Original Article

Association of parity with cord blood TSH level variations

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ABSTRACT

Background: Thyroid hormones are important regulators of fetal neurodevelopment and are critical for brain development. The hormones released by the thyroid gland are tri-iodothyronine [T3] and tetra-iodothyronine [T4] which is under the control of thyroid stimulating hormone [TSH] released from the pituitary gland. This hormone is, in turn, under the control of thyrotropin releasing hormone from hypothalamus. Congenital hypothyroidism (CH) is inadequate thyroid hormone production in the newborn infants and is one of the most common preventable causes of mental retardation. Thus, early detection and treatment of CH prevent intellectual disability and optimizes growth and developmental outcomes. Indian Academy of Paediatrics recommends the use of cord blood samples for screening for CH. Different researchers have used different cutoffs for cord blood TSH (CBTSH) levels. A value of >20 mIU/ml for recall of retesting and neonates who have CBTSH values >20 mIU/ml was advised free T3, T4, and TSH assessment after 3 days of life. Various maternal and perinatal factors have been found to affect cord blood thyroid hormone levels, particularly CBTSH. A study of the influence of these factors is, therefore, necessary to improve the interpretation of screening data. This could result in lower recall rates and lessen the anguish of parents awaiting the diagnosis. **Materials and Methods**: This prospective and cross-sectional study was conducted in the Department of Obstetrics and Gynecology, MIMER Medical College and BSTR hospital, Talegaon Dabhade for duration of 1 year 6 months. All parturients coming to the labor ward were included in this study. Women not willing to participate in the study and neonates with major congenital anomalies were excluded from the study. A total of 960 neonates were studied, out of which 98 had high CBTSH levels ≥20 mIU/L. The effect of perinatal variables on CBTSH was analyzed statistically. All the data were entered in Microsoft Excel sheet and then transferred to SPSS software version 18 for statistical analysis. Appropriate tests were applied according to the type and distribution of data and differences were regarded as significant at values of $P < 0.05$. **Results**: The mean CBTSH level was 11.91 ± 7.2 mIU/L with 10.2% of neonates having high CBTSH levels >20 mIU/L. Significant association was found between the perinatal factor such as parity with high CBTSH levels ($P < 0.05$). No significant association was found between high CBTSH levels and gestational age, maternal age, premature rupture of membranes, induction of labor, gender of the baby, or antenatal complications such as preeclampsia, gestational diabetes mellitus, or anemia. **Conclusion**: Parity was found to be significant perinatal factors associated with high CBTSH values. Hence, CBTSH values should be interpreted in the light of these perinatal variables.

Key words: Congenital hypothyroidism, Cord blood thyroid stimulating hormone, Perinatal factors

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INTRODUCTION

Thyroid hormones are important regulators of fetal neurodevelopment and are critical for brain development.[1] The hormones released by the thyroid gland are tri-iodothyronine [T3] and tetra-iodothyronine [T4] which is under the control of thyroid stimulating hormone [TSH] released from the pituitary

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gland. This hormone is, in turn, under the control of thyrotropin releasing hormone from hypothalamus.

Congenital hypothyroidism (CH) is inadequate thyroid hormone production in the newborn infants and is one of the most common preventable causes of mental retardation. The worldwide incidence is 1:3000–4000 live births and the estimated incidence in India is 1:2500–2800 live births.[2] The other studies from India quote a prevalence of 1 in 1985 from Hyderabad[3] and 2.1 in 1000 from Kochi.[2] It is not only the most common pediatric endocrine disorder but is also the most common preventable and treatable cause of mental retardation. More than 95% of newborn infants with CH have few, if any clinical manifestations,[4] so it goes undetected. Thus, early detection and treatment of CH prevent intellectual disability and optimizes growth and developmental outcomes.[5]

Indian Academy of Paediatrics recommends the use of cord blood samples for screening for CH.[6] Cord blood TSH (CBTSH) had high sensitivity with a high false positive rate.[7] Cord blood screening has a lower recall rate and has the advantage of not being invasive, ease of collection, and avoids a second hospital visit when the mothers are discharged early thus decreasing the rate of missed samples. A high correlation has been found between cord blood and heel-prick blood TSH levels measured 48 h after birth, so, cord blood remains a very practical alternative for screening purposes more so in the rural population.[5,8] When CBTSH is measured for CH screening, it has high sensitivity but with a high false positive rates.[7]

A value of >20 mIU/ml for recall of retesting and neonates who have CBTSH values >20 mIU/ml was advised free T3, T4, and TSH assessment after 3 days of life. Various maternal and perinatal factors have been found to affect cord blood thyroid hormone levels, particularly CBTSH. A study of the influence of these factors is, therefore, necessary to improve the interpretation of screening data. This could result in lower recall rates and lessen the anguish of parents awaiting the diagnosis.

Various perinatal factors have been found to be associated with the variation of CBTSH levels.[9,10] Admission of the baby to newborn intensive care unit or any requirement of resuscitation has also been studied for effect on the CBTSH values. These levels may indicate the stress that the fetus is undergoing during the process of delivery. Thus, CBTSH levels can be used as an indicator for the prognosis of fetal outcome.

Thus, the study was conducted to find out the association between various perinatal factors and CBTSH levels.

MATERIALS AND METHODS

This prospective and cross-sectional study was conducted in the Department of Obstetrics and Gynecology, MIMER Medical College and BSTR hospital, Talegaon Dabhade for duration of 1 year 6 months. All parturients coming to the labor ward were included in this study. Women not willing to participate in the study and neonates with major congenital anomalies were excluded from the study. Case record proforma was filled, maternal medical and obstetric details were recorded after taking informed consent from each parturient.

The perinatal variables analyzed for their influence on CBTSH levels included the maternal variables such as parity, age of the mother, mode of delivery, maternal hypothyroidism, premature rupture of membranes, antenatal complications such as preeclampsia, gestational diabetes mellitus, anemia, and neonatal variables such as gestational age, gender, and birth asphyxia. Immediately, after delivery, 5 ml of cord blood sample was collected from the maternal end of the cord in a plain vacutainer and transported to the laboratory within 1 h for estimation of CBTSH levels. The sample was analyzed using electro-chemiluminescence immunoassay on Cobas e 411 analyser with functional sensitivity of 0.014 microIU/ml.

Statistical Analysis

All the data were entered in Microsoft Excel sheet and then transferred to SPSS software version 18 for statistical analysis. Appropriate tests were applied according to the type and distribution of data and differences were regarded as significant at values of $P < 0.05$.

RESULTS

A prospective and cross-sectional study was conducted to find out the association of maternal and neonatal factors with CBTSH levels. In the study, total of 1020 case sheets were studied of which only 960 neonates were found eligible having the CBTSH levels and hence included in the study.

Table 1 : Distribution of study groups as per cord blood TSH levels

Cord Blood TSH
n=960
%
<20 mIU/L
862
89.8%
≥20 mIU/L
98
10.2%
Total
960
100.0%

TSH: Thyroid stimulating hormone

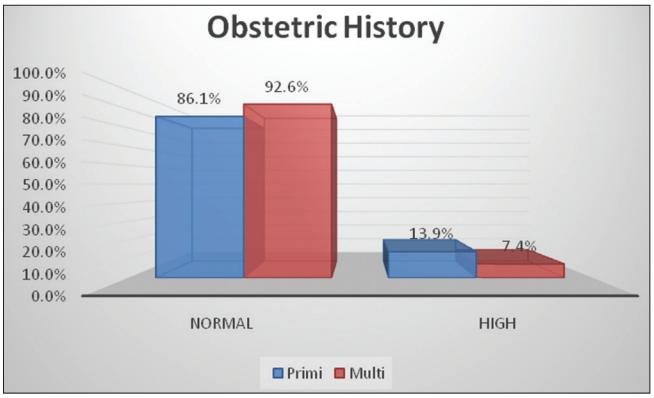
Table 2: Association of cord blood TSH levels with obstetric history

Obstetric History			
Cord Blood TSH	Total	Normal (<20 mIU/L)	High (≥20 mIU/L)
Primi	359	58	417
	86.1%	13.9%	100.0%
Multi	503	40	543
	92.6%	7.4%	100.0%
Total	862	98	960
	89.8%	10.2%	100.0%

P<0.01, TSH: Thyroid stimulating hormone

In the study, to decrease the recall rate, a cutoff value of ≥20 mlU/L was used for high CBTSH levels. Out of 960, 98 (10.2%) neonates had CBTSH above 20 mIU/ml. Mean CBTSH level was 11.91 ± 7.2 mIU/L (Range 1.71–55.6 mIU/L). At 72 h of life, repeat TSH, FT4, and FT3 were done. Out of these 98 neonates with high CBTSH levels, 2 (0.2%) were found to have high TSH satisfying the criteria for CH.

In the study, among the perinatal factors, parity was found to be significantly associated with high CBTSH levels. Statistically significant association was observed between primiparas and high CBTSH levels ($P < 0.01$).



Graph 1: Association of cord blood TSH levels with obstetric history

DISCUSSION

The main objective of the study was to find out association of various perinatal factors with CBTSH levels. We studied the association of various perinatal factors such as parity, mode of delivery, preeclampsia, anemia, gestational diabetes mellitus, induction of labor, premature rupture of membranes, and neonatal factors such as birth asphyxia, APGAR scores (at 1 min and 5 min), gestational age, birth weight, and gender.

Various authors have found association of various factors with an increase in CBTSH values, such as birth asphyxia and difficult deliveries,[11] perinatal stress events,[12,13] and instrumental delivery,[5] and no association with cesarean section as mode of delivery,[14] but the mechanisms are poorly understood.[15]

In the study, two groups were formed, as neonates born to primipara and the other group consisting of neonates born to multipara. In the group of neonates born to primipara mothers, 13.9% had high CBTSH levels (≥20 mIU/L) whereas in those born to multipara mothers, 7.4% had high CBTSH levels (≥20 mIU/L). We found significant increase in CBTSH levels among neonates of primipara mothers. Statistically significant association was found between primipara mothers and high CBTSH levels ($P < 0.05$) [Graph 1].

Gupta *et al*.[12] also observed higher CBTSH levels in primipara mothers (9.03 vs. 7.47 mIU/L; $P < 0.05$). Similar results were also observed by other authors.[5,11,13] Herbstman *et al*.[16] have proposed that this pattern might be related to environmental exposure, as some persistent chemicals are found at higher levels in

firstborn children.[16] In addition, the relatively more difficult labor associated with a first delivery compared to subsequent deliveries could increase TSH levels.[16]

Other factors such as birth weight, gestational age, and antenatal complications such as preeclampsia, gestational diabetes mellitus, and anemia did not have statistically significant association with CBTSH levels ($P > 0.05$).

CONCLUSION

Association between perinatal factors with CBTSH has been proven. Any rise in CBTSH should be interpreted and analyzed after taking these factors into consideration. Thus, CBTSH if interpreted in the light of these factors can help to reduce the rescreening number thereby saving a lot of cost and time. In the study, parity was the significant factor associated with high CBTSH levels. Other factors such as birth weight, gestational age and antenatal complications such as preeclampsia, gestational diabetes mellitus, and anemia did not have statistically significant association with CBTSH levels. Further larger studies are required to find out a correction in CBTSH cutoffs in accordance with perinatal factors.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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