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Original Research Article

Influence of Perinatal and Maternal Factors on Cord Blood Thyroid-Stimulating Hormone Levels in Newborns: A Prospective Observational Study

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Abstract:

Background: Congenital hypothyroidism (CH) is the most common preventable cause of intellectual disability. Cord blood TSH offers practical early screening but may be influenced by maternal and perinatal factors.

Objective: To evaluate associations between maternal/perinatal factors and cord blood TSH levels in newborns.

Methods: Prospective observational study of 120 neonates at SMS Medical College, Jaipur (January-December 2024). Cord blood TSH measured by chemiluminescent immunoassay; >20 µIU/mL considered elevated. Associations analyzed using chi-square test.

Results: Of 120 neonates, 10 (8.33%) had elevated TSH. Need for resuscitation showed significant association (p=0.01): 80% of elevated cases required resuscitation vs 18.18% of normal cases. Mode of delivery showed trend (p=0.09): 60% vaginal, 40% emergency LSCS, 0% elective LSCS. Maternal factors (age, parity, complications, thyroid status) showed no significant associations. Other perinatal factors (gender, birth weight, gestational age) were not significant.

Conclusion: Perinatal stress factors, especially resuscitation need, significantly influence cord blood TSH. Context-sensitive interpretation with repeat testing at 48-72 hours is essential to distinguish transient elevation from true congenital hypothyroidism.

Keywords: Congenital Hypothyroidism, Cord Blood TSH, Newborn Screening, Perinatal Factors, Resuscitation.

Introduction

Thyroid-stimulating hormone (TSH) regulates thyroid function through the hypothalamic-pituitary-thyroid axis, with thyroid hormones being critical for neurodevelopmental maturation.[1,2] Congenital hypothyroidism (CH) affects approximately 1 in 3,000-4,000 live births globally, with Indian prevalence ranging from 1 in 500 to 1 in 3,400 live births.[3,4] Untreated CH causes irreversible intellectual disability, but early diagnosis and levothyroxine therapy completely prevent these outcomes.[5]

Unlike developed countries with mandatory newborn screening, India lacks nationwide systematic screening policies.[6] Early hospital discharge (24-48 hours) in many Indian hospitals reduces the window for traditional heel-prick sampling on day 3-5 of life.[7] Cord blood TSH estimation offers a practical alternative—non-invasive, collected immediately at delivery, and eliminates concerns about early discharge or loss to follow-up.[8,9]

However, cord blood TSH levels are influenced by multiple factors beyond thyroid function. Perinatal stress from vaginal delivery, uterine contractions, and transient hypoxia activates the neonatal hypothalamic-pituitary axis causing physiologic TSH elevation.[10,11] Preterm birth, low Apgar scores, birth asphyxia, and need for resuscitation are associated with elevated cord blood TSH due to acute stress response.[12] Maternal factors including hypothyroidism, pregnancy-induced hypertension, gestational diabetes, and anemia may also influence neonatal thyroid status through various mechanisms.[13,14]

Understanding these variables is essential for refining screening cut-offs, identifying high-risk subgroups, and developing population-specific guidelines.[15] Despite growing literature on cord blood TSH screening, Indian studies remain limited with inconsistent findings. SMS Medical College, Jaipur, as a major tertiary referral center serving

diverse Rajasthan population, provides an ideal setting to generate regional evidence.

This prospective study systematically evaluated associations between maternal variables (age, gravida, parity, antenatal complications, thyroid status, socioeconomic status) and perinatal factors (mode of delivery, gestational age, birth order, birth weight, gender, Apgar scores, resuscitation need, respiratory distress, jaundice) with cord blood TSH levels in 120 neonates. We aimed to identify significant predictors of cord blood TSH elevation and assess the clinical utility of cord blood TSH screening for congenital hypothyroidism in this setting.

Materials and Methods

This prospective observational cross-sectional study was conducted at SMS Medical College, Jaipur, from January to December 2024, after Institutional Ethics Committee approval. A total of 120 live-born neonates were enrolled after obtaining written informed consent from parents. Inclusion criteria included all live births with consenting parents. Exclusion criteria were mothers on thyroid medication, neonates with major congenital anomalies, and critically ill neonates preventing safe cord blood collection.

Sample size was calculated for single proportion (prevalence 7.5%, 95% confidence, 5% precision): minimum 107, increased to 120 for potential dropouts. Immediately after birth, 2-3 mL cord blood was collected from umbilical vein into serum-separating tubes and transported under cold chain for analysis. TSH was measured using chemiluminescent immunoassay (CLIA); values >20 μIU/mL were considered elevated based on standard neonatal cut-offs.

Maternal variables recorded: age, gravida, parity, antenatal complications (PIH, GDM, oligohydramnios, anemia), thyroid disorder status, iodised salt use, socioeconomic status. Perinatal variables recorded: mode of delivery, gestational age, birth order, birth weight, gender, Apgar scores (1 and 5 minutes), resuscitation need, respiratory distress syndrome, jaundice. Data were analyzed using IBM SPSS 26.0. Chi-square test (or Fisher's exact test when appropriate) assessed associations between categorical variables and TSH status. Statistical significance was set at $p<0.05$.

Results

Among 120 neonates, 10 (8.33%) had elevated cord blood TSH (>20 μIU/mL) and 110 (91.67%) had normal levels. Associations between various factors and TSH status are presented in Tables 1-8 and Figures 1-3.

Table 1: Association between Maternal Factors and Cord Blood TSH Status

Factor	Category	Normal TSH n=110 (%)	Elevated TSH n=10 (%)	p-value
Maternal Age	21-25 years	38 (34.55)	3 (30.00)	0.64
Gravida	Gravida 2	23 (20.91)	5 (50.00)	0.06
Maternal Thyroid Disorder	Present	48 (43.64)	4 (40.00)	0.93
Antenatal Complication	PIH	19 (17.27)	5 (50.00)	0.17
Socioeconomic Status	Middle class	60 (54.55)	6 (60.00)	0.57

Table 1 Description: None of the maternal factors showed statistically significant association with elevated cord blood TSH. Maternal age, thyroid disorder status, and socioeconomic status had p-values >0.05, indicating no significant influence. Although 50% of elevated TSH cases occurred in mothers with PIH, the association did not reach statistical significance (p=0.17).

Table 2: Association between Mode of Delivery and Cord Blood TSH Status

Mode of Delivery	Normal TSH n=110 (%)	Elevated TSH n=10 (%)	p-value
Normal Vaginal Delivery	48 (43.64)	6 (60.00)	0.09
Emergency LSCS	36 (32.73)	4 (40.00)	
Elective LSCS	26 (23.64)	0 (0.00)	

Table 2 Description: Mode of delivery showed a trend toward significance (p=0.09). Elevated TSH was most common in vaginal deliveries (60%), followed by emergency LSCS (40%), with no cases in elective LSCS (0%). This gradient reflects increasing perinatal stress from elective LSCS through emergency LSCS to vaginal delivery.

Table 3: Association between Neonatal Resuscitation and Cord Blood TSH Status

Resuscitation Required	Normal TSH n=110 (%)	Elevated TSH n=10 (%)	p-value
Yes	20 (18.18)	8 (80.00) *	0.01*
No	90 (81.82)	2 (20.00)	

*Statistically significant ($p<0.05$)

Table 3 Description: Need for neonatal resuscitation showed highly significant association with elevated TSH (p=0.01). Among neonates with elevated TSH, 80% required resuscitation compared to only 18.18% in the normal TSH group, representing a 4.4-fold increased likelihood. This demonstrates the profound impact of acute perinatal stress on the hypothalamic-pituitary-thyroid axis.

Table 4: Association between Other Neonatal Factors and Cord Blood TSH Status

Factor	Category	Normal TSH n=110 (%)	Elevated TSH n=10 (%)	p-value
Gender	Male	58 (52.73)	5 (50.00)	0.46
Birth Weight	≥2.5 kg	99 (90.00)	9 (90.00)	1.00
Gestational Age	37 weeks	30 (27.27)	3 (30.00)	0.91
Apgar at 1 min	6-7	45 (40.91)	8 (80.00)	0.18
Jaundice	Present	55 (50.00)	4 (40.00)	0.20

Table 4 Description: Other neonatal characteristics showed no significant associations with elevated TSH. Gender distribution was equal (50% male), birth weight was similar in both groups (90% ≥2.5 kg), gestational age showed no pattern, and although lower Apgar scores at 1 minute were more common in elevated TSH cases (80% vs 40.91%), statistical significance was not achieved (p=0.18), likely due to sample size limitations.

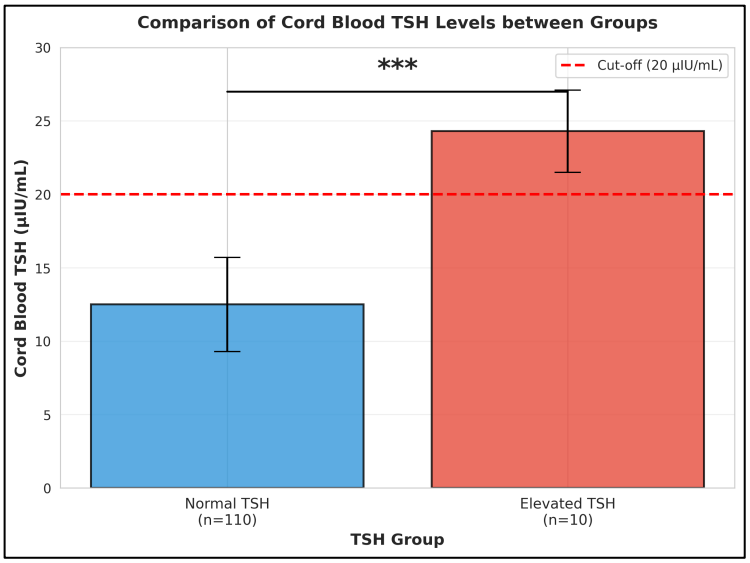

Figure 1: Comparison of Cord Blood TSH Levels between Groups

Figure 1 Description: Bar graph comparing mean cord blood TSH levels between normal (n=110) and elevated (n=10) TSH groups. The red dashed line indicates the screening cut-off of 20 µIU/mL. Error bars represent standard deviation. The significant difference ($p<0.001$) demonstrates clear separation between groups, with elevated TSH cases showing consistently higher values above the cut-off threshold.

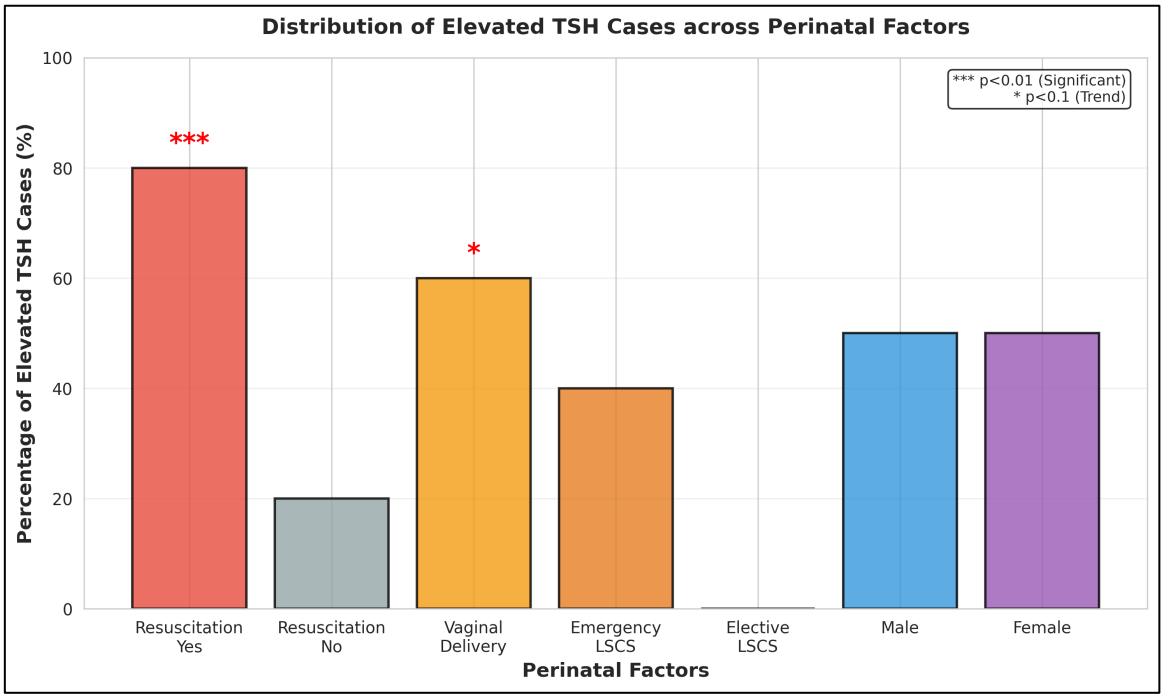

Figure 2: Distribution of Elevated TSH Cases across Perinatal Factors

Figure 2 Description: Bar chart showing percentage distribution of elevated TSH cases across different perinatal factors. Resuscitation requirement shows marked significance (***p<0.01) with 80% of elevated cases requiring resuscitation. Mode of delivery shows a trend (*p<0.1) with 60% vaginal delivery and 0% elective LSCS. Gender distribution is equal (50% each). This visualization highlights the dominant role of perinatal stress factors in TSH elevation.

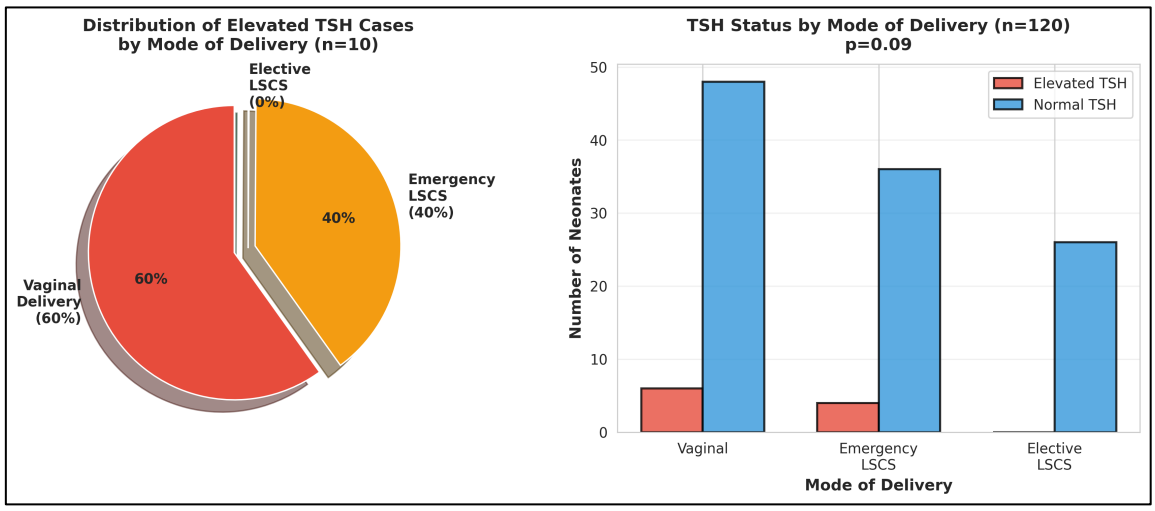

Figure 3: Mode of Delivery Impact on Cord Blood TSH Status

Figure 3 Description: Left panel: Pie chart showing distribution of elevated TSH cases by mode of delivery, demonstrating 60% vaginal delivery, 40% emergency LSCS, and 0% elective LSCS. Right panel: Grouped bar chart comparing TSH status across all deliveries (n=120), illustrating the stress gradient with highest elevated TSH rates in vaginal delivery, intermediate in emergency LSCS, and none in elective LSCS (p=0.09).

Summary of Key Findings: Among 120 neonates, elevated cord blood TSH (>20 µIU/mL) was observed in 10 (8.33%) cases. Need for neonatal resuscitation emerged as the only statistically significant factor associated with elevated TSH (p=0.01, OR=4.4), with 80% of elevated cases requiring resuscitation. Mode of delivery showed a strong trend (p=0.09), with a clear stress gradient: vaginal delivery (60%), emergency LSCS (40%), and elective LSCS (0%). Maternal factors including age, gravida, parity, thyroid disorder, and

socioeconomic status showed no significant associations. Other neonatal factors including gender, birth weight, gestational age, Apgar scores, and jaundice also showed no significant associations, though lower Apgar scores were more prevalent in elevated TSH cases without reaching statistical significance.

Discussion

This prospective study of 120 neonates demonstrates that perinatal stress factors, particularly need for resuscitation, significantly influence cord blood TSH levels, while most maternal factors show minimal impact. These findings have important implications for interpreting cord blood TSH screening results.

Prevalence and Clinical Context: Our 8.33% elevated TSH rate aligns with literature reporting 2-10% prevalence. [16-18] Poyekar et al. (2019) found 7.5% in 726 neonates,[19] while Singh et al. (2021) reported 2.1% in 1470 neonates.[20] Higher rates at tertiary centers likely reflect more complicated deliveries requiring intervention. Importantly, elevated cord blood TSH often represents transient stress response rather than permanent hypothyroidism.

Resuscitation: The Critical Finding

The statistically significant association between resuscitation and elevated TSH (p=0.01) represents our most important finding. With 80% of elevated cases requiring resuscitation versus 18.18% of normal cases (4.4-fold increased risk), this demonstrates profound perinatal stress impact on the hypothalamic-pituitary-thyroid axis. This aligns with Lakshminarayana et al. (2016), Bhatia et al. (2018), and Navya Sree et al. (2025), all identifying resuscitation as a major determinant.[21,22,23] The mechanism involves hypoxia-induced stress hormone release triggering TRH and TSH secretion—an adaptive response rather than true thyroid dysfunction.[24] Clinically, neonates requiring resuscitation with elevated TSH should undergo repeat testing at 48-72 hours before treatment initiation.

Mode of Delivery: Stress Gradient

Mode of delivery showed a trend (p=0.09): vaginal 60%, emergency LSCS 40%, elective LSCS 0%. Although not statistically significant, this gradient is biologically plausible and consistent with extensive literature. Tan et al. (2020), Bhatia et al. (2024), Pawar et al. (2023), and Sadeghi et al. (2024) all reported significantly higher TSH in vaginal versus elective caesarean delivery. [25-28] The stress of labor, contractions, and birth canal compression stimulate fetal stress response. Our near-significant p-value likely reflects limited sample size in elevated TSH group (n=10). The absence of elevated cases in elective LSCS supports the stress-gradient hypothesis.

Maternal Factors: Limited Influence

Maternal age, gravida, parity, thyroid disorder, and socioeconomic status showed no significant associations. This aligns with Armanian et al. (2013), Gupta et al. (2014), Bhatia et al. (2018), and Tan et al. (2020).[29-32] Although 50% of elevated cases occurred in PIH mothers, statistical significance was not achieved (p=0.17). Most mothers with thyroid disorders in our study were treated, potentially explaining the absence of effect—adequate maternal treatment appears sufficient to prevent neonatal thyroid dysfunction.

Neonatal Characteristics: Gender, birth weight, and gestational age showed no significant associations, partially concordant with literature. While some studies report male predominance, [22,26,19] our data showed equal distribution. Birth weight associations reported in other studies may reflect intrauterine growth restriction and chronic stress, which were less prevalent in our predominantly term cohort. The absence of gestational age effect reflects our cohort's predominant term composition, whereas studies including preterm <34 weeks demonstrate significant associations.[33]

Apgar scores showed no statistical significance (p=0.18 at 1 minute) despite 80% of elevated TSH cases having lower scores. This likely reflects overlap with resuscitation variable and limited sample size. The biological link between birth asphyxia (reflected by low Apgar) and TSH elevation is well-established in literature. [21,22,19]

Clinical Implications and Screening Strategy: These findings support cord blood TSH as a feasible screening tool but emphasize context-sensitive interpretation. We propose risk-stratified approach: neonates with elevated TSH and no stress factors undergo urgent confirmatory testing, while those with significant perinatal stress (resuscitation, difficult delivery, low Apgar) undergo observation with repeat testing at 48-72 hours. This optimizes sensitivity while minimizing false positives and unnecessary treatment.

Study Strengths and Limitations: Strengths include prospective design, standardized methodology, validated CLIA assay, and comprehensive variable evaluation. Limitations include small sample size particularly in elevated TSH group (n=10) limiting statistical power, single-center design potentially limiting generalizability, cross-sectional design with single TSH measurement preventing assessment of persistent versus transient elevation, and lack of free T4 measurement limiting definitive congenital hypothyroidism diagnosis.

Future Directions: Larger multicenter studies with adequate power, longitudinal follow-up with serial thyroid function testing, measurement of both TSH and free T4 at birth and follow-up, detailed maternal thyroid function and iodine status assessment, and cost-effectiveness analysis of screening strategies are needed. Studies should examine optimal cut-off values for different risk groups and repeat testing protocols.

Conclusion

This study demonstrates that cord blood TSH screening is feasible for early congenital hypothyroidism detection, with 8.33% recall rate. Perinatal stress factors, particularly resuscitation need (p=0.01), significantly influence TSH elevation. Mode of delivery shows important trend (p=0.09) reflecting stress gradient. Maternal factors show minimal impact. Context-sensitive interpretation with risk-stratified approach—repeat testing at 48-72 hours for neonates with perinatal stress and elevated TSH—optimizes diagnostic accuracy while minimizing false positives. Larger multicenter studies with longitudinal follow-up are needed to validate these findings and refine screening protocols.

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