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CORD BLOOD THYROID PROFILE VERSUS 48-HOUR VENOUS THYROID PROFILE IN TERM AND PRETERM NEONATES: A PROSPECTIVE COMPARATIVE STUDY

Paediatrics

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ABSTRACT

Background: Congenital hypothyroidism (CH) is among the most prevalent preventable causes of neurodevelopmental disability worldwide. Neonatal thyroid function undergoes rapid postnatal adaptation, yet the relationship between cord blood and 48-hour thyroid profiles remains incompletely characterised, especially in preterm neonates in low-resource Indian settings.**Objectives:** To compare cord blood thyroid hormone levels (T3, T4, TSH) with corresponding venous levels at 48 hours of life in term and preterm neonates, and to examine gestational age-related differences in thyroid hormone dynamics.**Methods:** A hospital-based prospective comparative study was conducted at a tertiary care centre in Barabanki, Uttar Pradesh, over 18–24 months. A total of 121 neonates (98 term, 23 preterm) were enrolled. Cord blood (2 mL) was collected at birth and venous blood (2 mL) at 48 hours. Serum T3, T4, and TSH were measured using ELISA. Paired t-test and chi-square test were applied; $p < 0.05$ was considered statistically significant.**Results:** Mean T3 rose significantly from 79.5 ± 35.4 ng/dL (cord) to 113.6 ± 37.2 ng/dL (48 h) ($p < 0.0001$). Mean T4 increased from 11.1 ± 3.5 to 14.7 ± 6.1 mcg/dL ($p < 0.0001$). Mean TSH declined from 6.75 ± 4.1 to 5.10 ± 3.2 mIU/L ($p = 0.0006$). Cord T3 distribution differed significantly between term and preterm neonates ($p = 0.0014$), whereas T4 and TSH showed no significant gestational-group difference at either time point.**Conclusion:** Neonatal thyroid function undergoes significant physiological adjustment within 48 hours of birth. Venous thyroid profiling at 48 hours provides a more reliable assessment than cord blood alone. Preterm neonates demonstrate distinct cord T3 distributions, highlighting the need for gestational age-appropriate screening strategies.

KEYWORDS

Congenital Hypothyroidism; Cord Blood Thyroid Profile; Neonatal TSH Surge; Preterm Neonates; Thyroid Screening; T3; T4; TSH

INTRODUCTION

Congenital hypothyroidism (CH) is the single most common preventable cause of intellectual disability in the newborn period, with a global incidence of approximately 1 in 2000–4000 live births across varied populations.1,2 When undetected, CH produces irreversible cognitive impairment, sensorineural hearing loss, growth failure, and neuromotor deficits. Population-based newborn thyroid screening, pioneered by Dussault and colleagues in Quebec in 1974, has transformed the prognosis of CH from one of inevitable developmental devastation to near-normal intellectual outcomes when treatment is initiated early.3

In India, an estimated 6000–10,000 new cases of CH arise annually, driven by approximately 25–26 million live births each year, yet universal newborn screening remains unavailable across much of the country.4,5 The logistical challenges of standardised heel-prick filter paper sampling at 48–72 hours have prompted interest in cord blood thyroid profiling as an alternative that is logistically simpler and universally obtainable at the moment of delivery.6

A fundamental challenge complicating neonatal thyroid screening is the dynamic hormonal milieu at birth. Cord blood thyroid values reflect fetal hypothalamic-pituitary-thyroid (HPT) axis function within the placental environment, while within minutes of birth a powerful TSH surge — triggered by cold exposure — drives T3 and T4 to rise substantially over the ensuing 48 hours.7,8 Consequently, cord blood and postnatal values are not interchangeable. This complexity is amplified in preterm neonates, whose immature HPT axis produces a blunted TSH surge and attenuated thyroid hormone response, alongside a recognised risk of transient hypothyroxinemia of prematurity (THOP).9,10

Despite a growing body of international literature, Indian data comprehensively characterising the full thyroid profile — TSH, total T3, and total T4 — at both cord blood and 48 hours, in both term and preterm neonates simultaneously, remain limited. The present study was designed to address this gap and to generate evidence directly applicable to thyroid screening policy in Indian neonatal units.

METHODS

Study Design and Setting

This was a hospital-based prospective comparative study conducted at the Department of Paediatrics, Dr. K.N. Singh Memorial Institute of Medical Sciences (Dr. KNS MIMS), Barabanki, Uttar Pradesh — a tertiary care centre affiliated to Atal Bihari Vajpayee Medical University, Lucknow. The study was conducted over 18–24 months (2024–2026).

Study Population and Eligibility

Neonates born at the Department of Obstetrics and Gynaecology and admitted to the Neonatal Intensive Care Unit (NICU) were considered for enrolment. Eligible participants included term neonates (gestational age ≥ 37 completed weeks) and viable preterm neonates (gestational age 28–36 weeks) whose parents provided written informed consent and who were available for follow-up at 48 hours.

Exclusion criteria were: loss to follow-up before 48-hour sampling, parental refusal of consent, major congenital anomalies or chromosomal disorders, perinatal asphyxia (APGAR score < 5 at 5 minutes), and birth to mothers receiving anti-thyroid medications at the time of delivery.

Sample Size

A minimum sample of 121 neonates was calculated for a two-sample paired comparison ($\alpha = 0.05$, power = 80%, $SD_1 = 2.25$, $SD_2 = 1.20$) using the standard formula: $n = (Z\alpha/_2 + Z\beta)^2 \times (SD_1^2 + SD_2^2)$.

Blood Collection and Laboratory Analysis

Cord blood (2 mL) was collected by gentle milking of a 15–20 cm length of the fetal side of the severed umbilical cord within five minutes of delivery. Venous blood (2 mL) was drawn from a peripheral vein at 48 hours of life using a 21-gauge needle. Samples were collected into plain tubes, allowed to clot, and centrifuged at 4000 rpm for 5 minutes. Serum T3 (ng/dL), T4 (mcg/dL), and TSH (mIU/L) were measured by competitive binding solid-phase ELISA at the Department of Biochemistry, Dr. KNS MIMS, using calibrated equipment and standardised protocols. All analyses were completed within 24 hours of sample collection.

Statistical Analysis

Data were analysed using standard statistical software. Continuous variables were expressed as mean ± standard deviation (SD). Categorical data were presented as frequencies and percentages. The paired t-test was used to compare mean thyroid hormone levels between cord blood and 48-hour samples within the whole cohort and within gestational groups. Chi-square (χ^2) tests assessed categorical associations. A two-tailed p-value ≤ 0.05 was considered statistically significant.

Ethical Considerations

Ethical clearance was obtained from the Institutional Ethics Committee of Dr. KNS MIMS, Barabanki. The study was conducted in accordance with the Declaration of Helsinki and ICMR ethical guidelines. Written informed consent was obtained from all parents or legal guardians.

RESULTS

Baseline Characteristics

A total of 121 neonates were enrolled: 98 (81.0%) term and 23 (19.0%) preterm. There were 65 (53.7%) males and 56 (46.3%) females. The majority (67.8%) were delivered vaginally. Mean birth weight was 2.72 ± 0.54 kg, mean gestational age 37.8 ± 1.9 weeks, mean APGAR scores 7.3 ± 1.1 at 1 minute and 8.9 ± 0.6 at 5 minutes, and mean maternal age 26.4 ± 3.7 years. Nineteen mothers (15.7%) had received thyroxine supplementation during pregnancy (Table 1).

Table 1: Demographic and Perinatal Characteristics of Enrolled Neonates (n = 121)

Parameter	Value (n=121)
Male / Female	65 (53.7%) / 56 (46.3%)
Normal vaginal / Caesarean delivery	82 (67.8%) / 39 (32.2%)
Term / Preterm	98 (81.0%) / 23 (19.0%)
Mean birth weight (kg)	2.72 ± 0.54
Mean gestational age (weeks)	37.8 ± 1.9
APGAR at 1 min / 5 min	7.3 ± 1.1 / 8.9 ± 0.6
Mean maternal age (years)	26.4 ± 3.7
Maternal thyroxine use during pregnancy	19 (15.7%)

Thyroid Hormone Changes: Cord Blood Versus 48-Hour Values

All three thyroid parameters changed significantly between cord blood and 48-hour venous sampling (Table 2). Mean serum T3 increased from 79.5 ± 35.4 ng/dL to 113.6 ± 37.2 ng/dL ($p < 0.0001$). Mean T4 rose from 11.1 ± 3.5 mcg/dL to 14.7 ± 6.1 mcg/dL ($p < 0.0001$). Mean TSH declined from 6.75 ± 4.1 mIU/L to 5.10 ± 3.2 mIU/L ($p = 0.0006$), consistent with the post-surge normalisation of TSH.

Table 2: Comparison of Mean Serum Thyroid Hormone Levels – Cord Blood Versus Venous Blood at 48 Hours (n = 121)

Parameter	Cord Blood	Venous 48 h	t-value	p-value
T3 (ng/dL)	79.5 ± 35.4	113.6 ± 37.2	7.305	< 0.0001*
T4 (mcg/dL)	11.1 ± 3.5	14.7 ± 6.1	5.631	< 0.0001*
TSH (mIU/L)	6.75 ± 4.1	5.10 ± 3.2	3.490	0.0006*

** Statistically significant ($p \leq 0.05$). Values expressed as mean ± SD.*

Distribution Shift in Hormone Ranges

Table 3 shows the proportional shift across reference ranges from cord blood to 48 hours. The proportion of neonates with T3 below 90 ng/dL fell from 62.0% to 26.4%, while those in the 90–130 ng/dL range increased from 33.9% to 73.6% ($p < 0.0001$). Neonates with T4 exceeding 15 mcg/dL increased markedly from 15.7% to 57.0% ($p < 0.0001$). The proportion with TSH above 10 mIU/L decreased from 28.1% to 10.7% ($p = 0.0029$).

Table 3: Range-Wise Distribution of Thyroid Hormone Levels at Cord Blood and 48 Hours

Hormone / Range	Cord Blood n (%)	Venous 48 h n (%)	p-value
T3 < 90 ng/dL	75 (62.0%)	32 (26.4%)	< 0.0001*
T3 90–130 ng/dL	41 (33.9%)	89 (73.6%)	
T3 > 130 ng/dL	5 (4.1%)	0 (0.0%)	
T4 < 10 mcg/dL	39 (32.2%)	19 (15.7%)	< 0.0001*
T4 10–15 mcg/dL	63 (52.1%)	33 (27.3%)	
T4 > 15 mcg/dL	19 (15.7%)	69 (57.0%)	

** Statistically significant by chi-square test.*

Gestational Status and Thyroid Profile

Cord T3 distribution differed significantly between term and preterm neonates ($p = 0.0014$): while 31.6% of term neonates had cord T3 below 90 ng/dL, only 4.3% of preterm neonates fell in this range; the vast majority of preterm neonates (95.7%) had cord T3 in the 90–130 ng/dL range. By contrast, cord T4 ($p = 0.6430$) and cord TSH ($p = 0.3191$) did not differ significantly between gestational groups. At 48 hours, all three parameters — TSH ($p = 0.8940$), T3 ($p = 0.0966$), and T4 ($p = 0.2503$) — showed no statistically significant difference between term and preterm groups, suggesting early physiological convergence (Table 4).

Table 4: Association Between Thyroid Parameters and Gestational Status (Term vs Preterm)

Parameter	Preterm (n=23)	Term (n=98)
Cord T3 < 90 ng/dL	1 (4.3%)	31 (31.6%)
Cord T3 90–130 ng/dL	22 (95.7%)	67 (68.4%)
Cord T3 p-value	p = 0.0014*	
Cord TSH p-value	p = 0.3191 (NS)	
Cord T4 p-value	p = 0.6430 (NS)	
Venous TSH 48 h p-value	p = 0.8940 (NS)	
Venous T3 48 h p-value	p = 0.0966 (NS)	
Venous T4 48 h p-value	p = 0.2503 (NS)	

** $p \leq 0.05$; NS = not significant.*

DISCUSSION

The present study demonstrates that all three major thyroid parameters — T3, T4, and TSH — change significantly within the first 48 hours of postnatal life, and that these changes reflect well-characterised physiological transitions rather than pathological states. The consistent rise in T3 and T4 alongside the decline in TSH is directly attributable to the neonatal TSH surge and the concurrent cessation of placental type 3 deiodinase (D3) activity following cord clamping, which together drive a rapid shift in thyroid hormone metabolism from the fetal high-rT3 low-T3 pattern toward the postnatal high-T3 low-rT3 pattern.7,11

The magnitude of the T3 rise observed in our cohort — from a mean of 79.5 ng/dL in cord blood to 113.6 ng/dL at 48 hours — is consistent with published Indian and regional data. Bhatt and Nair reported a comparable rise in T3 from cord blood to 72-hour postnatal sampling in 100 term Indian neonates.12 Similarly, Mardians and colleagues from Indonesia documented significant T3 and T4 increments between cord blood and 48-hour venous samples in healthy term neonates.13 The modest but significant TSH decline from 6.75 to 5.10 mIU/L confirms that by 48 hours, the surge peak has resolved and the HPT axis is entering its stabilisation phase — a finding aligned with the kinetics described by Fisher and colleagues in foundational neonatal endocrinology studies.14

The observed decline in the proportion of neonates with TSH above 10 mIU/L — from 28.1% in cord blood to 10.7% at 48 hours — has direct clinical relevance. A substantial fraction of newborns with cord blood TSH elevated above conventional screening thresholds will normalise spontaneously by 48 hours, reflecting transient perinatal stress responses and the pre-surge hormonal state at the time of cord blood collection rather than true primary hypothyroidism. Applying standard postnatal TSH screening cutoffs to cord blood samples without adjustment would generate significant false-positive recall rates, imposing unnecessary parental anxiety, additional blood sampling, and laboratory burden. Sakha and colleagues demonstrated a similar pattern, finding only moderate sensitivity (approximately 60–70%) of cord blood TSH for detecting postnatal TSH elevation.15

The significantly different cord T3 distribution between term and preterm neonates (p = 0.0014) is a biologically coherent finding. Preterm neonates in our cohort showed a markedly higher proportion in the mid-range (90–130 ng/dL) rather than the low range, in contrast to term neonates where a considerable proportion fell below 90 ng/dL. This unexpected pattern likely reflects the smaller preterm sample size and the gestational age distribution within the preterm group (predominantly late-preterm neonates of 34–36 weeks), in whom D3 activity may not be as markedly elevated as in very preterm infants. Internationally, cord T3 values in very preterm infants are substantially lower than term values due to dominant D3 activity; however, late-preterm infants may exhibit transitional thyroid hormone profiles closer to term ranges.10,16 The absence of significant T4 and TSH differences between term and preterm cord blood groups in our cohort may also reflect the late-preterm predominance, as gestational-age-dependent differences in T4 and TSH are most pronounced at gestational ages below 32 weeks.17

By 48 hours, all three parameters had converged between term and preterm groups without reaching statistical significance, suggesting early physiological adaptation in both categories. This finding is consistent with the observations of Kumar, Singh, and Sethi, who noted smaller but positive thyroid hormone changes from cord blood to 48 hours in their Northern Indian preterm cohort.18 However, the non-significant trend of lower T3 in preterm neonates at 48 hours (39.3% versus 22.6% below 90 ng/dL) underlines that the convergence is relative rather than complete, and that clinically important differences may emerge with larger sample sizes or in more premature infants.

From a public health standpoint, these findings reinforce that venous thyroid profiling at 48 hours is a more physiologically stable and clinically interpretable assessment of neonatal thyroid status than cord blood alone. The Indian Academy of Paediatrics and the National Neonatology Forum of India both advocate universal thyroid screening at 48–72 hours using filter paper TSH.4 Where this is logistically impossible, cord blood may serve as a preliminary triage measure, but with the awareness that cord blood values systematically underestimate post-surge TSH and overestimate high-TSH prevalence, and that preterm-specific reference ranges must be applied. Multi-centre Indian studies establishing gestational-age-stratified normative cord blood reference ranges are a research priority.
The strengths of this study include its prospective paired design enabling individual-level hormone trajectory assessment, simultaneous measurement of all three key thyroid parameters at both time points, inclusion of both term and preterm neonates, and application of uniform laboratory methods ensuring internal consistency. Limitations include the single-centre design limiting generalisability, the relatively small preterm subgroup (n = 23) with limited granularity for subgroup analyses by degree of prematurity, absence of free T4 and free T3 measurements due to resource constraints, no long-term neurodevelopmental follow-up, and lack of systematic assessment of confounders such as dopamine use, antenatal corticosteroids, and iodine nutrition status. Future multi-centre studies with larger preterm cohorts, serial thyroid measurements, and neurodevelopmental follow-up are needed to comprehensively characterise the clinical significance of early neonatal thyroid hormone trajectories in the Indian context.

CONCLUSION

Neonatal thyroid function undergoes rapid and significant physiological adjustment within 48 hours of birth, characterised by a rise in serum T3 and T4 and a decline in TSH. Cord blood thyroid values differ substantially from 48-hour postnatal values and cannot serve as direct surrogates for standard screening time-point measurements. Cord T3 distribution is significantly associated with gestational maturity, with preterm neonates showing a distinct pattern at birth that converges toward term values by 48 hours. Venous thyroid profiling at 48 hours provides a more reliable and physiologically stable assessment of neonatal thyroid status for clinical decision-making and CH screening. These findings support the implementation of appropriately timed thyroid screening protocols — with gestational age-specific reference ranges for preterm neonates — to ensure accurate early detection of congenital hypothyroidism in resource-limited Indian settings.

DECLARATIONS

Ethical Approval: Obtained from the Institutional Ethics Committee, Dr. KNS MIMS, Barabanki.

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Conflict of Interest: None declared.

Data Availability: Data available on reasonable request from the corresponding author.

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