

Effect of maternal and neonatal factors on cord blood thyroid stimulating hormone

Sheetal G. Lakshminarayana, Nidhish P. Sadanandan, A. K. Mehaboob¹, Lakshminarayana R. Gopaliah²

Departments of Physiology and ¹Pediatrics, MES Medical College, ²Department of Nephrology, E.M.S. Memorial Co-operative Hospital and Research Centre, Perinthalmanna, Malappuram, Kerala, India

ABSTRACT

Background: Congenital hypothyroidism (CH) is most common preventable cause of mental retardation in children. Cord blood Thyroid Stimulating Hormone (CBTSH) level is an accepted screening tool for CH. **Objectives:** To study CBTSH profile in neonates born at tertiary care referral center and to analyze the influence of maternal and neonatal factors on their levels. **Design:** Cross retrospective sectional study. **Methods:** Study population included 979 neonates (males = 506 to females = 473). The CBTSH levels were estimated using electrochemiluminescence immunoassay on Cobas analyzer. Kit based cut-offs of TSH level were used for analysis. All neonates with abnormal CBTSH levels, were started on levothyroxine supplementation 10 µg/Kg/day and TSH levels were reassessed as per departmental protocol. **Results:** The mean CBTSH was 7.82 µIU/mL (Range 0.112 to 81.4, SD = 5.48). The mean CBTSH level was significantly higher in first order neonates, neonates delivered by assisted vaginal delivery and normal delivery, delivered at term or preterm, neonates with APGAR score <5 and those needing advanced resuscitation after birth. The CBTSH level >16.10 and <1.0 µIU/mL was found in 4.39 % and 1.02 % neonates respectively. The prevalence rate of CBTSH level >16.1 µIU/mL was significantly higher in neonates delivered by assisted vaginal delivery and normal delivery, term and preterm neonates, APGAR score of <5, presence of fetal distress, need for resuscitation beyond initial steps and in those with birth weight of <1.5 Kg. Three neonates were confirmed to have CH after retesting of TSH level. **Conclusions:** The CBTSH estimation is an easy, non-invasive method for screening for CH. The cutoff level of CB TSH (µIU/mL) >16.10 and <1.0 led to a recall of 5.41% of neonates which is practicable given the scenario in our Country. The mode of delivery and perinatal stress factors have a significant impact on CBTSH levels and any rise to be seen in the light of these factors. The prevalence rate of CH after recall was ~3 in 1000 live births.

Key words: Cord blood thyroid stimulating hormone, congenital hypothyroidism, newborn screening

INTRODUCTION

Congenital hypothyroidism (CH) is the most common preventable cause of mental retardation with a global incidence of 1:2500–1:4000 live births.^[1-4] Clinical diagnosis is difficult at birth, and the time of initiation of therapy is a critical determinant of outcome. Screening for early

diagnosis of CH is mandatory in most of the developed countries for early diagnosis and treatment.^[4]

Neonatal screening methods measure thyroid stimulating hormone (TSH) level in either cord blood (CB) sample or that obtained from heel prick (HP) sample at 3–4 days of life. CBTSH estimation has the advantages of being easy to collect, noninvasive, and low rates of follow-up loss as the results would be available before the mother leaves the hospital, enabling repeat sampling if needed at the earliest, which is critical for early institution of

Corresponding Author: Dr. Lakshminarayana R. Gopaliah, Department of Nephrology, E.M.S. Memorial Co-operative Hospital and Research Centre, Perinthalmanna, Malappuram - 679 322, Kerala, India. E-mail: drlng23@gmail.com

Access this article online

Quick Response Code:



Website:
www.ijem.in

DOI:
10.4103/2230-8210.179998

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Cite this article as: Lakshminarayana SG, Sadanandan NP, Mehaboob AK, Gopaliah LR. Effect of maternal and neonatal factors on cord blood thyroid stimulating hormone. Indian J Endocr Metab 2016;20:317-23.

treatment if necessary. Various maternal and perinatal factors are known to affect the CBTSH levels.^[5-13] Neonatal TSH level can also be used as one of the indicators for monitoring iodine sufficiency of the population.^[14] A study by Seth *et al.* did not find statistically significant difference in mean TSH values in serum obtained from CB and HP at 4th–7th day-of-life.^[15]

There are very few studies in India on screening for CH and the effects of various factors on CBTSH levels.^[5-11] This study presents an analysis of various maternal and neonatal factors on CBTSH level, studied in neonates born at a Tertiary Care Medical College Hospital in Kerala, India.

Objectives

The objectives of the study were to analyze the profile of CBTSH levels and the effect of maternal and neonatal factors on their levels, in neonates born at MES Medical College Hospital, Perinthalmanna, a tertiary care, referral hospital in North Kerala. The factors studied were parity of mother (birth order), maternal medical and obstetric conditions, mode of delivery, indication for cesarean section, birth weight, gestational age, gender, weight, requirement of resuscitation beyond initial steps, and the Apgar score.

MATERIALS AND METHODS

Study design and subjects

This cross-sectional, retrospective study was a study conducted in Neonatology Unit of MES Medical College Hospital, Perinthalmanna, Malappuram, Kerala. Our hospital is tertiary care multi-specialty referral hospital with all specialties and super-specialty departments. All consecutive neonates delivered from January 2013 to January 2014 were included in the study. The neonates with major life-threatening malformations, those with antenatally detected central nervous system malformations and neonates whose mothers were on any known anti-thyroid drugs were excluded from the study.

Following variables were recorded and analyzed:

- Neonatal factors: CBTSH level, birth weight, length at birth, birth order, date and time of delivery, gender, mode of delivery, Apgar score, MORO reflex, need for resuscitation, respiratory distress syndrome, neonatal jaundice, and hemoglobin level
- Maternal factors: Maternal age, maternal medical history (diabetes mellitus, hypertension, and thyroid diseases).

CB samples of all the babies born were collected and sent for CBTSH estimation. Blood samples (2 mL) were

collected in a sterile container drawn from the umbilical vein with the help of a 5cc syringe, from 15 to 20 cm length of the umbilical cord severed at the time of birth of the baby. The samples were analyzed within 4 h using electrochemiluminescence immunoassay on Cobas analyzer. Normal value of TSH in neonates as per the kit was 1.00–16.10 μ IU/mL. Values >16.1 and <1.0 μ IU/mL were considered abnormal. All neonates who had CBTSH values in abnormal range were advised repeat TSH assessment within 14 days of life.

The neonates with abnormal CBTSH levels (<1 or >16.1 μ IU/mL) were started on supplemental levothyroxine of 10 μ g/kg/day and TSH levels were recalled at 1st, 3rd, 6th, and 12th months after delivery, to confirm thyroid illness. CH was diagnosed if the values if TSH >10 μ IU/mL along with T4 <6.5 μ g/dl and FT4 <0.8 ng/dl.

Statistical analysis was performed using SPSS (version 17) by SPSS Inc., Illinois, USA for Windows. The quantitative variables (CBTSH level, birth weight) have been described as mean \pm standard deviation (SD) and range. The birth order, mode of delivery, resuscitation (routine or advanced), gestational and maternal age categories, Apgar score categories, timing of CB sampling, and maternal comorbidities were summarized as counts and percentages. One-way ANOVA test was used to assess the effect of maternal and neonatal factors on mean CBTSH level. The Chi-square test was used to assess the trends in the prevalence of abnormal CBTSH level and its relation to neonatal and maternal factors. The multivariate regression analysis of variables was done to find out their effect on CBTSH level. A $P < 0.05$ was taken as statistically significant. The study was approved by Hospital Ethics Committee.

RESULTS

A total of 1012 neonates were born at MES Medical College Hospital, Perinthalmanna, India, during the study period from January 2013 to January 2014 of which 979 whose records were complete with all the necessary variables as per protocol were included in the study. The clinical profile of subjects according to neonatal and maternal factors is summarized in Table 1.

The mean value of CBTSH was 7.82 μ IU/mL (range 0.112–81.4, SD = 5.48). Mean birth weight of the neonates was 2.75 kg (range 0.72–4.32 kg, SD = 0.57). The cord TSH levels from 1.00 to 16.10 μ IU/mL was taken as normal. The males (506) to females (473) ratio was 1.07:1.

CBTSH >16.10 μ IU/mL was found in 43 (4.39%) neonates with range of 16.4–81.40 μ IU/mL (mean = 26.17). CBTSH

Table 1: Profile of subjects according to neonatal factors along with mean CBTSH levels

Parameter	Number of subjects	Percentage	Mean CBTSH ($\mu\text{IU/mL}$)	Standard deviation
All subjects	979	100	7.82	5.48
Birth order				
First	319	32.58	8.10	6.57
Second	291	29.72	7.81	4.95
Third or more	369	37.69	7.56	4.80
Mode of delivery				
Normal	344	35.13	7.91	6.47
Assisted vaginal	27	2.76	13.36	10.47
LSCS (elective)	266	27.17	7.69	4.88
LSCS (emergency)	342	34.93	7.39	3.79
Gestational age (weeks)				
37-41 (term)	786	80.28	7.90	5.73
32-36 (preterm)	118	12.05	7.96	4.60
<32 (extreme preterm)	58	5.92	7.26	3.75
>40 (post term)	17	1.74	5.27	3.27
Birth weight (Kg)				
<1.5	35	3.57	7.89	5.85
1.5-2.5	267	27.27	7.88	6.29
2.6-4.0	674	68.84	7.79	5.12
>4.0	3	0.31	7.90	2.42
Gender				
Males	506	51.69	7.94	5.81
Females	473	48.31	7.69	5.11
Apgar score at birth				
<5	15	1.53	9.70	7.99
5-7	46	4.70	8.08	5.46
>7	918	93.77	7.78	4.96
Resuscitation				
Routine care	941	96.12	7.81	5.45
Beyond initial care	38	3.88	8.14	6.25
Timing of sample				
7 am to 7 pm	685	69.97	7.72	4.55
7 pm to 7 am	294	30.03	8.05	7.20

LSCS: Lower segment caesarean section, CBTSH: Cord blood thyroid stimulating hormone

level <1.0 was found in 1.02% (10) of neonates with range of 0.113–0.917 $\mu\text{IU/mL}$ (mean = 0.57).

The cord blood thyroid stimulating hormone level and neonatal factors

The relation of neonatal factors and mean CBTSH level are shown in Table 1. The mean CBTSH ($\mu\text{IU/mL}$) was higher in neonates delivered by assisted vaginal (13.36) and normal vaginal mode (7.91) or than lower segment caesarean section (LSCS) (elective [7.69] or emergency [7.39]); the difference was that it was statistically significant ($P < 0.01$). The mean CBTSH was higher in neonates belonging to term (7.90) and preterm (7.96) gestational age than postterm (5.27) or extreme preterm (7.26); it was statistically significant ($P = 0.01$).

The mean CBTSH was higher in the first (8.10) and second (7.81) child than the third or more (7.56) birth order; it was statistically significant ($P = 0.03$). The mean CBTSH was higher in neonates with fetal distress or needing advanced

resuscitation after birth (8.14) than neonates receiving routine care (7.81); it was statistically significant ($P < 0.01$). The mean CBTSH was higher in those with Apgar score of <5 (9.70) than those with score of 5–7 (8.08) and >7 (7.78); it was statistically significant ($P < 0.01$).

The mean CBTSH was marginally higher in those with birth weight of more than 4 kg (7.90) than those belonging to categories of 2.6–4.0 kg (7.79), <1.5 kg (7.89), and 1.5–2.5 kg (7.88), and the variation was statistically not significant ($P = 0.65$). The mean CBTSH was slightly higher males (7.94) than females (7.69); it was statistically not significant ($P = 0.13$). The mean CBTSH was slightly higher when time of birth was between 7 pm to 7 am (8.05) and 7 am to 7 pm (7.72); however, it was statistically not significant ($P = 0.54$).

The relation of neonatal factors and CBTSH level-based categories are shown in Table 2. CBTSH more than 16.1 and >1.0 $\mu\text{IU/mL}$ was noted in 4.39% (43) and 1.02% (10) of neonates, respectively. The prevalence rate of CBTSH >16.1 $\mu\text{IU/mL}$ was higher in neonates delivered by normal delivery (5.23%) and assisted vaginal delivery (22.22%) as compared to cesarean section (elective [4.51] or emergency [2.04]), and it was statistically significant ($P < 0.01$).

The prevalence rate CBTSH >6.1 $\mu\text{IU/mL}$ was more in neonates belonging to term (4.77%) and preterm (4.24%) gestational age than extreme preterm (1.72%) or postterm (0%); it was statistically significant ($P < 0.01$).

The prevalence rate CBTSH >16.1 $\mu\text{IU/mL}$ was higher in the first (5.33%) child than the second (4.12%) and third or more (3.79%) birth order; however, the variation was not statistically significant ($P = 0.66$). The prevalence rate CBTSH >16.1 $\mu\text{IU/mL}$ was higher in females (4.86%) than males (3.95%); it was statistically not significant ($P = 0.59$).

The prevalence rate CBTSH >16.1 $\mu\text{IU/mL}$ was higher in those with Apgar score of <5 (20%) than those with score of 5–7 (6.52%) and >7 (4.03%); it was statistically significant ($P = 0.039$). The prevalence rate CBTSH >16.1 $\mu\text{IU/mL}$ was higher in neonates with fetal distress or needing advanced resuscitation after birth (10.52%) than neonates receiving routine care (4.14%); it was not statistically significant ($P = 0.098$).

The prevalence rate CBTSH >16.1 $\mu\text{IU/mL}$ was the highest in those with birth weight of <1.5 kg (5.71%), followed by than those weighing 1.5–2.5 kg (4.87%), 2.6–4.0 kg (4.15%), and >4.0 kg (0%); variation was

Table 2: Effect of neonatal factors on CBTSH levels

CBTSH categories	Parameter	CBTSH (micro IU/mL) n (%)			Total	P value (Chi square test CBTSH level vs neonatal factors)
		1-16.1	>16.1	<1		
All subjects		926 (94.58)	43 (4.39)	10 (1.02)	979	
Birth order	First	298 (32.18)	17 (5.33)	4 (1.25)	319	0.01
	Second	275 (29.70)	12 (4.12)	4 (1.37)	291	
	Third or more	353 (38.12)	14 (3.79)	2 (0.54)	369	
Mode of delivery	Normal	322 (34.77)	18 (5.23)	4 (1.16)	344	<0.01
	Assisted vaginal	21 (2.27)	6 (22.22)	0	27	
	LSCS (elective)	252 (27.21)	12 (4.51)	2 (0.75)	266	
	LSCS (emergency)	331 (35.74)	7 (2.04)	4 (1.17)	342	
Gestational age (weeks)	37-41 (term)	746 (80.56)	37 (4.77)	3 (0.38)	786	<0.01
	32-36 (preterm)	110 (11.90)	5 (4.24)	3 (2.54)	118	
	< 32 (extreme preterm)	56 (6.05)	1 (1.72)	1 (1.72)	58	
	> 40 (post term)	14 (1.51)	0	3 (17.64)	17	
Birth weight (Kg)	<1.5	30 (3.24)	2 (5.71)	3 (8.57)	35	0.001
	1.5-2.5	250 (27.00)	13 (4.87)	4 (1.50)	267	
	2.6-4.0	643 (69.44)	28 (4.15)	3 (0.45)	674	
	>4.0	3 (0.32)	0	0	3	
Gender	Males	482 (52.05)	20 (3.95)	4 (0.79)	506	0.589
	Females	444 (47.95)	23 (4.86)	6 (0.13)	473	
Apgar score at birth	<5	12 (1.29)	3 (20)	0	15	0.039
	5-7	43 (4.64)	3 (6.52)	0	46	
	>7	871 (94.06)	37 (4.03)	10 (0.10)	918	
Resuscitation	Routine care	893 (96.44)	39 (4.14)	9 (0.96)	941	0.098
	Beyond initial care	33 (3.56)	4 (10.52)	1 (2.63)	38	
Timing of sample	7 am to 7 pm	649 (70.09)	28 (4.09)	8 (1.17)	685	0.617
	7 pm to 7 am	277 (29.91)	15 (5.10)	2 (0.68)	294	

CBTSH: Cord blood thyroid stimulating hormone

statistically significant ($P = 0.001$). The prevalence rate CBTSH $>16.1 \mu\text{IU/mL}$ was slightly higher when time of birth was between 7 pm to 7 am (5.10%) and 7 am to 7 pm (4.09%); however, it was statistically not significant ($P = 0.617$).

The cord blood thyroid stimulating hormone level and maternal factors

The relation of maternal factors and mean CBTSH level are shown in Table 3. The mean CBTSH ($\mu\text{IU/mL}$) was slightly higher if the maternal age (years) is more than 35 (7.94) in comparison to age groups of 26–34 (7.79) and 18–25 (7.84) but was not statistically significant ($P = 0.42$).

The mean CBTSH level was higher in neonates whose mothers had hypertension (8.95) followed by those with of both hypertension and diabetes mellitus (8.40), no maternal comorbidities (7.66), diabetes mellitus only (7.46) and was least in those with hypothyroidism (7.45); however, it was statistically insignificant ($P = 0.56$).

The relation of maternal factors and CBTSH level categories are shown in Table 4. The prevalence rate CBTSH $>16.1 \mu\text{IU/mL}$ was slightly higher if the maternal age (years) is 18–25 (4.76%) followed by 26–34 (4.25%) and >35 (0%) but was statistically insignificant ($P = 0.98$).

The prevalence rate CBTSH $>16.1 \mu\text{IU/mL}$ was higher in neonates whose mothers had hypertension (7.81%) followed by those with of both hypertension and diabetes mellitus (5.88%), no maternal comorbidities (4.05%), diabetes mellitus only (2.63%) and was least in those with hypothyroidism (0%); however, it was statistically insignificant ($P = 0.19$).

All neonates with abnormal CBSTH levels were started on levothyroxine supplementation $10 \mu\text{g/kg/day}$, and TSH levels were reassessed as per the protocol. Three neonates were confirmed to have CH and are on regular follow-up in the outpatient department; they are euthyroid on levothyroxine supplements. The prevalence rate of CH in the present study is 3 (1 male and 2 females) out of 979 ($\sim 3/1000$).

DISCUSSION

CH is the most common preventable cause of mental retardation in children. The CBTSH estimation has the advantages of being easy to collect, noninvasive, and low rates of follow-up loss as the results would be available before the mother leaves the hospital, enabling repeat sampling if needed at the earliest, which is critical for early institution of treatment if necessary. This study

Table 3: Effect of neonatal factors on cord blood thyroid stimulating hormone levels

Parameter	CBTSH ($\mu\text{IU/mL}$)			Total	P (Chi-square test CBTSH level vs. neonatal factors)
	1–16.1 n (%)	>16.1 n (%)	<1 n (%)		
All subjects	926 (94.58)	43 (4.39)	10 (1.02)	979	
Birth weight (kg)					
<1.5	30	2 (5.71)	3 (8.57)	35	0.001
1.5–2.5	250	13 (4.87)	4 (1.50)	267	
2.6–4.0	643	28 (4.15)	3 (0.45)	674	
>4.0	3	0	0	3	
Gender					
Males	482	20 (3.95)	4 (0.79)	506	0.589
Females	444	23 (4.86)	6 (0.13)	473	
Apgar score at birth					
<5	12	3 (20)	0	15	0.039
5–7	43	3 (6.52)	0	46	
>7	871	37 (4.03)	10 (0.10)	918	
Resuscitation					
Routine care	893	39 (4.14)	9 (0.96)	941	0.098
Beyond initial care	33	4 (10.52)	1 (2.63)	38	
Timing of sample					
7 am to 7 pm	649	28 (4.09)	8 (1.17)	685	0.617
7 pm to 7 am	277	15 (5.10)	2 (0.68)	294	

CBTSH: Cord blood thyroid stimulating hormone

Table 4: Effect of maternal factors on cord blood thyroid stimulating hormone levels

Parameter	CBTSH ($\mu\text{IU/mL}$)			Total	P (Chi-square test maternal factor vs. CBTSH category)
	1–16.1 n (%)	>16.1 n (%)	<1.0 n (%)		
All subjects	926 (94.58)	43 (4.39)	10 (1.02)	979	
Maternal age (years)					
18–25	474	24 (4.76)	6 (1.19)	504	0.98
26–34	424	19 (4.25)	4 (0.89)	447	
≥ 35	28	0	0	28	
Maternal complications					
HTN	117	10 (7.81)	1 (0.78)	128	0.19
Gestational diabetes	37	1 (2.63)	0	38	
HTN and gestational diabetes	15	1 (5.88)	1 (5.88)	17	
Hypothyroidism	7	0	0	7	
No complications	750	32 (4.05)	7 (0.89)	789	

CBTSH: Cord blood thyroid stimulating hormone, HTN: Hypertension

presents an analysis of effect of maternal and neonatal factors on CBTSH level, studied in neonates born at MES Medical College Hospital, Perinthalmanna, Kerala, India.

In our study, the mean TSH level was 7.82 $\mu\text{IU/mL}$ comparable to other studies with levels of mean TSH ranging from 6.13 to 10.^[5,6,8,10] The mean CBTSH was higher than 10 $\mu\text{IU/mL}$ few studies.^[7,9,11]

In our study, mean CBTSH was significantly raised in neonates delivered by assisted vaginal delivery and normal delivery than those delivered by LSCS finding correlating with other studies.^[10,12] Neonates born at full-term gestational age had significantly higher mean CBTSH than those born at age of pre- and post-term or extreme preterm. Neonates who had fetal distress or low Apgar

score (<5) or those requiring resuscitation beyond initial steps had significantly higher CBTSH, correlating with previous studies.^[10,12]

Gender had varying effect on CBTSH level significant in a few^[10,12] and insignificant in other^[9,11] studies. Gender had no significant effect on mean CBTSH level in the present study. The mean CBTSH level was significantly higher in the first and second child than the third or more finding similar to an earlier study.^[10] Birth weight also shown to have varying effect on CBTSH level did not have significant effect in the present study similar to one of the studies;^[9] CBTSH level was found to be higher in small for gestational age neonates in another study.^[12] Low birth weight newborns had significantly lower TSH than normal or high birth weight in one of the studies.^[8]

Maternal comorbidities, birth weight, and gestational age did not have significant effect on CBTSH level in the present study, findings correlating with previous studies.^[8,10] However; in one study, CBTSH level showed an increasing trend with maternal age.^[11]

Researchers have used different CBTSH cut-off levels ranging from 10 to 20 $\mu\text{IU}/\text{mL}$ for recall and rescreening, to make it more cost-effective.^[5,7,8,10,11] The kit cut-off values were used in the present study as there were no normative data for the local population. The previous studies also had used cut-off values based on the kit for analysis.^[5,7,10-12]

Recall rates were varied widely based on cut-off levels of CBTSH levels and geographic location of study, 1.83–11.45%^[10] if the CBTSH cut-off $>20 \mu\text{IU}/\text{mL}$.^[5,7,10] The recall rate was 29.53% in one of the studies using CBTSH cut-off $>13.2 \mu\text{IU}/\text{mL}$.^[11] When the CBTSH cut-off level was raised to $40.0 \mu\text{IU}/\text{mL}$, none of the variables examined were significant.^[12]

In the present study, CBTSH >16.1 and $<1.0 \mu\text{IU}/\text{mL}$ were considered abnormal as per the kit. The abnormal CBTSH levels of $>16.1 \mu\text{IU}/\text{mL}$ in 43 and $<1.0 \mu\text{IU}/\text{mL}$ in 10 neonates were leading to a recall of 5.41% (53 out of 979). The recall rate reduces to 0.6% (~ 6 neonates) and 0.31% (~ 3 neonates) if the CBTSH cut-off is >30 and $>40 \mu\text{IU}/\text{mL}$, respectively; however, higher cut-off has risk of underestimate the risk of CH. A 5-year prospective study from Thailand used cut-off value of 30 to begin with and had a recall rate of 1.1% in a large sample size of 35,390 neonates. Modification in cut-off value to 40 lead to a fall in recall rate to 0.43%.^[16]

The neonates with abnormal CBTSH were started on levothyroxine supplements, and TSH was reassessed as per the protocol at 1st, 3rd, 6th, and 12th months after delivery. CH was confirmed in 3 neonates, with prevalence rate of ~ 3 in 1000, during follow-up as per the protocol mentioned above. Higher cut-off values of CBTSH for recall lowers the recall rate and improves the economic and practical logistics. Our figures have shown a comparable trend as with the normative data for CBTSH values as reported by various workers.^[12,15]

The prevalence rate of higher CBTSH level ($>16.1 \mu\text{IU}/\text{mL}$) was significantly more in neonates delivered by assisted vaginal delivery followed by normal delivery and LSCS. The prevalence rate of higher CBTSH was more in full-term neonates than and pre- or post-term. The prevalence rate of higher CBTSH level was significantly more in those with birth weight of $<1.5 \text{ kg}$ or Apgar score of <5 or with fetal distress or needing advanced

resuscitation after birth. The birth order/parity, gender, time of birth, maternal age, and maternal comorbidities did not have any significant effect on prevalence rate of CBTSH $>16.1 \mu\text{IU}/\text{mL}$.

On multivariate regression analysis, mode of delivery, gestational age, and Apgar score had significant effect on prevalence rate of higher CBTSH ($>16.1 \mu\text{IU}/\text{mL}$). Gender, time of CB sampling/birth time, birth weight, parity, maternal age, and maternal comorbidities did not have significant effect on prevalence of higher CBTSH level.

CH was confirmed in 3 neonates (females: 2, males: 1) during the follow-up. The prevalence rate of CH in the present study was ~ 3 in 1000 neonates, with female to male ratio of 2:1. The previous studies from India have reported varying rates prevalence of CH 3:430, 1:476, 1:1700, 1:2481, and 1:2804.^[11,17-20]

Limitations

Our study is based on single-center experience; hence, we need large population-based or multicenter studies in future to estimate the prevalence of CH in India. The present study used kit based cut-off for CBTSH, we also need multicenter national data using uniform analysis kits find out the normative range for the population. We need national protocol based on consensus for screening and treatment of CH, which is nonexistent at present.

CONCLUSIONS

The CBTSH estimation has the advantages of being easy to collect, noninvasive method for screening for CH. The cut-off level of CBTSH ($\mu\text{IU}/\text{mL}$) >16.10 and <1.0 led to a recall of 5.41% which is practicable give the scenario in our country. Higher cut-off values can further reduce the recall rates and needs to be studied.

The assisted vaginal or normal mode of delivery, presence of fetal distress or low Apgar score (<5) or requirement resuscitation beyond initial steps had significant effect on CBTSH level. Gender, parity and birth weight, maternal age, and maternal comorbidities did not have significant effect on CBTSH level.

We therefore conclude that perinatal stress factors and mode of delivery have a significant impact on CBTSH levels, and any rise in CBTSH should be seen in the light of these factors and those with higher CBTSH needs to be recalled for retesting at later date. CH was confirmed in 3 neonates with prevalence rate of ~ 3 in 1000 live births.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Desai MP. Congenital hypothyroidism: Screening dilemma. *Indian J Endocrinol Metab* 2012;16 Suppl 2:S153-5.
- Sareen N, Pradhan R. Need for neonatal screening program in India: A national priority. *Indian J Endocrinol Metab* 2015;19:204-20.
- Agrawal P, Philip R, Saran S, Gutch M, Razi MS, Agroiya P, *et al.* Congenital hypothyroidism. *Indian J Endocrinol Metab* 2015;19:221-7.
- American Academy of Pediatrics, Rose SR; Section on Endocrinology and Committee on Genetics, American Thyroid Association, Brown RS; Public Health Committee, Lawson Wilkins Pediatric Endocrine Society, Foley T, *et al.* Update of newborn screening and therapy for congenital hypothyroidism. *Pediatrics* 2006;117:2290-303.
- Manglik AK, Chatterjee N, Ghosh G. Umbilical cord blood TSH levels in term neonates: A screening tool for congenital hypothyroidism. *Indian Pediatr* 2005;42:1029-32.
- Meghana KP, Kamble BD, Suryawanshi PB, Melinkeri RR. Umbilical cord TSH levels in term small for gestational age neonates. *Indian J Res* 2013;2:294-5.
- Sangeeta N, Kamala L, Paras K, Gomi B, Ajitkumar Y, Ranbir SL, *et al.* Assessment of umbilical cord TSH in term neonates in Manipur. *IOSR J Dent Med Sci* 2013;9:14-7.
- Chandrika DN, Madhava K, Dinesh MN, Nagesha KM. Status of pituitary-thyroid axis of newborns and its relationship with anthropometry and maternal factors at birth. *Int J Pharma Bio Sci* 2012;3:B51-7.
- Rashmi, Seth A, Sekhri T, Agarwal A. Effect of perinatal factors on cord blood thyroid stimulating hormone levels. *J Pediatr Endocrinol Metab* 2007;20:59-64.
- Gupta A, Srivastava S, Bhatnagar A. Cord blood thyroid stimulating hormone level – Interpretation in light of perinatal factors. *Indian Pediatr* 2014;51:32-6.
- Raj S, Baburaj S, George J, Abraham B, Singh S. Cord blood TSH level variations in newborn – Experience from a rural centre in Southern India. *J Clin Diagn Res* 2014;8:PC18-20.
- Chan LY, Leung TN, Lau TK. Influences of perinatal factors on cord blood thyroid-stimulating hormone level. *Acta Obstet Gynecol Scand* 2001;80:1014-8.
- Miyamoto N, Tsuji M, Imataki T, Nagamachi N, Hirose S, Hamada Y. Influence of mode of delivery on fetal pituitary-thyroid axis. *Acta Paediatr Jpn* 1991;33:363-8.
- Li M, Eastman CJ. Neonatal TSH screening: Is it a sensitive and reliable tool for monitoring iodine status in populations? *Best Pract Res Clin Endocrinol Metab* 2010;24:63-75.
- Seth A, Rashmi M, Bhakhri BK, Sekri T. Neonatal thyroid screening: Relationship between cord blood thyroid stimulating hormone levels and thyroid stimulating hormone in heel prick sample on 4th to 7th day-of-life. *Indian J Endocrinol Metab* 2014;18:125-6.
- Mahachoklertwattana P, Phuapradit W, Siripoonya P, Charoenpol O, Thuvasethakul P, Rajatanavin R. Five-year thyrotropin screening for congenital hypothyroidism in Ramathibodi Hospital. *J Med Assoc Thai* 1999;82 Suppl 1:S27-32.
- Rama Devi AR, Naushad SM. Newborn screening in India. *Indian J Pediatr* 2004;71:157-60.
- Desai MP, Colaco MP, Ajgaonkar AR, Mahadik CV, Vas FE, Rege C, *et al.* Neonatal screening for congenital hypothyroidism in a developing country: Problems and strategies. *Indian J Pediatr* 1987;54:571-81.
- Desai MP, Upadhye P, Colaco MP, Mehre M, Naik SP, Vaz FE, *et al.* Neonatal screening for congenital hypothyroidism using the filter paper thyroxine technique. *Indian J Med Res* 1994;100:36-42.
- Mathew J. Burden of thyroid diseases in India. Need for aggressive diagnosis. *Med Update* 2008;18:334-41.