Increased Congenital Hypothyroidism Detection in Preterm Infants with Serial Newborn Screening

Dinushan C. Kaluarachchi, MBBS[1], David B. Allen, MD[1], Jens C. Eickhoff, PhD[2], Sandra J. Dawe, PhD[3], and Mei W. Baker, MD[1,3]

Objectives To determine the incidence of congenital hypothyroidism in preterm infants and to identify associated risk factors.

Study design A population-based cohort study was performed in preterm infants born at <32 weeks of gestational age between 2012 and 2016 in Wisconsin. Newborn screening (NBS) results and demographic data were obtained from the Wisconsin State Laboratory of Hygiene. Congenital hypothyroidism was subdivided to early TSH elevation (eTSH) and delayed TSH elevation (dTSH). Multivariate logistic regression analyses were performed to identify demographic factors associated with dTSH.

Results A total of 3137 preterm infants born at 22-31 weeks of gestational age were included in the study. Mean gestational age was 28.4 ± 2.4 weeks and mean birth weight was 1191 ± 399 g. Forty-nine infants were diagnosed with congenital hypothyroidism. The overall incidence of congenital hypothyroidism was 1.56%, including a 0.13% incidence of eTSH and a 1.43% incidence of dTSH. Birth weight <1000 g, multiple gestation, and initial TSH level were identified as independent predictors for dTSH.

Conclusion Targeted serial NBS in Wisconsin led to a higher rate of diagnosis of congenital hypothyroidism in preterm infants than has been reported previously. The majority (92%) of congenital hypothyroidism cases were diagnosed with dTSH. Birth weight <1000 g, multiple gestation, and elevated initial TSH level were associated with increased risk for development of dTSH. We recommend obtaining targeted serial NBS in preterm infants (<32 weeks of gestational age) to improve the detection of congenital hypothyroidism. *(J Pediatr 2019;207:220-5).*

The reported incidence of congenital hypothyroidism has increased significantly over the last few decades; recent reports have noted an incidence of 1:1400-1:1700.[1-3] This increasing incidence is thought to be due to changes in birth demographics and methodological shifts in newborn screening (NBS).[4,5] Detection of congenital hypothyroidism in preterm infants has been recognized as a contributor to this increased incidence of congenital hypothyroidism.[4]

Infants born preterm account for approximately 10% of all births in the US.[6] Survival of extremely premature infants has increased significantly over last few decades owing to advancements in perinatal medicine.[7] As a result, an increasing number of preterm infants, particularly those surviving extremely preterm birth, now undergo NBS. An increasing number of NBS programs now collect a routine second specimen for delayed TSH elevation (dTSH) in hospitalized infants, the majority of whom are born preterm.[8] Some NBS programs, including Wisconsin's NBS program, perform serial screenings in preterm infants.

The objectives of the present study were to determine the incidence of congenital hypothyroidism in preterm infants, to determine whether NBS of preterm infants contributes significantly to the increased incidence of congenital hypothyroidism, and to identify associated risk factors using a statewide preterm birth cohort of infants born before 32 weeks of gestation in Wisconsin between 2012 and 2016.

Methods

In this population-based cohort study of preterm infants in Wisconsin, the study cohort was drawn from the NBS database maintained by the Wisconsin state NBS program. All infants born before 32 weeks of gestation between 2012 and 2016 who

dTSH	Delayed thyroid-stimulating hormone elevation
ELBW	Extremely low birth weight
eTSH	Early thyroid-stimulating hormone elevation
FT4	Free thyroxine
NBS	Newborn screening
NICU	Neonatal intensive care unit
TSH	Thyroid-stimulating hormone
VLBW	Very low birth weight

From the [1]Department of Pediatrics; [2]Department of Biostatistics and Medical Informatics, University of Wisconsin-Madison; and [3]Wisconsin State Laboratory of Hygiene, University of Wisconsin School of Medicine and Public Health, Madison, WI

The authors declare no conflicts of interest.

https://doi.org10.1016/j.jpeds.2018.11.044

Table I. Screening cutoffs and associated actions/recommendations by age at the time of specimen collection

Age at time of collection	Possible abnormal with recommendation of repeat NBS notified by written report	Possible abnormal with recommendation of repeat NBS notified by phone call	Abnormal with confirmatory testing notified by phone call
0-25 h	37-43 μIU/mL	44-49 μIU/mL	≥50 μIU/mL
26-96 h	30-36 μIU/mL	37-49 μIU/mL	≥50 μIU/mL
97-312 h			≥17 μIU/mL
≥313 h			≥15 μIU/mL

underwent NBS in the Wisconsin state NBS program were eligible for inclusion in the study. We excluded infants whose first NBS was done after 96 hours of life, infants who died without a diagnosis of congenital hypothyroidism, and infants with incomplete data.

The Wisconsin state NBS program uses a primary thyroid-stimulating hormone (TSH) test strategy to screen for congenital hypothyroidism. The NBS program performs serial screenings for infants with an extended hospital stay. After the initial screening at 24-48 hours, in infants with a birth weight <2200 g, a second specimen is collected at 2 weeks of life, a third specimen is collected at 28-30 days of life or at discharge, whichever comes first, and specimens are collected monthly thereafter until discharge. NBS TSH level was measured by solid-phase, time-resolved fluoroimmunoassay from dried newborn blood spots using the AutoDELFIA platform (PerkinElmer, Waltham, Massachusetts). TSH measurements were converted to estimated serum levels using the following conversion factor: 1 μU/mL blood = 2.22 μU/mL serum (assuming 55% hematocrit). The abnormal TSH ranges and actions for observed concentrations based on age at the time of collection is presented in **Table I**.

NBS results for congenital hypothyroidism and demographic data (ie, gestational age, birth weight, race, sex, and multiple gestation) were obtained from the Newborn Screening Laboratory at the Wisconsin State Laboratory of Hygiene. The demographic data are reported on NBS cards. Gestational age determination was performed by obstetric care providers using best obstetric gestational age estimates. Extremely preterm infants were defined as preterm infants born before 28 weeks of gestation. Extremely low birth weight (ELBW) infants were defined as infants with birth weight <1000 g. Confirmed cases of congenital hypothyroidism were subdivided into early TSH elevation (eTSH), defined as congenital hypothyroidism detected on initial NBS performed between 0 and 96 hours of age, and delayed TSH elevation (dTSH), defined as normal initial screening with congenital hypothyroidism detected on subsequent screening. A diagnosis of dTSH was made based on a persistent serum TSH level >8 μIU/mL after a positive NBS.

We also measured the incidence of subclinical hypothyroidism, defined as TSH 6-15 μIU/ml on NBS at 1 month of age (28-35 days) and last NBS after 1 month of age of infants who didn't have a positive NBS.

Data analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina). Continuous variables were reported as mean ± SD, and categorical variables were reported as count and percentage. Multivariate logistic regression analyses were performed to identify demographic factors associated with dTSH. A 2-sided *P* value <.05 was used to determine the significance of variables in all analyses.

The University of Wisconsin-Madison's Institutional Review Board approved the study with a waiver of consent.

Results

A total of 334 444 infants underwent NBS in Wisconsin between 2012 and 2016. Among that birth cohort, 3858 infants (1.2%) were born before 32 weeks of gestational age. After exclusion of 721 infants based on predefined exclusion criteria, the final study cohort comprised 3137 infants (**Figure 1**). Mean gestational age and birth weight were 28.4 ± 2.3 weeks and 1196 ± 397 g, respectively. The study cohort comprised 33% extremely preterm infants and 34% ELBW infants; 53% were male, and 62% were Caucasian.

Forty-nine infants were diagnosed with congenital hypothyroidism, and the overall incidence of congenital hypothyroidism among preterm infants born before 32 weeks was 1.56% (1 of 64). Congenital hypothyroidism with eTSH was identified in 4 infants, for an incidence of 0.13% (1 of 784); 45 cases of dTSH were identified, for an incidence of 1.43% (1/70) (**Table II**). The incidence of dTSH in the different subgroups of the study cohort is presented in **Table III**.

On multivariate logistic regression analysis, birth weight categories 501-1000 g and ≤500 g were significantly associated with

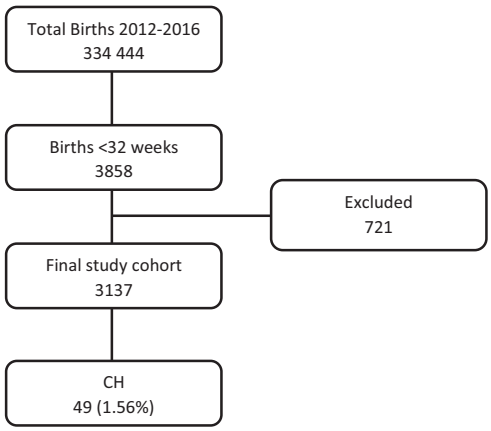

Figure 1. Study population. *CH*, congenital hypothyroidism.

Table II. Incidence of congenital hypothyroidism

Category	No. of cases	Incidence, cases/100 births (95% CI)
Early TSH elevation	4	0.13 (0.05-0.33)
Delayed TSH elevation	45	1.43 (1.07-1.91)
Overall	49	1.56 (1.18-2.06)

the development of dTSH (Table IV). Multiple gestation and initial TSH values of 5-10, 15-20, and >20 μIU/mL were also significantly associated with dTSH. Gestational age category was not associated with dTSH in multivariate logistic regression analysis.

Infants with dTSH were identified at a mean age of 46.5 days. NBS performed at 2 weeks identified the greatest number of infants with dTSH (n = 18). NBS performed at 1 month, 2 months, and after 2 months identified 10, 9, and 8 infants with dTSH, respectively. Fifteen of the infants with dTSH had markedly elevated TSH level >100 μIU/mL at the time of diagnosis. Infants with marked TSH elevation did not differ from those with lower TSH elevations in terms of demographic characteristics or TSH level on initial NBS (Table V), but they were diagnosed at a significantly earlier age (mean, 20.5 days vs 59.5 days).

Confirmatory TSH measurements were available for 48 infants, and confirmatory free thyroxine (FT4) levels were available for 39 infants (2 infants with eTSH and 37 infants with dTSH). Confirmatory TSH and FT4 levels for 37 infants with dTSH are presented in Figure 2. Confirmatory TSH levels ranged from 8 μIU/mL to 525 μIU/mL. Confirmatory FT4 levels ranged from 0.2 to 1.43 ng/dL. One infant with eTSH and 19 infants with dTSH had low FT4, defined as <0.8 ng/dL.

Among infants without a positive NBS, 348 infants (11%) had a TSH level of 6-15 μIU/mL on the NBS at 1 month (ie, 25-35 days), including 68 infants (2%) with a TSH level of 10-15 μIU/mL. An even greater number of patients had a mildly elevated TSH level on their last NBS performed after age 1 month: 400 infants with TSH 6-10 μIU/mL and 84 infants with TSH 10-15 μIU/mL.

Table III. Characteristics of population and incidence of congenital hypothyroidism according to subgroup

Characteristics	Number of subjects	dTSH	No congenital hypothyroidism
Gestational age, wk			
22-24	229	5 (2.2)	224 (97.8)
25-27	793	25 (3.2)	768 (96.8)
28-29	827	8 (1.0)	819 (99.0)
30-31	1284	7 (0.5)	1277 (99.5)
Birth weight, g			
≤500	52	4 (7.7)	48 (92.3)
501-1000	1026	36 (3.5)	990 (96.5)
1001-1500	1318	4 (0.3)	1314 (99.7)
>1500	737	1 (0.1)	736 (99.9)
Sex			
Male	1659	24 (1.4)	1635 (98.6)
Female	1474	21 (1.4)	1453 (98.6)
Race			
Caucasian	1954	29 (1.5)	1925 (98.5)
African American	757	10 (1.3)	747 (98.7)
Other	279	4 (1.4)	275 (98.6)
Unknown	143	2 (1.4)	141 (98.6)
Gestation			
Singleton	2355	29 (1.2)	2326 (98.8)
Multiple	778	16 (2.1)	762 (97.9)
Initial TSH level, μIU/mL			
<5	2113	20 (0.9)	2093 (99.1)
5-10	664	12 (1.8)	652 (98.2)
10-15	210	5 (2.4)	205 (97.6)
15-20	85	5 (5.9)	80 (94.1)
>20	61	3 (4.9)	58 (95.1)

Table IV. Risk factors for dTSH on multivariate logistic regression analysis, comparing dTSH with no congenital hypothyroidism among preterm infants born before 32 weeks of gestation

Risk factors	OR	95% CI	*P* value
Gestational age, wk			
22-24	2.6	0.9-7.2	.06
25-27	2.1	0.6-7.7	.26
28-29	4.0	1.0-17.1	.05
30-31	Reference		
Birth weight, g			
≤500	108.7	9.2-999.0	.0002
501-1000	36.1	4.1-319.5	.001
1001-1500	2.7	0.3-25.5	.38
>1500	Reference		
Sex			
Male	Reference	0.4-1.4	
Female	0.75		.36
Race			
Caucasian	Reference	0.4-1.7	
African American	0.78	0.4-3.1	.52
Other	1.04		.94
Gestation			
Singleton	Reference	1.2-4.4	
Multiple	22.3		.01
Initial TSH			
<5	Reference	1.5-7.1	
5-10	3.3	0.9-9.1	.002
10-15	2.9	2.8-26.3	.07
15-20	8.6	1.8-28.6	.0002
>20	7.3		.004

Discussion

This study confirms that the rate of congenital hypothyroidism identified through NBS is much higher in preterm infants compared with term-born infants. We have identified associations between dTSH and lower birth weight, multiple gestation, and elevated initial TSH level. We also have determined the incidence of dTSH for different patient subgroups among preterm infants.

The overall incidence of congenital hypothyroidism in our population-based cohort of preterm infants born at <32 weeks of gestation was 1.56% (1 in 64). The overall incidence of congenital hypothyroidism was 1.9% (1 of 52) in very low birth weight (VLBW) infants and 3.7% (1 of 27) in ELBW infants. The incidence of congenital hypothyroidism in our cohort is greater than that reported previously.[9,10] During the study

Table V. Comparison between dTSH cases with dried blood spot TSH >100 μIU/mL and TSH <100 μIU/mL at the time of diagnosis

Variables	dTSH cases (n = 45)	dTSH cases with TSH <100 μIU/mL (n = 30)	dTSH cases with TSH <100 μIU/mL (n = 15)	*P* value
Gestational age, wk, mean ± SD	26.7 ± 2.2	26.9 ± 2.2	26.3 ± 2.3	.40
Birth weight, g, mean ± SD	752.0 ± 256.9	731.1 ± 229.3	793.7 ± 309.4	.76
Male sex, n (%)	24 (53)	18 (60)	6 (40)	.22
Race, n (%)				
Caucasian	29 (64)	20 (71)	9 (60)	.62
African American	10 (22)	6 (21)	4 (27)	
Other	4 (9)	2 (7)	2 (13)	
Unknown	2 (4)	2 (7)	0 (0)	
Singleton gestation, n (%)	29 (64)	17 (57)	12 (80)	.18
Initial TSH, μIU/mL, mean ± SD	7.7 ± 7.7	7.6 ± 7.6	7.8 ± 8.1	.89
Time of diagnosis, d, mean ± SD	46.5 ± 45.2	59.5 ± 50.1	20.5 ± 11.5	.007

period, the overall incidence of congenital hypothyroidism in Wisconsin was 1 in 579 in infants born at 32-36 weeks of gestation and 1 in 1488 in infants born at ≥37 weeks of gestation. Even though infants born at <32 weeks of gestation accounted for approximately 1% of births in Wisconsin during the study period, these very preterm and extreme preterm infants accounted for 17% of all congenital hypothyroidism cases detected by the NBS program. These data concur with a previously reported 14-fold higher incidence of congenital hypothyroidism in VLBW infants compared with non-VLBW infants in the New England NBS program.[9] Similarly, congenital hypothyroidism with dTSH occurred in 1 of 95 VLBW infants, according to a recent study by the Rhode Island NBS program.[11] Mild cases of congenital hypothyroidism and dTSH account for this increased incidence of congenital hypothyroidism among preterm infants.[2] Taken together, these reports

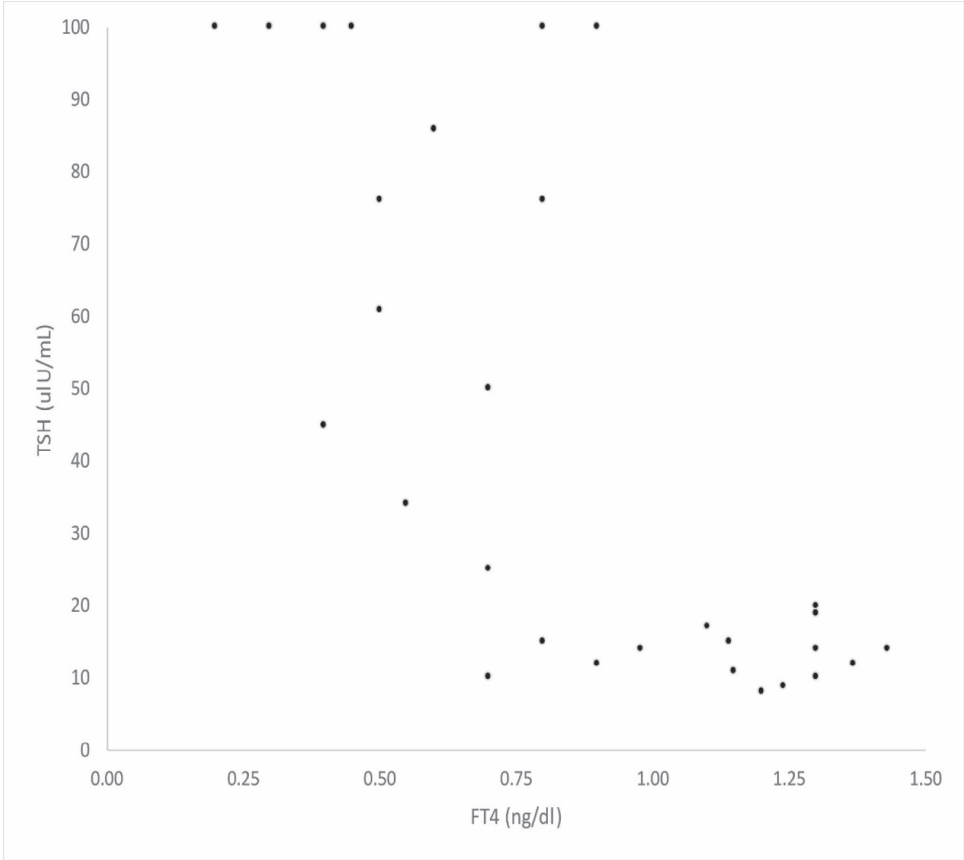

Figure 2. Confirmatory TSH and FT4 levels at the time of diagnosis for infants with dTSH (n = 37). TSH values >100 μIU/mL are truncated at 100 μIU/mL.

and our present findings support the idea that the higher overall incidence of congenital hypothyroidism is due, at least to a significant degree, to increased survival of VLBW and ELBW infants and more rigorous NBS methodology.

In the present study, the incidence of dTSH was 1.8% (1 in 54) in VLBW infants and 3.7% (1 in 27) ELBW infants. The incidence of dTSH was higher than that reported by Woo et al in a study in which the TSH cutoff after 96 hours was similar to that in our study.[11] This increase is likely due to the greater number of screenings and the timing of screenings in the Wisconsin NBS program. In the Wisconsin NBS program, repeat screenings are performed at 2, 4, 8, and, if still being treated, 12 weeks, compared with screenings at 2, 6, and 10 weeks in the Rhode Island NBS program.

Infants with dTSH were detected in increased frequency in younger gestational age and lower birth weight groups. Birth weight categories of 501-1000 g and ≤500 g were independently associated with dTSH. Previous reports have identified birth weight as associated with dTSH.[12] It is possible that eTSH and dTSH with markedly elevated TSH levels are the same disease process detected by NBS at different time points based on infants' hypothalamic-pituitary-thyroid response. Extremely preterm or ELBW infants may have an attenuated hypothalamic-pituitary-thyroid response that could delay the rise in TSH detected on initial NBS. A possible alternative explanation for the late TSH rise may be recovery from sick euthyroid syndrome, given that extremely preterm or ELBW infants are more likely than infants born at older gestational age to be critically ill from cardiorespiratory disease related to prematurity. A recent case-control study concluded that the variables associated with dTSH likely reflect the severity of infants' clinical condition in the neonatal intensive care unit (NICU).[13] Another explanation for the increased detection of dTSH in younger and smaller infants might be the increased frequency of NBS. In this cohort, extremely preterm infants born at <28 weeks underwent an average of 4 NBSs, compared with 3 screenings in infants born at 28-31 weeks.

Similar to our present findings, other studies have identified an association between dTSH and multiple gestation.[12] Elevated initial TSH level was also independently associated with dTSH. A similar association was reported in a study of preterm and term infants requiring admission to NICU.[14] It is likely that in some infants with mildly elevated TSH levels on initial screening, elevated TSH levels persist for several weeks.

Currently, many NBS programs in the US obtain routine or discretionary repeat NBSs to detect dTSH.[15] Some individual NICUs perform their own thyroid function screening in countries and states that do not obtain a repeat NBS.[12-17] Because these infants are under the care of neonatology providers for a period of weeks to months, whether repeat screenings should be done at the state level or the individual NICU level remains a matter of debate. For states in which repeat NBS is not routinely done, our present findings suggest that it would still be prudent to obtain repeat thyroid function screenings similar to any other NICU screening, such as a screening head ultrasound for intraventricular hemorrhage or a screening eye examination for retinopathy of prematurity. Moreover, if screening after age 1 month had not been performed, 17 infants (38% of those with dTSH) would have gone undetected. Thus, we recommend serial screening for dTSH in preterm infants born at <32 weeks of gestation to improve detection rates.

Preterm infants are at an elevated risk for adverse neurodevelopmental outcomes owing to complications associated with prematurity.[18,19] However, although preterm infants with dTSH may have a smaller mean head circumference,[11] the extent to which mild thyroid dysfunction contributes to neurodevelopmental outcomes remains uncertain. Despite several decades of experience with this mild form of congenital hypothyroidism, only limited evidence exist on the effects and natural history of this disease. Although most cases of mild congenital hypothyroidism and dTSH appear to be transient, a significant proportion of infants (23%-47%) develop permanent congenital hypothyroidism or hyperthyrotropinemia.[20,21]

In addition to the infants diagnosed with congenital hypothyroidism, 484 infants (15%) in our study cohort had a mildly elevated TSH level (6-15 μIU/mL) on their last NBS before discharge from the NICU. However, these TSH measurements on NBS were not confirmed with serum measurements. These infants were not diagnosed with thyroid dysfunction and did not undergo follow-up studies performed in accordance with the current NBS protocol. This group of infants may have subclinical hypothyroidism.[8,22] According to 2014 European Thyroid Association's guidelines for the management of subclinical hypothyroidism in pregnancy and in children, a serum TSH concentration >5 mU/L after age 1 month can be considered abnormal.[22] However, gestational age-specific TSH cutoffs for diagnosing subclinical hypothyroidism in preterm infants are not available at this time. The effects and natural history of this form of thyroid dysfunction also remain unclear.

Limitations of this study include its retrospective design, although the data were collected prospectively by the NBS program. Information on maternal characteristics, perinatal characteristics, or neonatal outcomes by birth cohort is lacking, because these data were not available to the NBS program. Patients with chromosomal or multiple congenital anomalies could not be excluded, because this information also was not available to the NBS program. There is a slight probability that some infants born at <32 weeks and weighing >2200 g at birth were excluded from serial NBS. The natural history of congenital hypothyroidism and long-term outcomes of the patients diagnosed with congenital hypothyroidism were also not available to the NBS program. Finally, although our study cohort is the largest cohort of preterm infants analyzed for congenital hypothyroidism to date, data from the Wisconsin NBS program might not be generalizable to other NBS programs owing to differences in racial composition. The NBS screening protocol described here includes more frequent screenings than are specified in the current consensus guidelines.[23] The TSH cutoff beyond 96 hours of life differs across state NBS programs,[15] and thus the incidence of dTSH in the present study might not be directly comparable with that reported in other NBS programs.

Further studies are needed to determine the natural history of congenital hypothyroidism diagnosed by NBS in preterm

infants, that is, the persistence versus resolution of congenital hypothyroidism in this group and, in those demonstrating persistent congenital hypothyroidism, its effects on growth and neurodevelopment. ■

Submitted for publication Aug 21, 2018; last revision received Oct 31, 2018; accepted Nov 26, 2018

Reprint requests: Dinushan C. Kaluarachchi, MBBS, 411 McConnell Hall, 1010 Mound St, Madison, WI 53715. E-mail: kaluarachchi@pediatrics.wisc.edu

References

1. Corbetta C, Weber G, Cortinovis F, Calebiro D, Passoni A, Vigone MC, et al. A 7-year experience with low blood TSH cutoff levels for neonatal screening reveals an unsuspected frequency of congenital hypothyroidism (CH). Clin Endocrinol (Oxf) 2009;71:739-45.
2. Mitchell ML, Hsu HW, Sahai I. The increased incidence of congenital hypothyroidism: fact or fancy? Clin Endocrinol (Oxf) 2011;75:806-10.
3. Mengreli C, Kanaka-Gantenbein C, Girginoudis P, Magiakou MA, Christakopoulou I, Giannoulia-Karantana A, et al. Screening for congenital hypothyroidism: the significance of threshold limit in false-negative results. J Clin Endocrinol Metab 2010;95:4283-90.
4. Wassner AJ, Brown RS. Congenital hypothyroidism: recent advances. Curr Opin Endocrinol Diabetes Obes 2015;22:407-12.
5. Ford G, LaFranchi SH. Screening for congenital hypothyroidism: a worldwide view of strategies. Best Pract Res Clin Endocrinol Metab 2014;28:175-87.
6. Hamilton BE, Martin JA, Osterman MJ, Curtin SC, Matthews TJ. Births: final data for 2014. Natl Vital Stat Rep 2015;64:1-64.
7. Stoll BJ, Hansen NI, Bell EF, Walsh MC, Carlo WA, Shankaran S, et al. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993-2012. JAMA 2015;314:1039-51.
8. LaFranchi SH. Newborn screening strategies for congenital hypothyroidism: an update. J Inherit Metab Dis 2010;33(Suppl 2):S225-33.
9. Larson C, Hermos R, Delaney A, Daley D, Mitchell M. Risk factors associated with delayed thyrotropin elevations in congenital hypothyroidism. J Pediatr 2003;143:587-91.
10. Mandel SJ, Hermos RJ, Larson CA, Prigozhin AB, Rojas DA, Mitchell ML. Atypical hypothyroidism and the very low birthweight infant. Thyroid 2000;10:693-5.
11. Woo HC, Lizarda A, Tucker R, Mitchell ML, Vohr B, Oh W, et al. Congenital hypothyroidism with a delayed thyroid-stimulating hormone elevation in very premature infants: incidence and growth and developmental outcomes. J Pediatr 2011;158:538-42.
12. Kaluarachchi D, Colaizy T, Pesce L, Tansey M, Klein J. Thyroid dysfunction in very low birth weight premature infants. J Perinatol 2017;37:277-82.
13. Zung A, Bier Palmon R, Golan A, Troitzky M, Eventov-Friedman S, Marom R, et al. Risk factors for the development of delayed TSH elevation in neonatal intensive care unit newborns. J Clin Endocrinol Metab 2017;102:3050-5.
14. Zung A, Yehieli A, Blau A, Almashanu S. Characteristics of delayed thyroid-stimulating hormone elevation in neonatal intensive care unit newborns. J Pediatr 2016;178:135-40.e1.
15. Kilberg MJ, Rasooly IR, LaFranchi SH, Bauer AJ, Hawkes CP. Newborn screening in the US may miss mild persistent hypothyroidism. J Pediatr 2018;192:204-8.
16. Lee JH, Kim SW, Jeon GW, Sin JB. Thyroid dysfunction in very low birth weight preterm infants. Korean J Pediatr 2015;58:224-9.
17. Uchiyama A, Sugihara S, Kusuda S. National survey on concepts for congenital hypothyroidism screening in neonatal intensive care units in Japan. Pediatr Int 2016;58:1311-5.
18. Serenius F, Källén K, Blennow M, Ewald U, Fellman V, Holmström G, et al. Neurodevelopmental outcome in extremely preterm infants at 2.5 years after active perinatal care in Sweden. JAMA 2013;309:1810-20.
19. Serenius F, Ewald U, Farooqi A, Fellman V, Hafström M, Hellgren K, et al. Neurodevelopmental outcomes among extremely preterm infants 6.5 years after active perinatal care in Sweden. JAMA Pediatr 2016;170:954-63.
20. Vigone MC, Caiulo S, Di Frenna M, Ghirardello S, Corbetta C, Mosca F, et al. Evolution of thyroid function in preterm infants detected by screening for congenital hypothyroidism. J Pediatr 2014;164:1296-302.
21. Ford GA, Denniston S, Sesser D, Skeels MR, LaFranchi SH. Transient versus permanent congenital hypothyroidism after the age of 3 years in infants detected on the first versus second newborn screening test in Oregon, USA. Horm Res Paediatr 2016;86:169-77.
22. 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;3:76-94.
23. Léger J, Olivieri A, Donaldson M, Torresani T, Krude H, van Vliet G, et al. European Society for Paediatric Endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. J Clin Endocrinol Metab 2014;99:363-84.