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Gil Rosen

Dana-Dwek Children's Hospital, Tel Aviv Sourasky Medical Center

Anat Lavie

Tel Aviv Sourasky Medical Center

Michal Yackobovitch-Gavan

Tel Aviv University

Shlomo Almashanu

Ministry of Health

Meital Priel

Dana-Dwek Children's Hospital, Tel Aviv Sourasky Medical Center

Ariel Many

Tel Aviv Sourasky Medical Center

Yael Lebenthal

Dana-Dwek Children's Hospital, Tel Aviv Sourasky Medical Center

Avivit Brener (✉ avivitb@tlvmc.gov.il)

Dana-Dwek Children's Hospital, Tel Aviv Sourasky Medical Center

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Congenital hypothyroidism can dictate the mode of delivery and intra-labor medication usage

Gil Rosen, MD¹, Anat Lavie, MD², Michal Yackobovitch-Gavan, PhD³, Shlomo Almashanu, PhD⁴, Meital Priel, MD⁵, Ariel Many, MD, PhD², Yael Lebenthal, MD¹, Avivit Brenner, MD¹

¹Pediatric Endocrinology and Diabetes Unit, Dana-Dwek Children's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel affiliated with the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. (gilrosen1@gmail.com) (yaelleb@tlvmc.gov.il) (avivitb@tlvmc.gov.il)

²Department of Obstetrics and Gynecology, Lis Maternity and Women's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel affiliated with the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. (netkin@hotmail.com) (arielm@tlvmc.gov.il)

³Department of Epidemiology and Preventive Medicine, School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (michalyg2000@gmail.com)

⁴The National Newborn Screening Program, Ministry of Health, Tel-Hashomer, Israel (shlomo.almashanu@sheba.health.gov.il)

⁵Department of Pediatrics, Dana-Dwek Children's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel affiliated with the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel (moshe.meital@gmail.com)

Correspondence: Dr. Avivit Brenner

Pediatric Endocrinology and Diabetes Unit
Dana Dwek Children's Hospital
Tel Aviv Sourasky Medical Center
6 Weizmann Street, Tel Aviv 6423906, Israel
Telephone: +972-3-6972513, Fax: +972-3-6974306
Email: avivitb@tlvmc.gov.il

Abstract

Pregnancy and parturition reflect the complex interaction between physiologic conditions of the mother and her offspring, and fetal health characteristics may affect maternal health throughout pregnancy and delivery. We investigated the characteristics of the mother-infant dyad of term infants detected by the National Newborn Screening Program as having congenital hypothyroidism (CH) (131 out of 108,717; 0.12%). Three years of surveillance in our Pediatric Endocrine Clinic revealed that 65 had transient CH and 66 had permanent CH. A higher proportion of deliveries of CH infants required vacuum assistance, and more infants with CH were born through a cesarean section compared to the general population ($p<0.001$). Medication during labor also differed, with higher rates of oxytocin ($p<0.001$) and antibiotics ($p=0.008$) administered to mothers of CH infants. A multivariate logistic regression model revealed an increased demand for oxytocin administration during the labor of a CH infant in a hypothyroidism severity-dependent manner, expressed as a threefold risk associated with permanent but not transient CH. Our findings of increased utilization of medical interventions during the labor and delivery of CH infants suggest that the prenatal fetal thyroid function affects the development and progress of labor and delivery, in response to oxytocin.

Introduction

Pregnancy and parturition reflect the complex interaction between the state of health of the mother and her offspring. The Developmental Origins of Health and Disease (DOHaD) hypothesis (formerly “fetal programming”) postulated that exposure to maternal conditions affecting the intrauterine environment may have consequences on their offspring’s health during infancy, childhood, and even adulthood^{1, 2}. There is also evidence that fetal health characteristics may affect maternal health outcomes throughout pregnancy and delivery³. A better understanding of the bidirectional nature of health characteristics may assist in creating an integrated obstetric medical approach which will take into consideration the mother-infant dyad rather than separate mother and infant.

Neonatal thyroid screening aims to detect infants with congenital hypothyroidism (CH) in order to initiate thyroid hormone replacement therapy as soon as possible and prevent mental retardation⁴. The screen detects infants with anatomic (agenesis or ectopic dysgenesis) or genetic thyroid disorders leading to permanent CH, as well as infants with transient abnormal thyroid function who do not require lifelong thyroid replacement therapy^{5, 6}. In transient CH, the appropriate maturation of the hypothalamic-pituitary-thyroidal axis may be interrupted by maternal, perinatal, or neonatal factors⁷.

The evolution of environmental, social, and medical influences may have diverse effects on the mother-infant dyad. The past decade has witnessed an increase in the utilization of obstetric interventions, such as assisted reproduction therapy⁸, the number of medications administered during pregnancy and labor, and a rise in the rates of caesarean sections⁹. Importantly, these medical and surgical interventions may influence the hypothalamic-pituitary-thyroidal axis function⁷. In this study, we aimed to investigate characteristics of the mother-infant dyad of infants detected as having CH in order to identify contributing and non-contributing factors.

Patients and methods

Study Population. We conducted a retrospective cohort study of term infants (gestational age ≥ 37 weeks) delivered liveborn at Lis Maternity and Women's Hospital, Tel-Aviv Sourasky Medical Center (TASMC) between January 1, 2010 and December 30, 2017. Data on maternal, pregnancy, delivery, and perinatal characteristics of the mother-infant dyads were retrieved from the hospital's electronic database that became available from 2010. Newborn screening for CH among full-term newborns was routinely practiced by a single screen of total T4 (TT4) at 48-72 hours of age, with a subsequent measurement of thyroid-stimulating hormone (TSH) when low levels of TT4 were obtained¹⁰. Infants detected by the neonatal screen are routinely referred to TASMC's Pediatric Endocrine Unit in Dana Dwek Children's Hospital for further evaluation and surveillance. The Israeli National Newborn Screening Program Database was linked with the electronic medical files of the Pediatric Endocrine Unit to generate a list of infants with CH born at Lis Maternity Hospital. The medical files of those infants were searched for maternal, perinatal, neonatal, and disease course characteristics. Infants were categorized as having transient or permanent CH according to the necessity of l-thyroxine treatment after the age of 3 years.

Data collection. The information in the electronic medical files contains both self-reported patient information and physician's notes on diagnoses, management, and surveillance. The information retrieved from the maternity hospital database included maternal age, number of the current pregnancy, number of previous live births, smoking during pregnancy, reported weight before pregnancy and measured weight before delivery, medical background (gestational diabetes, thyroid disease, chronic medication use), number of fetuses (singleton, twins), type of delivery (spontaneous vaginal, vacuum extraction, cesarean section [elective

or urgent]), medications administered during delivery (Pitocin® [oxytocin injection, USP], anesthesia [epidural, spinal, or general] and antibiotics) and newborn data (gestational age [GA, weeks], birth weight [kilograms], and APGAR score at 1 and 5 minutes after birth).

The data retrieved from medical files of infants diagnosed with CH included additional data on sociodemographic (socioeconomic position [SEP] by home address, ethnicity), conception-related (spontaneous, assisted fertilization therapy), and CH-related characteristics (neonatal thyroid screen test results [TT4, TSH], confirmatory thyroid test results [TSH, FT4] and thyroid imaging [scintigraphy and ultrasonography]). Corrected birth weight z-scores were calculated for infants with CH by means of PediTools Electronic Growth Chart Calculators, based upon the Fenton growth chart for preterm infants¹¹. Appropriate birth weight for gestational age (AGA) was defined as corrected birth weight z-scores of -1.28 to 1.28, small for gestational age (SGA) as birth weight z-scores <-1.28, and large for gestational age (LGA) as birth weight z-scores >1.28.

SEP was analyzed by home address according to the Israel Central Bureau of Statistics' Characterization and Classification of Statistical Areas within Municipalities and Local Councils by the Socio-Economic Level of the Population 2015¹². SEP was determined by cluster of localities of residence, ranging from 1 to 10, with 1 being the lowest rating and 10 the highest. The SEP index is an adjusted calculation of 14 variables that measure social and economic levels in the domains of demographics, education, standard of living, and employment (ranging from the lowest -2.797 to the highest 2.590).

Ethics. The study was approved by the Ethics Committee of the Tel-Aviv Sourasky Medical Center according to the Helsinki Declaration. Informed consent by the participants was waived since the data were retrieved from the subjects' medical records and all personal

identification was omitted. The data were handled in accordance with the principles of Good Clinical Practice.

Statistical analysis. Data were analyzed by the IBM SPSS software (IBM SPSS Statistics for Windows, Version 27, Armonk, NY: IBM Corp.). Continuous data are presented as mean $\pm$ standard deviation (SD, normal distribution) or median (interquartile range [IQR], skewed distribution), and as number and percentage for categorical variables. Differences in continuous data between groups were examined using independent-sample t-tests (normally distributed data) or Mann-Whitney U-tests (skewed data). The Chi-squared tests (or Fisher's exact test for small count tables) were used to examine the differences in categorical data. Stepwise multivariate logistic regression models were used to evaluate the selected factors (including delivery-related and infant characteristics) correlated with the diagnosis of CH and transient vs. permanent CH. A p value of ≤ 0.05 was considered significant.

Results

During the study period, 117,529 infants were liveborn in Lis Maternity and Women's Hospital of TASMC. Excluded from the study were 8810 preterm infants and two infants diagnosed with 21 trisomy. Of 108,717 infants born at term during the study period, 131 (0.12%) were detected by the National Newborn Screening Program as having CH. Three years of surveillance in the Pediatric Endocrine Clinic revealed that 65 (49.6%) had transient CH and 66 (50.4%) had permanent CH. Thyroid scintigraphy demonstrated athyreosis in 10 (7.6%) infants, an ectopic thyroid gland in 30 (22.9%), and dysharmonogenesis in six (4.6%). Thyroid scintigraphy performed in infants with transient CH revealed normal uptake.

Characteristics of mother-infant dyads with CH compared to the general population are presented in Table 1. The median age of the mothers was 32 years (range 15-50 years),

and the median maternal pre-pregnancy weight was 59 kg (range 31- 130 kg), with a median weight gain during pregnancy of 13 kg (range 0- 40 kg). In addition, 4.9% of the mothers were smokers, and 6.2% were diagnosed with gestational diabetes. There was no significant difference between the groups for any of these parameters. The distribution of mode of delivery differed between groups, with fewer CH infants born by spontaneous vaginal delivery compared to the general population (55.7% vs. 72.2%, $p < 0.001$). The frequency of maternal medication use during labor differed significantly between groups, with increased administration of oxytocin (43.5% vs. 34.9%, $p < 0.001$), antibiotics (8.4% vs. 3.9%, $p = 0.008$), and anesthesia (87.8% vs. 76.3%, $p < 0.001$) to mothers of CH infants compared to the general population. The CH infants were born at a median GA of 39 weeks (range 37-44), and 51.3% were males. The median birthweight of the infants of the general population was 3.270 kilograms (range 1.165-8.810 kg), and the median birthweight of the CH infants was significantly lower ($p = 0.002$).

The characteristics of the mother-infant dyads of CH infants stratified according to the diagnosis of transient and permanent CH is presented in Table 2. Maternal age, gravidity, and parity did not differ between the two groups. The median SEP cluster of the cohort was 7 (range 2- 10), the index was 0.783 (range -1.305 to 2.667), the vast majority were Jewish, and there were no significant differences in SEP or ethnicity between the transient and permanent CH groups. The mothers did not differ in weight prior to delivery and weight gain during pregnancy, or in their smoking or medical history. Five percent of the pregnancies followed assisted reproductive therapy, most of them after in vitro fertilization treatment. The mode of delivery and extent of medication administration during labor did not differ between the groups. The majority of infants with transient CH were males, while the majority of infants with permanent CH were females, a difference that did not reach statistical significance. The infants with transient CH were born at an earlier GA ($p = 0.011$). The median birth weight z-

scores for all the CH infants were -0.34 (range -2.36 to 2.85), and 7.7% of the infants with transient CH were born SGA vs 18.2% of infants with permanent CH (p = non-significant for all). Infants with permanent CH had lower TT4 levels and higher TSH levels on thyroid screening tests (p = 0.03 and p < 0.001, respectively), and lower FT4 levels and higher TSH levels on confirmatory thyroid testing compared to those with transient CH (p < 0.001 for both).

Multivariate forward logistic regression models to evaluate the factors associated with the diagnosis of any CH, transient and permanent CH in the general population and permanent CH in the CH group are presented in Table 3. The analysis performed on the entire cohort revealed that the administration of oxytocin during labor was associated with the diagnosis of permanent CH (odds ratio [OR]=2.77, p < 0.001), and that none of the neonatal or maternal characteristics were associated with the diagnosis of transient CH. The analysis of the entire CH group revealed that birth weight z-scores and screening TSH levels were significantly associated with the diagnosis of permanent CH (OR=1.52, p = 0.05 and OR=0.99, p < 0.001 respectively).

Discussion

The aim of this study was to analyze the characteristics of the mother-infant dyad of CH infants in order to identify contributing and non-contributing factors. The analyses revealed increased utilization of medical intervention during the labor and delivery of the infants with any CH. Although the mothers of CH infants did not differ in age, weight, and obstetric and medical background, the labor process of the CH infants was different than that of the general population. Our findings suggest that the labor and delivery of CH infants required increased utilization of medical intervention. Specifically, the statistical analyses revealed an increased demand for oxytocin administration during the labor of a CH infant in a hypothyroidism

severity-dependent manner, and showed a threefold risk in those with permanent CH but not with transient CH. These findings suggest that the prenatal fetal thyroid function has a role in the development and progress of labor and delivery in response to oxytocin.

Maternal characteristics, such as older age^{13, 14} and obesity¹⁵, have been linked with various adverse pregnancy outcomes, including complications during pregnancy and delivery leading to increased morbidity in the newborn. In our study, maternal age and maternal parity did not differ, and maternal weight prior to conception and weight gain during pregnancy were similar for mothers of infants with CH as for those in the general population. As such, neither maternal age nor maternal obesity and their implications provided any explanations for the differences in the delivery of infants with CH.

Only 55% of infants with CH were born through a spontaneous vaginal delivery. A higher proportion of CH deliveries required vacuum assistance, and more infants with CH were born by means of a cesarean section compared to the general population. Cesarean delivery has short- and long-term implications upon the health of both mother and infant^{16, 17}. Infants born through cesarean delivery may have compromised adaptation to the extrauterine environment manifested by transient CH. This assumption did not hold true in our study, since the rate of cesarean deliveries did not differ between transient and permanent CH, and the type of delivery did not predict transient CH. The mode of delivery determines the acquisition of the newborn's intestinal microbiota, and the beneficial exposure of the newborn to the maternal vaginal microbiota is prevented in cesarean birthing^{18, 19}. This early-life experience, which may be influenced by fetal hypothyroidism, may affect development of the early immune system with possible implications upon allergic, autoimmune, and metabolic morbidities during childhood and adulthood^{20- 22}.

The rate and mode of anesthesia utilization differed between the deliveries of CH infants and the general population. Anesthesia was administered to more mothers of CH

infants, and a higher proportion underwent spinal anesthesia. This may be attributed to the increased demand for instrumental and surgical deliveries of CH infants. Spinal anesthesia may result in sustained spinal hypotension with the complication of neonatal acidosis²³. It could be assumed that the acid-base compromise would contribute to the development of transient CH, however, the type of anesthesia did not differ between our transient and permanent CH infants nor was it identified as a predictive factor for transient CH.

The fetal thyroid milieu may play a role in initiating and maintaining uterine contractions during delivery in response to endogenous oxytocin. Fetal hypothyroidism had been found to reduce uterine contractions (amplitude and frequency) in response to oxytocin administration in rat mothers²⁴. Another animal study linking oxytocin administration during delivery and maternal thyroid function reported that administration of intravenous oxytocin to rats decreased their TSH, FT4, and FT3 levels²⁵. Thus, oxytocin administration may transiently affect the thyroid axis function of the mother and augment a pre-existing maternal condition. However, maternal hypothyroidism is not the explanation for the findings in our study, since all mothers are screened for hypothyroidism during pregnancy and treated appropriately²⁶. Moreover, only 7% of the mothers of our CH infants were diagnosed as having thyroid disease, and they were all treated and monitored during the index pregnancy. Noteworthy, we found oxytocin administration during delivery as a predictor solely of permanent CH. Our findings support the role of prenatal fetal hypothyroidism in the abnormal progression of delivery, since oxytocin administration was even more prominent in the deliveries of infant with permanent CH, most of them having an anatomical explanation.

In this study we chose not to include premature infants in order to limit the effects of maternal, obstetric, and infantile medical conditions other than CH on the process of delivery. Premature infants are overrepresented in the CH screen detection group due to the lack of age-specific thyroid function cutoffs as well as to various medical conditions complicating

prematurity²⁷. It is plausible that the premature delivery of CH infants will be affected in a distinctive GA-stratified manner by fetal hypothyroidism. Further studies are warranted to characterize the mother-infant dyad of premature CH infants.

Our study is not without limitations. Since the data of the SEP grading and ethnic origin of mothers from the general population was lacking, we could not evaluate the contribution of these factors. Also missing were data on the quantitative thyroid function of infants from the general population, precluding the establishment of thresholds. The major strengths of this large-scale observational study lie in the uniformity of the obstetric approach of a single medical center and the comprehensiveness of data from the Pediatric Endocrine Clinic which enabled drawing conclusions on well-distinguished transient and permanent CH groups.

In conclusion, the investigation of the mother-infant dyads of CH infants revealed that the labor and delivery process of a CH infant is characterized by increased use of instrumentation and medications. The interaction between neonatal fetal thyroid and exogenous oxytocin administration suggests a role for prenatal fetal thyroid function in the development and progression of delivery in response to oxytocin.

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Author Contributions

G.R. made a substantial contribution to the curation of data, interpretation of data, and drafting of the article. A.L. made a substantial contribution to the curation of data, interpretation of data, and revision of the manuscript for important intellectual content. M.Y-G. performed the statistical analysis, interpreted the data, and revised the manuscript for

important intellectual content. S.A. made a substantial contribution to the curation of data and revised the manuscript for important intellectual content. M.P. made a substantial contribution to the curation of data and revised the manuscript for important intellectual content. A.M. made a substantial contribution to the interpretation of data analysis and revised the manuscript for important intellectual content. Y.L. made a substantial contribution to the design of the study, interpretation of data analysis, and revised the manuscript for important intellectual content. A.B. made a substantial contribution to the conception and design of the study, interpretation of data analysis and drafting of the article, and critically revised the manuscript, incorporating contributions from the coauthors. A.B. is the guarantor of this work, and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final version.

Competing Interests: The authors declare no competing interests.

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Table 1. Characteristics of mothers and their infant offspring with congenital hypothyroidism compared to the general population.

	General population	Congenital hypothyroidism	<i>p</i> value
Number	108,586	131	
Mother			
Age at delivery, years	32 [29, 36]	31.8 [28.5, 35.7]	0.226
Primiparous	45,498 (41.9)	51 (38.9)	0.274
Number of current pregnancy	2 [1, 3]	2 [1,3]	0.709
Number of previous live births	1 [0, 2]	1 [0, 2]	0.448
Twin pregnancy, n (%)	2,606 (2.4)	8 (6.1)	0.013
Weight, kg			
Before pregnancy	59.0 [53.0, 67.0]	59.6 [51.8, 72.3]	0.926
Weight gain during pregnancy	13 [10, 16]	12 [10, 15]	0.650
Health conditions affecting pregnancy, n (%)			
Smoking	5321 (4.9)	4 (3.1)	0.212
Gestational diabetes	6732 (6.2)	10 (7.6)	0.502
Medication administered during labor, n (%)			
Oxytocin	37,897 (34.9)	57 (43.5)	<0.001
Antibiotics	4235 (3.9)	11 (8.4)	0.008
Anesthesia, n (%)			
Epidural	65,369 (60.2)	77 (58.8)	<0.001
Spinal	16,179 (14.9)	37 (28.2)	
General	1303 (1.2)	1 (0.8)	
Mode of delivery, n (%)			
Spontaneous vaginal	78,399 (72.2)	73 (55.7)	<0.001
Vacuum extraction	7384 (6.8)	12 (9.2)	
Elective cesarean section	12,379 (11.4)	24 (18.3)	
Urgent cesarean section	10,424 (9.6)	22 (16.8)	
Infant			
Male sex, n (%)	55,726 (51.3)	65 (49.6)	0.381
Gestational age, weeks	39 [38, 40]	39 [38, 40]	0.806
Birth weight, kg	3.270 [2.995, 3.560]	3.100 [2.855, 3.500]	0.002
APGAR score			
1 minute	9 [9, 9]	9 [9, 9]	0.162
5 minutes	10 [10, 10]	10 [10, 10]	0.455
The data are expressed as number and (percent), median [interquartile range]. Bold indicates statistical significance. APGAR = appearance (skin color), pulse, grimace (reflex), activity (muscle tone) and respiration; kg = kilograms; n = number; y = years.			

Table 2. Characteristics of the mothers and their infant offspring with congenital hypothyroidism (transient vs. permanent).

	Transient hypothyroidism	Permanent hypothyroidism	<i>p</i> value
Number	65	66	
Mother			
Age at delivery, years	31.7 ± 5.0	32.0 ± 4.5	0.543
Socioeconomic position			
Cluster	7 [5, 9]	7 [5, 8.3]	0.985
Index	0.783 [0.050, 1.644]	0.744 [0.077, 1.649]	0.798
Ethnicity, n (%)	n=45	n=37	
Israeli Jews	43 (95.6)	34 (91.9)	0.092
Israeli Arabs	1 (2.2)	1 (2.7)	
Other	1 (2.2)	2 (5.4)	
Obstetric characteristics			
Primiparous	24 (36.9)	23 (34.8)	0.803
Number of current pregnancy	2 [1, 3]	2 [1, 3]	0.612
Number of previous live births	1 [0, 2]	1 [0, 2]	0.816
Twins	5 (7.7)	3 (4.5)	0.446
Conception, n (%)			
Assisted reproductive therapy	4 (6.2)	3 (4.5)	0.342
Intrauterine insemination	1 (1.5)	0 (0)	
In vitro fertilization	3 (4.6)	3 (4.5)	
Weight, kg			
Before pregnancy	56.5 [51.3, 70.0]	60.5 [51.8, 73.0]	0.496
Weight gain during pregnancy	12 [10, 15.3]	12 [10.3, 15]	0.722
Health conditions affecting pregnancy, n (%)			
Smoking	2 (3.1)	2 (3.0)	0.988
Gestational diabetes	7 (10.8)	3 (4.5)	0.206
Thyroid disease	5 (7.7)	4 (6.1)	0.604
Medication administered during labor, n (%)			
Oxytocin	35 (53.8)	39 (59.1)	0.545
Antibiotics	6 (9.2)	5 (7.6)	0.733
Anesthesia, n (%)			
Epidural/spinal	59 (90.8)	55 (83.3)	0.344
General	0 (0)	1 (9.1)	
Presentation, n (%)			
Vertex	56 (86.2)	62 (93.9)	0.328
Breech/legs	9 (14.1)	4 (6.1)	
Mode of delivery, n (%)			
Vaginal spontaneous	33 (50.8)	40 (60.6)	0.447
Vacuum extraction	7 (10.8)	5 (7.6)	
Elective cesarean section	15 (23.1)	9 (13.6)	
Urgent cesarean section	10 (15.4)	12 (18.2)	
Infant			
Male sex, n (%)	37 (56.9)	28 (42.4)	0.097
Gestational age, weeks	39 [38, 40]	40 [38, 40]	0.011
Birth weight, z-score	-0.26 [-0.80, 0.24]	-0.46 [-0.99, 0.41]	0.349

Small for gestational age, n (%)	5 (7.7)	12 (18.2)	0.075
APGAR score			
1 minute	9 [9, 9]	9 [9, 9]	0.811
5 minutes	10 [10, 10]	10 [10,10]	0.399
Thyroid screen test			
Total thyroxine, mcg/dL	8.46 [6.94, 9.37]	7.14 [5.35, 8.91]	0.030
Thyroid-stimulating hormone, mU/L	22.2 [18.0, 29.4]	116.0 [31.4, 399.9]	<0.001
Confirmatory thyroid tests			
Thyroid-stimulating hormone, mU/L	26.4 [9.9, 56.5]	100.0 [88.5, 150.0]	<0.001
Free thyroxine, ng/dL	1.12 ± 0.41	0.80 ± 0.38	<0.001
Thyroid scintigraphy, n (%)			
Performed	15 (23.1)	56 (84.8)	<0.001
Abnormal findings	0 (0)	46 (82.1)	<0.001
Thyroid ultrasound, n (%)			
Performed	2 (3.1)	9 (13.6)	0.029
Abnormal findings	0 (0)	8 (88.9)	0.015
L-thyroxine treatment, n (%)			
Treated	24 (36.9)	66 (100)	<0.001
<p>The data are expressed as number and (percent), median [interquartile range] and mean ± standard deviation. Socioeconomic position (SEP) is defined by the cluster of localities of residence, ranging from 1 (the lowest SEP) to 10 (the highest SEP). The SEP index is an adjusted calculation of 14 variables that measure social and economic levels in the domains of demographics, education, standard of living, and employment (ranging from the lowest -2.797 to the highest 2.590). Bold indicates statistical significance. APGAR = appearance (skin color), pulse, grimace (reflex), activity (muscle tone) and respiration; kg = kilograms; n = number; y = years.</p>			

Table 3. Multivariate logistic regression analysis of characteristics of mother-infant dyads contributing to the diagnosis of congenital hypothyroidism.

General population - congenital hypothyroidism¹

	β	<i>p</i> value	OR	95% CI for OR	
				Lower	Upper
Constant					
Number of previous births	0.200	0.009	1.22	1.05	1.42
Oxytocin administration	0.927	<0.001	2.53	1.59	4.01

General population - permanent congenital hypothyroidism¹

	β	<i>p</i> value	OR	95% CI for OR	
				Lower	Upper
Constant					
Number of previous births	0.202	0.036	1.22	1.01	1.48
Oxytocin administration	1.020	0.001	2.77	1.52	5.06
Gestational age	0.278	0.030	1.32	1.03	1.70

Congenital hypothyroidism - permanent congenital hypothyroidism²

	β	<i>p</i> value	OR	95% CI for OR	
				Lower	Upper
Constant					
Birth weight z-score	0.421	0.052	1.524	0.996	2.333
Screen TSH	-0.100	<0.001	0.990	0.985	0.995

¹ Multivariate forward logistic regression model included the following parameters: maternal age, number of current pregnancy, number of previous births, weight before pregnancy, weight gain during pregnancy, type of delivery, anesthesia, oxytocin and antibiotics administration, gestational week, and birth weight.

² Multivariate forward logistic regression model included the following parameters: maternal age, number of current pregnancy, number of previous births, socioeconomic position, weight before pregnancy, weight gain during pregnancy, type of delivery, anesthesia, oxytocin and antibiotics administration, gestational week, birth weight z-score, thyroid screen test (TSH, TT4), and thyroid confirmatory test (TSH, TT4).

OR = odds ratio; CI = confidence interval; TSH = thyroid stimulating hormone; TT4 = total thyroxine