2020;30(12):1732-1744.
32. Akcay T, Turan S, Guran T, Unluguzel G, Haklar G, Bereket A. T4 plus T3 treatment in children with hypothyroidism and inappropriately elevated thyroid-stimulating hormone despite euthyroidism on T4 treatment. Horm Res Paediatr. 2010;73(2):108-14.
33. Paone L, Fleisch AF, Feldman HA, Brown RS, Wassner AJ. Liothyronine Improves Biochemical Control of Congenital Hypothyroidism in Patients with Central Resistance to Thyroid Hormone. J Pediatr. 2016;175:167-172.e1.
34. Saba C, Guilmin-Crepon S, Zénaty D, Martinerie L, Paulsen A, Simon D, Storey C, Dos Santos S, Haignere J, Mohamed D, Carel JC, Léger J. Early Determinants of Thyroid Function Outcomes in Children with Congenital Hypothyroidism and a Normally Located Thyroid Gland: A Regional Cohort Study. Thyroid. 2018;28(8):959-967.
35. McGrath N, Hawkes CP, Mayne P, Murphy NP. Optimal timing of repeat newborn screening for congenital hypothyroidism in preterm infants to detect delayed thyroid-stimulating hormone elevation. J Pediatr. 2019;205:77–82.
36. Cavarzere P, Camilot M, Popa FI, Lauriola S, Teofoli F, Gaudino R, Vincenzi M, Antoniazzi F. Congenital hypothyroidism with delayed TSH elevation in low-birthweight infants: incidence, diagnosis and management. Eur J Endocrinol. 2016;175:395-402.
37. Olivieri A, Stazi MA, Mastroiacovo P, Fazzini C, Medda E, Spagnolo A, De Angelis S, Grandolfo ME, Taruscio D, Cordeddu V, Sorcini M; Study Group for Congenital Hypothyroidism. A population-based study on the frequency of additional congenital malformations in infants with congenital hypothyroidism: data from the Italian Registry for Congenital Hypothyroidism (1991-1998). J Clin Endocrinol Metab. 2002 87(2):557-62.
38. Jeremy H Jones, Malcolm DC Donaldson. J Pediatr Endocrinol Metab. 2009;22(11):1017-1125. Audit of Initial Management of Congenital Hypothyroidism in the United Kingdom Comparison of UK Practice with European and UK Guidelines
39. Luke Cielonko, Tyler Hamby, John S Dallas, Luke Hamilton, Don P Wilson. J Pediatr Endocrinol Metab. 2017;30(5):583-586. Provider variability in the initial diagnosis and treatment of congenital hypothyroidism.

Table 1. Characteristics of participants

Age and Experience	**Mean ± SD**	**Median (Range)**
Age (year)	42.0±9.6	40 (30-74)
Experience in pediatric endocrinology (year)	8.7±9.5	4.6 (0.2-40)
Place of Work and Title	**n**	**%**
University Hospital	44	46.3
Ministry of Health Training and Research Hospital	31	32.6
State Hospital	11	11.6
Private/Foundation University Hospital	5	5.3
Others	4	4.4
Fellow	27	28.4
Consultant	36	37.9
Assistant professor	6	6.3
Associated professor	7	7.4
Professor	19	20.0

Table 2. Treatment approaches in newborns with elevated TSH and normal FT4 levels

	TSH 6-20 mU/l		**TSH 20-40 mU/l**
Responses	**1-3 weeks old**	**3-4 weeks old**	**1-3 weeks old**
Starting treatment immediately (%)	-	23.2	24.2
n		22	23
Monitoring without treatment (%)	94.7	24.2	28.4
n	90	23	27
Decision based on FT4 level (%)	3.2	26.3	42.1
n	3	25	39
Decision based on thyroid imaging (%)	2.1	22.1	1.1
n	2	21	1
Various individual approaches (%)*	-	4.2	4.2
n		4	4

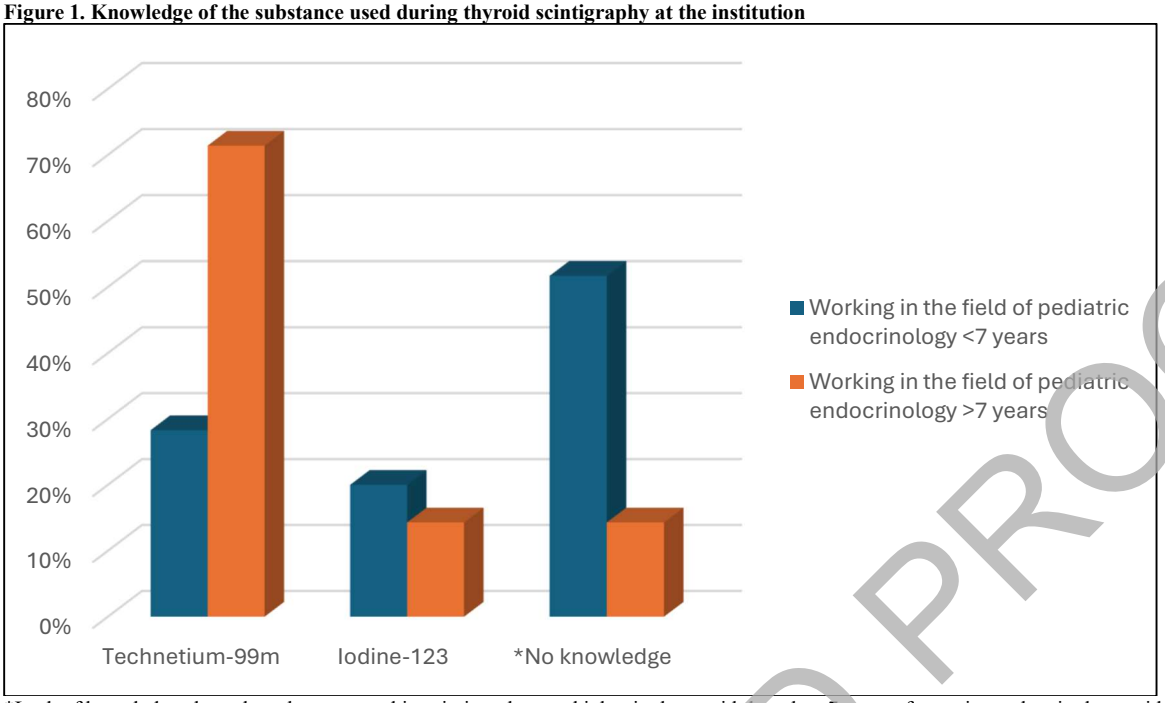
* Other approaches include decisions based on TSH trend, a different TSH threshold or clinical findings

Table 3. Attitudes toward determining the etiology of CH and possible associated problems

Requested test	Responses (n=95)			
	Never	**Rarely**	**Often**	**Always**
Thyroid ultrasound (n)	0	3	22	70
%		3.1	23.2	73.7
Thyroid scintigraphy (n)	24	62	6	3
%	25.2	65.3	6.3	3.2
Urinary iodine level (n)	28	36	19	12
%	29.4	37.9	20	12.7
Mother's urine iodine (n)	45	42	6	2
%	47.4	44.2	6.3	2.1
Breast milk iodine (n)	84	11	0	0
%	88.4	11.6		
Urinary iodine/creatinine (n)	58	28	6	3
%	61	29.5	6.3	3.2
Thyroglobulin (n)	1	27	36	31
%	1	28.4	37.9	32.6
Thyroid autoantibodies (n)	18	37	21	19
%	19	39	22	20
Genetic tests (n)	16	70	9	0
%	16.8	73.7	9.5	
Knee X-ray (n)	55	34	5	1
%	57.9	35.8	5.3	1
Echocardiography (n)	6	57*	28§	4
%	6.3	60	29.5	4.2
Abdominal ultrasound (n)	10	60*	21§	4
%	10.5	63.2	22.1	4.2

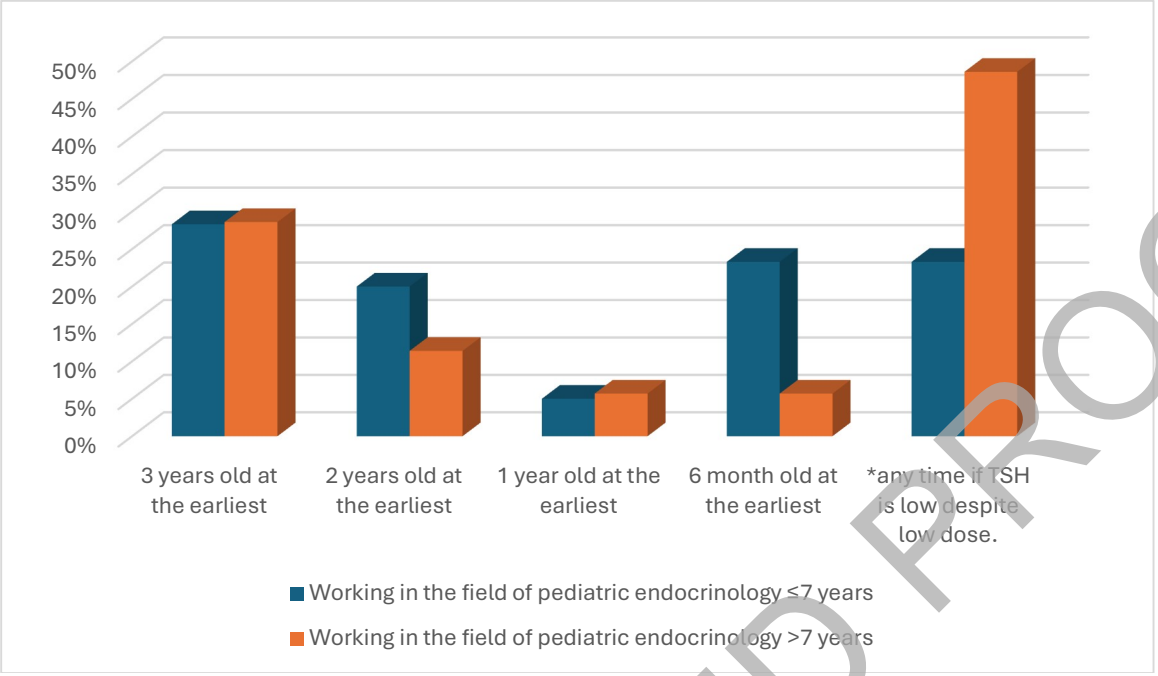
These imaging studies are only requested if there are dysmorphic findings on physical examination* or in cases of thyroid dysgenesis§.

Figure 1. Knowledge of the substance used during thyroid scintigraphy at the institution



*Lack of knowledge about the substance used in scintigraphy was higher in those with less than 7 years of experience than in those with more experience ($p<0.05$)

Figure 2. Approaches to the timing of drug withdrawal in patients with eutopic thyroid and receiving low-dose therapy



*Physicians with over 7 years of experience can discontinue medication if TSH is low, even with a lower dose, more frequently than those with less experience ($p<0.05$)