Original Article

Congenital hypothyroidism screening with umbilical cord blood thyroid-stimulating hormone at birth and peripheral venous blood thyroid-stimulating hormone after 72 h at a hospital in suburban area of Chhattisgarh

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ABSTRACT

Background: Primary congenital hypothyroidism (CH) is the most common cause of hypothyroidism in infancy and early childhood. Neonatal screening programs for the detection of CH in the neonatal period are widespread and in most screening programs, blood samples are collected at 5–6 days age. **Objective:** The objective of the study was to obtain cord blood (CB) samples at birth and the peripheral venous blood sample of thyroid-stimulating hormone (TSH) at 72 h. **Materials and Methods:** This cross-sectional observational study was done at a tertiary suburban center and a total of 1470 newborn delivered was enrolled after satisfying the inclusion criteria. Umbilical CB TSH sample was taken at birth and peripheral venous sample for TSH was taken at 72 h. TSH values more than 20 μIU/mL, in both groups, were taken as an upper limit of normal. **Results:** Out of 1470 samples collected, among those with umbilical cord sample, 31 (2%) had a value >20 μIU/mL, while only one baby had a value of TSH >20 μIU/mL at 72 h of life and was diagnosed as CH. **Conclusion:** The incidence of CH is 1 out of 1470 neonates. Female gender, maternal age, and lower socioeconomic status of parents have a significant impact on umbilical cord TSH Levels.

Key words: Congenital hypothyroidism, Cord blood, Peripheral venous thyroid-stimulating hormone

Congenital hypothyroidism (CH) frequently remains unrecognized in newborn (due to subtle clinical features) during infancy and early childhood and present to the clinic with irreversible clinical consequences [1]. The permanent impairment of intellectual and neurological functions indicates the crucial role of thyroid hormones on the developing brain in the early years of life. Beyond 3 years of age, when thyroid hormone-dependent brain growth is completed, the effects of thyroid deprivation are more evident on physical growth, metabolic functions, and skeletal maturation with less impairment of intellectual functions.

Permanent primary CH is the most common cause of hypothyroidism in infancy and early childhood. The worldwide incidence of CH is 1 in 4000 births [2] but in India, it varies from 1:500–600 to 1:3400 in various screening programs. In India, most cases are often missed due to the absence of an adequate health care system, education, and neonatal screening. Neonatal screening programs for the detection of CH in the neonatal period are widespread in the developed [3,4] as well as in the developing countries [5,6] but in India, it has not been mandated as a state program. Major hindrances for establishing an effective screening program in India are the cost involved, non-availability of demographic data, and the true incidence of disease in question, massive annual birth cohort, etc.

In most of the screening programs, blood samples are collected at 5–6 days of age but a large number of babies being discharged early (as in our hospital), and the absence of a follow-up system has led to the use of cord blood thyroid-stimulating hormone (CB-TSH) levels as a screening marker for detection of CH [7]. The present study was conducted to screen neonates, find the incidence of CH, and generate CB values of TSH or T4 at a hospital in suburban area of Chhattisgarh.

MATERIALS AND METHODS

A prospective cross-sectional observational study was conducted among newborns delivered by normal/cesarean section between March 2016 and February 2017 at a hospital in Bhilai, Chhattisgarh. The study protocol was reviewed by the Institutional Ethical Committee of the hospital and was granted ethical clearance.

The sample size was calculated using the formula $4\ PQ/e^2$, where P=prevalence, Q=1−prevalence, and e=Allowable error.

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As per the available research data, the prevalence of CH ranges from 1:500 to 1:3400 [7,8]. There are no baseline data or such study was available from our hospital or from this region. Due to the low prevalence and limitation of numbers of deliveries in our institution, we used an average number of deliveries per year in our hospital as a sample size for the present study.

All newborn delivered in our hospital during the study period were enrolled. The babies with very low birth weight (VLBW) (<1500 g), not well, on dopamine, and one of the twins were excluded. Furthermore, cases of perinatal deaths, consanguineous marriage, mother on antithyroid drugs, those who lack adequate follow-up, cases with application of povidone-iodine on the umbilical cord, or where proper CB sample could not be obtained, were excluded from the study.

Of the total 1776 newborns delivered during the study period, 306 newborns were excluded as per the exclusion criteria. Only 1470 newborns were involved in our study after obtaining informed consent from either of the parents. The first sample was collected in each newborn after birth within 20 min through the umbilical cord of the newborn and sent for TSH estimation. After the third postnatal day, the newborn with elevated CB-TSH level (cutoff value 20 μIU/mL) was further evaluated. In these newborns, the TSH value was obtained from the venous sample after 3 days of life [9,10]. The sample was analyzed within 4 h of collection, using the chemiluminescent immunoassay method [8,11]. Values, more than 20 μiu/ml, were considered abnormal [12]. The data regarding the mother's age, parity, and socioeconomic status (SES) were collected. Other information related to the neonate gender, birth weight, gestational age, and mode of delivery was also obtained.

Statistical Analysis

For all the statistical analysis, MS EXCEL and SPSS 16 (Statistical Package for Social Science) version were used. Percentage, frequency, and Chi-square test were used. $p<0.05$ was taken as statistical significance.

RESULTS

Among 1470 newborns, 727 (49.46%) were female and 743 (50.54%) were male. Most of the babies (68.9%) had a gestational age of 37–38 weeks and more than half (60.27%) had birth weight between 2.50 and 3.00 kg. Demographic details of study population have been given in Table 1.

Based on the method of sampling, 1439 (97%) babies were found to have CB-TSH ≤20 μIU/mL, 5 (0.30%) babies have TSH between 20.01 and 30 μIU/mL, 14 (0.90%) babies with TSH between 30.01 and 40.0 μIU/mL, 6 (0.40%) babies with TSH between 40.01 and 50.0 μIU/mL, 3 (0.20%) babies had TSH between 50.01 and 60.0 μIU/mL, and 3 (0.20%) babies had TSH >60.01 μIU/mL. While from peripheral blood cord sampling, 1469 (99.9%) had TSH <20 μIU/mL and only 1 baby had TSH >20 μIU/mL. Out of 31 babies, 30 (96.77%) babies have T4 were normal and only 1 (3.23%) baby had T4 level <2 ng/dl (low T4 due to thyroid gland dysgenesis with high CB-TSH at birth and peripheral venous blood TSH after 72 h).

We found that a higher level of CB-TSH (>20 μIU/mL) is significantly associated with an increase in maternal age ($p=0.02$). A statistical significance was found with the level of CB-TSH (>20 μIU/mL) and parents of neonates who belong to lower SES ($p=0.001$). The association of parity with CB-TSH was found non-significant (Table 2). Female neonates had a significantly higher level of CB-TSH (>20 μIU/mL) than male neonates ($p=0.03$). The association of gestational age, mode of delivery, and birth weight with CB-TSH was found non-significant (Table 3).

DISCUSSION

CH is the most common preventable cause of mental retardation in children. Screening of CH through CB-TSH and peripheral venous blood TSH (after 72 h of birth) was done in the present study. In the present study, the cutoff value of TSH was taken as 20 μIU/mL as taken in previous studies [8,12]. Shanghvi *et al*. [13] have taken a cutoff value of TSH of 40 while many other studies have taken a cutoff value of TSH <20 μIU/mL [14-17]. We found one confirmed case of CH with peripheral venous blood TSH of 38.44 μIU/mL. If we had taken 40 μIU/mL cutoff value of TSH, we would have missed this case of CH. Modification in cutoff value to 40 μIU/mL leads to a fall in recall rate to 0.43% [18]. The abnormal CB-TSH levels >20 μIU/mL in 31 neonates were leading to a recall rate of 2.10% (31/1470).

Table 1: Demographic profile of the newborns and their mothers (n=1470)

Characteristics	Variables	n (%)
Maternal age (years)	18–25	571 (38.84)
	26–35	874 (59.46)
	>35	25 (1.7)
Parity	Primiparous	609 (41.42)
	Multiparous (>1)	861 (58.57)
Gestational age (weeks)	32–36	179 (12.18)
	37–38	1013 (68.91)
	39–40	233 (15.85)
	>40	45 (3.06)
Mode of delivery	Lower segment caesarean section	906 (61.63)
	Normal vaginal	564 (38.37)
Socioeconomic status	Lower	221 (15.03)
	Upper lower	388 (26.39)
	Lower middle	515 (35.03)
	Upper middle	286 (19.45)
	Upper	60 (4.08)
Birth weight	1.5–2.500	397 (27.01)
	2.501–3.00	886 (60.27)
	3.001–3.500	131 (8.91)
	3.501–4.000	37 (2.52)
	>4.001	19 (1.29)

Table 2: Maternal characteristics and umbilical cord blood TSH (µIU/mL)

Maternal characteristics	Variables	Cord blood TSH		Total	Chi-square	p value
		<20	>20			
Maternal age	18–25	564 (38.36%)	07 (0.47%)	571 (38.84%)	7.065	**0.0292***
	26–35	852 (57.95%)	22 (1.49%)	874 (59.45%)		
	>35	23 (1.56%)	2 (0.136%)	25 (1.70%)		
Parity	Multiparous	839 (57.07%)	22 (1.49%)	861 (58.57%)	2.005	0.1567
	Primiparous	600 (40.81%)	9 (0.61%)	609 (41.42%)		
Socioeconomic status	Lower	211 (14.35%)	10 (0.68%)	221 (15.03%)	18.3	**0.001***
	Upper Lower	374 (25.44%)	14 (0.95%)	388 (26.39%)		
	Lower Middle	509 (34.62%)	6 (0.4%)	515 (35.03%)		
	Upper Middle	285 (19.38%)	1 (0.06%)	286 (19.45%)		
	Upper	60 (4.08%)	0	60 (4.08%)		

***Denotes statistical significance**

Table 3: Neonatal characteristics and umbilical cord blood TSH (µIU/mL)

Neonatal characteristics	Variables	Cord blood TSH		Total	Chi-square	p value
		<20	>20			
Gender of baby	Females	706 (49.02%)	21 (1.42%)	727 (49.45%)	4.236	**0.0396***
	Males	733 (49.86%)	10 (0.68%)	743 (50.54%)		
Birth weight of baby	1.5–2.5	390 (26.53%)	07 (0.47%)	397 (27.00%)	7.574	0.1085
	2.501–3.00	867 (58.97%)	19 (1.29%)	886 (60.27%)		
	3.001–3.5	128 (8.70%)	3 (0.20%)	131 (8.91%)		
	3.501–4.0	37 (2.51%)	0	37 (2.51%)		
Gestational age	32–36	179 (12.17%)	0	179 (12.17%)	5.859	0.1187
	37–38	991 (67.41%)	22 (1.49%)	1013 (68.91%)		
	39–40	225 (15.30%)	8 (0.54%)	233 (15.85%)		
	>40	44 (2.99%)	1 (0.06%)	45 (3.06%)		
Mode of delivery	LSCS	883 (60.06%)	23 (1.56%)	906 (61.63%)	2.113	0.1461
	Normal vaginal	556 (37.82%)	8 (0.54%)	564 (38.36%)		

In the present study, peripheral venous blood sample was taken after 72 h of birth in all 1470 neonates. The abnormal venous TSH levels >20 µIU/mL were found only in one neonate. The confirmation of diagnosis was done by free T4 estimation and the underlying etiology was confirmed by ultrasonography neck, X-ray of both knee, and Tc 99 m scan.

Various maternal and neonatal factors have varying effects on CB-TSH. We found that mothers of older age groups have statistically significant higher CB-TSH levels (µIU/mL), while other studies have varying effects. The results of our study were in concordance with the study of Raj *et al*. [14] while discordance with the study of Lakshminarayana *et al*. [15] (no effect of maternal age on CB-TSH). Birth order has no effect on CB-TSH (µIU/mL) in our study while Lakshminarayana *et al*. [15] found higher CB-TSH level in first birth order babies than third or more. When the SES of the mothers was compared, the mothers having lower SES had a higher level CB-TSH value than other classes of SES and this difference was statistically significant (p=0.001) in the present study.

Regarding mode of delivery, we found no effect on CB-TSH while studies of Raj *et al*. [14] and Lakshminarayana *et al*. [15] noted that vaginally delivered neonates had higher level CB-TSH than those who delivered by lower segment caesarean section (LSCS). Our hospital being a tertiary care center and referral center for many rural hospitals gets many cases of complicated pregnancies (pregnancy-induced hypertension, eclampsia, and twins) and difficult deliveries (obstructed labor and cephalopelvic disproportion) where many times LSCS was indicated. That's why we had more number of LSCS deliveries than NV deliveries.

The gestational age and birth weight of babies have no effect on CB-TSH in the present study while Lakshminarayana *et al*. [15] and Desai *et al*. [19] found that full-term neonates had significantly higher CB-TSH than those born pre- and post-term or extreme pre-term. Zion and Raheemunnisa found that the majority of the neonates (84.2%) were born at term >37 weeks [20]. Gupta *et al*. [8] and Lakshminarayana *et al*. [15] also found no effect of birth weight on CB-TSH but Zion and Raheemunnisa found that CB-TSH was high in low birth weight neonates (12.85+5.85) as compared to normal birth weight neonates (9.16+8.2) [20]. Furthermore, we found that the female sex of new-born had higher CB-TSH while others found no effect of sex of neonate on CB-TSH [8,14,15]. All pre-term (<37 week) and VLBW babies should be followed up for 3 months due to delayed rise of TSH and to avoid missing any case of CH.

In our study, the mean value of CB-TSH was 11.53±6.63 μIU/mL while other studies show a wide variation from 6.13 to 12.88 μIU/mL [7,8,15,21]. Our range is very close to the mean value found by Raj *et al*. [14] and Rashmi *et al*. [22].

Only one case of CH was confirmed (female) during the follow-up having a high CB-TSH at birth 66.57 μIU/mL, high peripheral venous blood TSH after 72 h of birth 38.44 μIU/mL, and low T4 0.65 ng/dl (due to thyroid gland dysgenesis). Thus, the rate of CH in the present study was 1:1470 neonates. The rates prevalence of CH found in various studies are 1:476 [12], 3:430 [14], 1:1700 [21], 1:2481 [23], and 1:2804 [24]. A study conducted by Bhatia and Rajwaniya found the incidence of CH as 1 in 1824 term neonates [25]. A recent study found the incidence of CH to be 6 out of 73 newborns [20].

Our study is based on single-center experience, which is not covering a larger population for study and lack of follow-up. This study can provide baseline data for future studies in this region, owing to the scarcity of the literature on local data. More studies should be done with a larger sample size, from rural areas, lower socioeconomic status, and longer follow-up periods to consolidate the evidence.

CH is a treatable cause of mental retardation, so the practicing pediatricians should incorporate screening for CH in every child at the time of birth as evidence supports that screening and diagnosis of CH at the appropriate time and initiation of early treatment with an adequate dose of thyroxine changes the outcome of a child with CH.

CONCLUSION

In the present study, we found only one case of CH having a high CB-TSH, peripheral venous blood TSH, and low T4. The cutoff value of TSH (both for CB and peripheral venous blood) >20 μIU/mL has a good recall rate and which is practicable in a given scenario in our country. Elderly mothers, the female gender of neonates, and the lower socioeconomic status of parents have a significant impact on UCBTSH Levels.

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