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Original Research Article

Association of maternal and perinatal factors with umbilical cord blood thyroid profile in newborns: a prospective observational study

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ABSTRACT

Background: Congenital hypothyroidism (CH) is a preventable cause of intellectual disability. Cord blood thyroid-stimulating hormone (TSH) is widely used for newborn screening; however, several perinatal factors may influence TSH levels and increase false-positive results. Objectives were to evaluate the effect of maternal and perinatal factors on cord blood thyroid profiles in neonates.
Methods: A hospital-based cross-sectional observational study was conducted among 90 neonates. Cord blood samples collected at birth were analyzed for TSH levels. Maternal age, parity, gestational age, mode of delivery, weight of the baby, gender, and birth asphyxia were recorded. A student's t test, one-way ANOVA, and chi-square test were used to analyze the data. Statistical significance was considered at $p<0.05$.
Results: The mean cord blood TSH level was 13.53±6.22 µIU/ml. Elevated TSH (>20 µIU/ml) was observed in 14.4% of neonates. Higher cord blood TSH levels were significantly associated with parity ($p=0.010$), mode of delivery ($p<0.001$), and birth asphyxia ($p=0.006$). Assisted vaginal delivery was associated with the highest mean TSH level (20.76 µIU/ml). Cord blood TSH levels were not significantly associated with maternal age, gestational age, birth weight, and gender.
Conclusions: Cord blood TSH is a useful screening test for CH. However, interpretation should be based on perinatal factors, mainly mode of delivery, parity, and birth asphyxia, to minimize false positive results and improve screening accuracy.

Keywords: Cord blood TSH, Perinatal factors, Birth asphyxia

INTRODUCTION

Congenital hypothyroidism (CH) is one of the most common preventable causes of intellectual disability and is an important cause of neurodevelopmental impairment if left untreated.[1] Thyroid hormones are important for fetal and neonatal brain development, including neuronal migration, myelination, synapsis formation, and growth.[2] Early diagnosis and initiation of treatment still remain the cornerstone to achieve optimum neurodevelopment.[3,4]

India has reported a higher incidence ranging from 1 in 2,500 to 1 in 2,800 live births.[5,6] Due to transplacental delivery of maternal thyroid hormones, most affected newborns are clinically asymptomatic at birth. Hence, newborn screening helps early detection and management of CH.[2]

TSH samples are usually collected 48-72 hours after birth. However, cord blood TSH estimation is increasingly done in institutional deliveries, as it allows sample collection immediately after birth, avoids resampling of newborns, and improves screening coverage, particularly in resource-limited settings.[7,8]

Cord blood TSH concentrations are influenced by the physiological neonatal TSH surge that occurs immediately after birth and by several maternal and perinatal factors.[9] Gestational age, birth weight, parity,

mode of delivery, birth asphyxia, maternal age, and perinatal stress have all been reported to influence neonatal thyroid hormone levels, potentially leading to transient TSH elevation and false-positive screening results.[10,11] Such false-positive results may increase anxiety in parents, necessitating repeat testing.

Previous studies evaluating the association of perinatal factors and cord blood TSH levels have shown inconsistent results because of differences in study populations, laboratory diagnosis, and screening cut-off values.[12,13] Identifying the influence of these factors is important for accurate interpretation of neonatal thyroid screening and for improving the specificity of CH screening programs.

Therefore, the present study was undertaken to evaluate the association of various perinatal factors with cord blood thyroid hormone levels among neonates and to identify perinatal factors that significantly influence cord blood TSH levels.

METHODS

Study design and setting

A hospital-based cross-sectional observational study was conducted in the Department of Paediatrics, Cheluvamba Hospital, Mysore Medical College and Research Institute (MMC and RI), Mysuru, Karnataka, over a period of 18 months from March 2024 to September 2025 after obtaining approval from the Institutional Ethics Committee.

Study participants

The study included 90 singleton live-born neonates delivered at Cheluvamba Hospital between 28 and 42 completed weeks of gestation. Written informed consent was obtained from the parents or legal guardians before enrolment. Singleton live-born neonates, with a gestational age between 28 and 42 completed weeks and parents or legal guardians who provided written informed consent were included in our study.

Neonates with major congenital malformations, multiple gestations, neonates born to mothers with known thyroid disorders or euthyroid goitre and those receiving antithyroid drugs or thyroid hormone replacement therapy during pregnancy were excluded from our study.

Sample size

The minimum sample size was calculated using the standard formula for comparison of means with a 95% confidence interval, 80% power, an expected mean difference of 0.97, and a standard deviation of 3.28. The calculated sample size was 90 neonates, who were enrolled consecutively until the required sample size was achieved.

Data collection

Maternal and neonatal data were collected using a predesigned and pretested case record proforma. Maternal variables included age and parity. Neonatal variables included sex, gestational age, birth weight, mode of delivery, Apgar scores, birth asphyxia, and requirement of resuscitation.

Cord blood sample collection

Immediately after delivery and clamping of the umbilical cord, approximately 3-5 mL of cord blood was collected aseptically from the placental end of the umbilical cord into a sterile plain vacutainer. Samples were transported to the central laboratory, allowed to clot, and centrifuged to separate serum.

Serum TSH, triiodothyronine (T3), and thyroxine (T4) concentrations were estimated using a standard chemiluminescent immunoassay as per the manufacturer's instructions and institutional laboratory protocol.

The 24 neonates with elevated cord blood TSH values suggestive of CH underwent repeat thyroid function testing after seven days of life to differentiate transient hypothyroidism from CH, in accordance with standard newborn screening recommendations.[2]

Outcome measures

The primary outcome was cord blood TSH concentration. The association between cord blood TSH levels and perinatal factors, including maternal age, parity, gestational age, birth weight, neonatal sex, mode of delivery, and birth asphyxia, was evaluated.

Statistical analysis

Data were entered into Microsoft excel and analyzed using statistical package for the social sciences (SPSS) version 28.0. Continuous variables were expressed as mean and standard deviation, whereas categorical variables were expressed as frequency and percentage. A student's t test was used for comparison between two groups, one-way analysis of variance (ANOVA) for comparison among more than two groups, and the chi-square test for categorical variables. A $p<0.05$ was considered statistically significant.

Ethical considerations

The study was approved by the institutional ethics committee of Mysore Medical College and Research Institute, Mysuru, prior to the commencement of the study. Written informed consent was obtained from the parents or legal guardians of all study participants. The study was conducted in accordance with the ethical principles outlined in the declaration of Helsinki.

RESULTS

In our study, mean cord blood TSH values were 13.53±6.52 µIU/ml. Of the 90 newborns studied, 13 (14.4%) had elevated cord blood TSH levels (>20 µIU/mL) requiring further evaluation, while 77 (85.6%) had normal TSH levels (Figure 1).

Out of 90, the majority of mothers (34.4%) belonged to the 20-25 years age group, followed by 26-30 years (28.9%), 31-35 years (20.0%), >35 years (10.0%), and <20 years (6.7%). No association was observed between cord blood TSH values and maternal age. Mean values of cord blood TSH were comparable across various subgroups of maternal age (p>0.05).

More than half of the mothers (62.2%) were primiparous, while 37.8% were multiparous. The mean cord blood TSH for babies born to primipara mothers was 14.8±6.4 µIU/ml, and for babies born to multipara mothers was 11.45±5.4 µIU/ml. The TSH levels of cord blood in babies of primipara were higher than those of multipara (p<0.01).

Female newborns (52.2%) slightly more than male newborns (47.8%). No association was observed between cord blood TSH values and the gender of the baby. Mean values of cord blood TSH was comparable between male and female neonates (p>0.05). Normal vaginal delivery was the most common mode (40.0%), followed by elective LSCS (27.8%), emergency LSCS (26.7%), and assisted vaginal delivery (5.6%). Assisted vaginal delivery had the highest mean TSH followed by normal vaginal delivery (20.76±1.39 µIU/ml and 15.48±6.11 µIU/ml respectively). Cord blood TSH levels were significantly higher in assisted vaginal delivery than in normal vaginal delivery (p<0.01).

Most of the newborns (64.4%) were term babies (37-40 weeks), 18.9% were late preterm, 10.0% were post-term, while 6.7% were very preterm. No association was observed between TSH values in cord blood and gestation.

The majority (60.0%) had normal birth weight (2500-3499 g), followed by low birth weight (21.1%), high birth weight (14.4%), and very low birth weight (4.4%). No correlation was found between birth weight and cord blood TSH values.

Birth asphyxia was present in 11.1% of newborns and was absent in 88.9% (APGAR score ≥7 at 5 minutes). The mean cord blood TSH was 19.6±6 µIU/ml for babies born with birth asphyxia and 12.8±5.9 µIU/ml for babies born without birth asphyxia. Significantly, higher mean cord blood TSH levels were observed in babies with birth asphyxia (p<0.01) (Table 1).

A significant inverse correlation was observed between cord blood TSH and gestational age and birth weight (p<0.01) i.e.; higher TSH values were observed with decreasing gestation age and low birth weight.

Parity, mode of delivery, and birth asphyxia are important determinants of cord blood TSH levels, while maternal age, gestational age, birth weight, and neonatal sex do not significantly influence cord blood TSH concentrations in the study population.

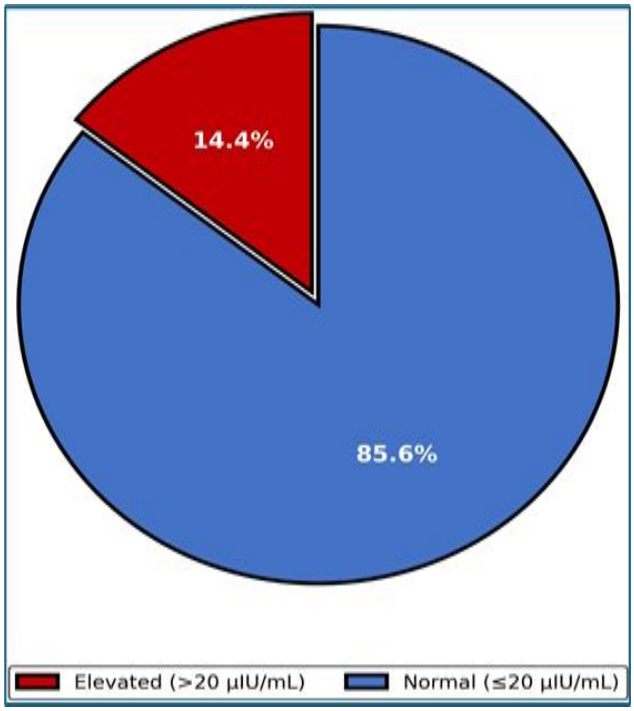

Figure 1: Distribution of elevated cord blood TSH.

Table 1: Demographic profile of mothers and newborns and their association with cord blood TSH levels.

Characteristics	N (%)	Mean±SD	P value
Maternal age (in years)			
<20	6 (6.7)	13.99±8.24	0.324
20-25	31 (34.4)	12.67±5.6	
26-30	26 (28.9)	15.39±5.6	
31-35	18 (20)	11.71±6	
>35	9 (10)	14.46±8.5	
Parity			
Primipara	56 (62.2)	14.80±6.4	0.010*
Multipara	34 (37.8)	11.45±5.4	

Continued.

Characteristics	N (%)	Mean±SD	P value
Mode of delivery			
Normal vaginal delivery	36 (40)	15.48±6.1	0.001*
Assisted vaginal delivery	5 (5.6)	20.76±1.4	
Emergency LSCS	24 (26.7)	10.33±4.9	
Elective LSCS	25 (27.8)	12.36±6.1	
Gender			
Male	43 (47.8)	12.47±7.1	0.127
Female	47 (52.2)	14.50±5.2	
Gestation			
28-32 weeks (very preterm)	6 (6.7)	18±6.3	0.058
33-36 weeks (late preterm)	17 (18.9)	15.6±4.9	
37-40 weeks (term)	58 (64.4)	12.9±5.9	
>40 weeks (post-term)	9 (10)	10.8±8.4	
Birth weight (in gm)			
<1500 (VLBW)	4 (4.4)	19.7±4.8	0.158
1500-2499 (LBW)	19 (21.1)	14.4±6.7	
2500-3499 (normal)	54 (60)	13.0±6.2	
≥3500 (high)	13 (14.4)	12.2±5.3	
Birth asphyxia			
Present (APGAR <7 at 5 min)	10 (11.1)	19.6±6	0.006*
Absent (APGAR ≥7 at 5 min)	80 (88.9)	12.8±5.9	

*Statistically significant (p<0.05)

DISCUSSION

The aim of the study was to investigate the association of perinatal factors and cord blood TSH in newborns. The mean TSH level in cord blood was 13.53±6.22 µIU/ml. The abnormal TSH levels (>20 µIU/ml) were detected in 14.4% of neonates. Associations were significant between cord blood TSH levels and parity, mode of delivery, and birth asphyxia. There was no significant association between cord blood TSH levels and maternal age, gestational age, birth weight, and gender.

Association was not significant between maternal age and cord blood TSH levels in the study. Studies done by Armanian et al, Lee et al, Tan et al and Fariduddin et al showed that maternal age alone would not affect neonatal thyroid function at birth.[10-14]

Parity and cord blood TSH levels were significantly associated. TSH levels of primiparous mothers were higher than those of multiparous mothers. Lakshminarayana et al, Garg et al, Poyekar et al and Katyayani et al found a significant increase in cord blood TSH levels among first-order births.[11,15-17] An exaggerated neonatal TSH surge could be due to stress with the first pregnancy and labor.

Mode of delivery and cord blood TSH levels were significantly associated. Neonates delivered by assisted vaginal delivery showed the highest mean TSH levels, whereas those delivered by caesarean section had the lowest levels. Studies by Armanian et al, Lee et al, Tan et al, McElduff et al and Aliefendioglu et al suggested higher cord blood TSH concentrations following vaginal and assisted vaginal deliveries compared with caesarean section.[10-12,18,19] Labor-related stress, release of catecholamine, hypoxia, and hypothalamic-pituitary-thyroid axis activation are a few hypotheses.

Birth asphyxia and cord blood TSH levels were significantly associated. Newborns with birth asphyxia had higher TSH levels than those without asphyxia. Studies by Khashana et al and Fariduddin et al showed hypoxic stress in the perinatal period affected thyroid hormone secretion in newborns. Some studies suggested thyroid hormone suppression in severe hypoxia, showing varied endocrine responses according to the severity and insult duration.[14,20]

Gestational age was not associated with cord blood TSH levels. Studies by Armanian et al, Lee et al, Tan et al and Fariduddin et al showed an opposite finding i.e., higher TSH levels among preterm neonates.[10-14] Birth weight was not associated with cord blood TSH levels, similar to observations in previous studies.[18-20] Gestational age was not associated with cord blood TSH levels. Similar to previous studies.[18-20]

A study shows significant association of perinatal factors i. e., parity, mode of delivery, and birth asphyxia, with cord blood TSH levels. For accurate analysis of thyroid screening in newborns, one has to have prior knowledge to reduce false-positives.

The inclusion of perinatal data into newborn screening improves the specificity of cord blood TSH-based screening of CH.

Limitations

The present study has certain limitations. It was conducted at a single tertiary care center with a relatively small sample size, which may limit the generalizability of the findings. Maternal iodine status and other potential confounding variables were not assessed. Larger multicenter studies with longer follow-up are recommended to validate these findings and establish population-specific reference values for cord blood TSH in Indian neonates.

CONCLUSION

Cord blood TSH is a useful screening tool for congenital hypothyroidism; However, its interpretation is significantly influenced by perinatal stress factors such as mode of delivery, parity, and birth asphyxia. The study establishes that perinatal stress has a measurable and significant effect on neonatal cord blood thyroid profile, and that incorporation of perinatal clinical context can improve the specificity, reliability, and practical value of neonatal thyroid screening programs.

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