# Comparative Study Of Thyroid Hormone Levels In Newborns With And Without Perinatal Asphyxia In Dr Sushila Tiwari Hospital

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**Keywords**
Perinatal Asphyxia; Thyroid Hormones; Hypoxic-Ischemic Encephalopathy; Neonatal Screening; TSH.

**Abstract**

**Background:** Perinatal asphyxia remains a leading cause of neonatal morbidity and mortality, particularly in low- and middle-income countries like India. While its neurological and systemic sequelae are well recognized, its endocrine effects—especially on the hypothalamic-pituitary-thyroid (HPT) axis—are less explored. Thyroid hormones are essential for early neurodevelopment, and hypoxia may impair their regulation, contributing to further neonatal complications.

**Objectives:** To compare thyroid hormone levels (T3, T4, TSH) between term neonates with and without perinatal asphyxia and to assess their association with hypoxic-ischemic encephalopathy (HIE) staging and neonatal outcomes in a tertiary care setting.

**Methods:** A cross-sectional, hospital-based study was conducted at Dr. Sushila Tiwari Hospital, Haldwani, including 130 term neonates—65 with perinatal asphyxia and 65 healthy controls. Blood samples were collected at 72 hours of life for thyroid hormone analysis. Clinical data including birth weight, mode of delivery, Apgar scores, and multi-organ function parameters were recorded. HIE was staged using Sarnat and Sarnat criteria. Statistical analysis was done using SPSS; $p<0.05$ was considered significant.

**Results:** Mean T3 and T4 levels were significantly lower, while TSH was markedly elevated in asphyxiated neonates ($p<0.001$). Thyroid dysfunction severity correlated with HIE stage and low birth weight. Multi-organ dysfunction and need for ventilatory support were significantly associated with altered thyroid status. Logistic regression identified low T3, severe HIE, and low maternal education as predictors of mortality.

**Conclusion:** Perinatal asphyxia significantly alters thyroid function, with prognostic implications. Routine screening for thyroid dysfunction may guide timely intervention.

## Introduction

Perinatal asphyxia, characterized by impaired gas exchange resulting in neonatal hypoxemia and hypercapnia, remains one of the most critical causes of neonatal morbidity and mortality worldwide.[1] It contributes to nearly 23% of neonatal deaths in India, posing a substantial public health challenge in low- and middle-income countries due to insufficient perinatal surveillance and delayed obstetric interventions.[1,2] The incidence in developing nations ranges between 3–6 per 1,000 live births, compared to <1 per 1,000 in developed countries.[3,4]

While the neurological consequences of perinatal asphyxia, particularly hypoxic-ischemic encephalopathy (HIE), have been well established, growing attention is now being directed to its endocrine sequelae, notably the suppression of the hypothalamic-pituitary-thyroid (HPT) axis.[5,6] Thyroid hormones, especially triiodothyronine (T3) and thyroxine (T4), are essential for neuronal growth, myelination, metabolic regulation, and thermogenesis during the neonatal period.[7,8] Hypoxia-induced suppression of the HPT axis leads to decreased T3 and T4 levels and variable TSH alterations, often described under non-thyroidal illness syndrome (NTIS).[9]

India contributes to nearly 40% of global low birth weight deliveries, of which a significant proportion are small-for-gestational-age (SGA) babies born at term. These neonates are under chronic intrauterine stress, often resulting in underdeveloped thyroid glands, which compromises thyroid hormone synthesis and affects neurodevelopmental outcomes.[10,11] Embryogenesis of the thyroid and HPT axis completes by 12 weeks of gestation, but functional maturity with thyroxine secretion begins mid-gestation. Until then, fetal thyroid hormone levels depend on transplacental maternal transfer, highlighting the vulnerability of the fetus to maternal and perinatal factors.[12]

Multiple studies have demonstrated an inverse relationship between the severity of HIE and thyroid hormone levels, suggesting their potential role as biomarkers for prognosis and indicators of multi-organ dysfunction.[13,14] T3 in particular has emerged as a critical determinant of neonatal recovery, with reduced levels linked to adverse neurodevelopmental outcomes.[15] Birth asphyxia, by reducing oxygen perfusion to vital organs, can disrupt thyroid metabolism at multiple levels—including synthesis, conversion, and receptor response—thereby worsening clinical outcomes. Several studies have reported conflicting thyroid hormone patterns in asphyxiated neonates, with some showing reduced T3, T4 and elevated TSH, while others found inconsistent trends with gestational age.[16-18]

Furthermore, maternal and neonatal risk factors such as low socioeconomic status and birth weight also appear to influence thyroid profiles.[19,20] Hence, this study compared thyroid hormone levels (T3, T4, TSH) in term neonates with and without perinatal asphyxia, and examined their association with HIE severity and early neonatal outcomes.

## Materials and Methods

This was a hospital-based cross-sectional study conducted in the Department of Pediatrics, Government Medical College, Haldwani. The institution's neonatal unit, equipped with advanced diagnostic and monitoring facilities, served as the setting for evaluating thyroid function in term neonates with and without perinatal asphyxia.

### Study Population

The study included 130 term neonates (≥37 weeks gestation), divided into two groups: 65 neonates diagnosed with perinatal asphyxia and 65 healthy controls without any birth complications. Neonates with congenital anomalies, preterm birth, known endocrine disorders, or incomplete records were excluded. Diagnosis of asphyxia was based on clinical criteria, including Apgar scores <7 at 5 minutes and need for active resuscitation.[12]

### Sample Size and Sampling Technique

The sample size was determined using the formula:

$$n = \frac{Z^2 \times P \times Q}{d^2}$$

where Z = 1.96 (95% CI), P = 8%, Q = 92%, and d = 10%. The calculated minimum was 113, which was rounded to 124 and adjusted to 130 to account for possible dropouts. A convenience sampling method was adopted, enrolling eligible neonates based on inclusion criteria during the study period.[12]

**Data Collection and Methodology**

Detailed maternal and neonatal histories were obtained, including gestational age, mode of delivery, Apgar scores, and resuscitation details. For all neonates, blood samples were collected at 72 hours of life to measure serum levels of T3, T4, and TSH using standard laboratory techniques. Serum was separated and stored at −20°C until analysis. Reference ranges were based on neonatal norms. In asphyxiated neonates, additional investigations included serum calcium (S.Ca), random blood sugar (RBS), complete blood count (CBC), liver function tests (LFT), and kidney function tests (KFT) to assess multi-organ dysfunction. Hypoxic-ischemic encephalopathy (HIE) was staged using the Sarnat and Sarnat criteria. Clinical outcomes such as need for ventilatory or inotropic support, neurological status, complications, and discharge outcome were recorded.

**Ethical Considerations**

Ethical clearance for this study was obtained from the Institutional Ethics Committee (IEC) of Government Medical College, Haldwani, under Letter No. 775/GMC/IEC/2023 / Reg. No. 730/IEC/R-01-05-2023. Written informed consent was obtained from the parents or legal guardians of all participating neonates prior to enrollment. Confidentiality and anonymity of patient data were strictly maintained throughout the study, in accordance with institutional and national ethical guidelines.

**Statistical Analysis**

Data were analyzed using SPSS. Descriptive statistics included means, SDs, medians, and percentages. Chi-square and t-tests were used for categorical and continuous variables, respectively. Shapiro-Wilk tested normality; Mann-Whitney U was applied for non-normal data. A p-value <0.05 was considered significant. Multivariate logistic regression identified predictors of thyroid dysfunction and outcomes.

**Results**

Among all the participants, no significant difference was observed in sex distribution, maternal age, or residence between groups. However, maternal illiteracy was significantly higher in the asphyxiated group (40% vs 12.3%, p=0.002), indicating maternal education as a potential risk factor. (See Table 1)

**Table 1: Sociodemographic Profile of Study Participants**

| Parameter | Category | Asphyxiated (n=65) | Controls (n=65) | p-value |
|---|---|---|---|---|
| **Sex Distribution** | Male | 38 (58.5%) | 35 (53.8%) | 0.62 |
| | Female | 27 (41.5%) | 30 (46.2%) | |
| **Maternal Age (years)** | Mean ± SD | 23.8 ± 3.2 | 24.5 ± 2.9 | 0.18 |
| | < 20 | 10 (15.4%) | 7 (10.8%) | 0.43 |
| | 20–25 | 40 (61.5%) | 38 (58.5%) | |
| | > 25 | 15 (23.1%) | 20 (30.7%) | |

| | | | | |
|---|---|---|---|---|
| **Socioeconomic Status (Kuppuswamy Scale)** | Upper Class | 3 (4.6%) | 6 (9.2%) | 0.30 |
| | Upper Middle | 9 (13.8%) | 14 (21.5%) | |
| | Lower Middle | 26 (40.0%) | 29 (44.6%) | |
| | Upper Lower | 22 (33.8%) | 15 (23.1%) | |
| | Lower Class | 5 (7.7%) | 1 (1.5%) | |
| **Residence** | Urban | 22 (33.8%) | 30 (46.2%) | 0.15 |
| | Rural | 43 (66.2%) | 35 (53.8%) | |
| **Maternal Education** | Illiterate | 26 (40.0%) | 8 (12.3%) | 0.002 |
| | Primary/Secondary | 39 (60.0%) | 57 (87.7%) | |

Asphyxiated neonates had significantly lower birth weight (p=0.001) and were more often delivered vaginally (p=0.008), possibly reflecting intrapartum-related hypoxia. Gestational age difference was not significant. (See Table 2)

**Table 2: Neonatal Characteristics & Mode Of Delivery**

| **Parameter** | **Asphyxiated (mean ± SD or N)** | **Controls (mean ± SD or N)** | **p-value** |
|---|---|---|---|
| **Gestational Age** | 38.1 ± 1.2 weeks | 38.4 ± 0.8 weeks | 0.11 |
| **Birth Weight** | 2.7 ± 0.3 kg | 3.0 ± 0.4 kg | 0.001* |
| **Mode of Delivery** | | | 0.008 |
| **- Vaginal** | 47 (72.3%) | 32 (49.2%) | |
| **- LSCS** | 18 (27.7%) | 33 (50.8%) | |

Figure 1 shows asphyxiated neonates had significantly lower T3 and T4 levels and higher TSH compared to controls, indicating transient hypothyroidism likely due to hypoxic stress, warranting early thyroid evaluation.

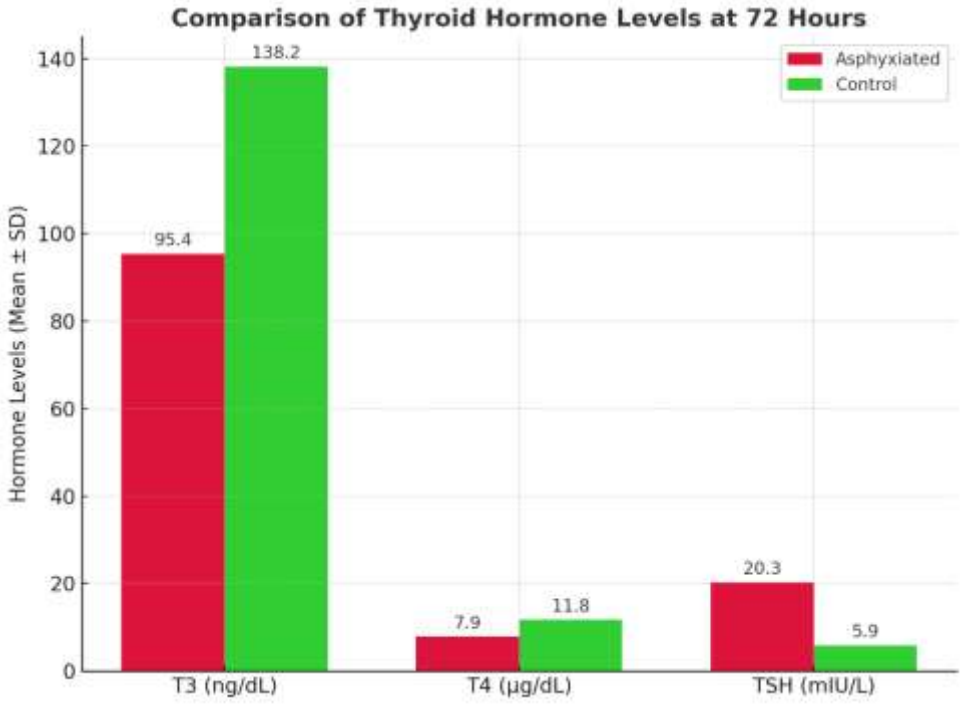


**Figure 1: Thyroid Hormone Levels at 72 Hours**

Thyroid dysfunction (low T3, T4, and elevated TSH) worsened with increasing HIE stage, showing a statistically significant inverse relationship between hormone levels and HIE severity (p=0.001). (See Table 3)

**Table 3: HIE Severity vs Thyroid Hormone Status (Normal vs Abnormal Counts)**

| HIE Stage | T3 Normal (N) (mean ± SD) | T3 Abnormal (N) (mean ± SD) | T4 Normal (N) (mean ± SD) | T4 Abnormal (N) (mean ± SD) | TSH Normal (N) (mean ± SD) | TSH Abnormal (N) (mean ± SD) | P-Value |
|---|---|---|---|---|---|---|---|
| Stage I (27) | 20 (109.3 ± 10.7) | 7 (87.6 ± 9.3) | 22 (9.3 ± 1.2) | 5 (7.4 ± 1.1) | 21 (11.7 ± 3.2) | 6 (17.9 ± 4.5) | 0.001 |
| Stage II (26) | 10 (91.4 ± 8.8) | 16 (74.8 ± 7.9) | 12 (8.1 ± 0.9) | 14 (5.8 ± 1.3) | 13 (17.8 ± 4.8) | 13 (22.3 ± 5.1) | |
| Stage III (12) | 3 (69.7 ± 6.2) | 9 (61.2 ± 5.7) | 4 (6.7 ± 0.7) | 8 (4.9 ± 0.8) | 5 (19.9 ± 5.5) | 7 (25.1 ± 6.9) | |

Renal, hepatic, and cardiac dysfunctions were significantly more frequent in asphyxiated neonates. Higher need for ventilation and inotropic support, with mortality (12.3% vs 0%, p=0.003), was seen only in the asphyxiated group. (See Table 4)

**Table 4: Multi-Organ Dysfunction, Organ-Specific Clinical Findings, and Clinical Outcomes**

| Variable | Category | Asphyxiated (n=65) | Controls (n=65) | p-value |
|---|---|---|---|---|
| **Organ Affected** | Renal | 20 (30.8%) | 1 (1.5%) | 0.001* |
| | Hepatic | 16 (24.6%) | 0 (0%) | 0.001* |
| | Cardiac | 14 (21.5%) | 0 (0%) | 0.001* |
| **Organ-Specific Clinical Findings** | Required Inotropic Support | 14 (21.5%) | 0 (0%) | - |
| | Hepatic Dysfunction | 16 (24.6%) | 0 (0%) | - |
| | Ventilation Requirement | 22 (33.8%) | 1 (1.5%) | - |
| **Clinical Outcomes** | Mortality | 8 (12.3%) | 0 (0%) | 0.003* |
| | Ventilation Needed | 22 (33.8%) | 1 (1.5%) | 0.001* |
| | Seizures | 15 (23.1%) | 0 (0%) | 0.001* |

Figure 2 shows that ventilation need increased with HIE severity—only 11.1% of Stage I neonates required ventilation compared to 26.9% in Stage II and 100% in Stage III—highlighting a strong correlation between advancing HIE stage and respiratory compromise.

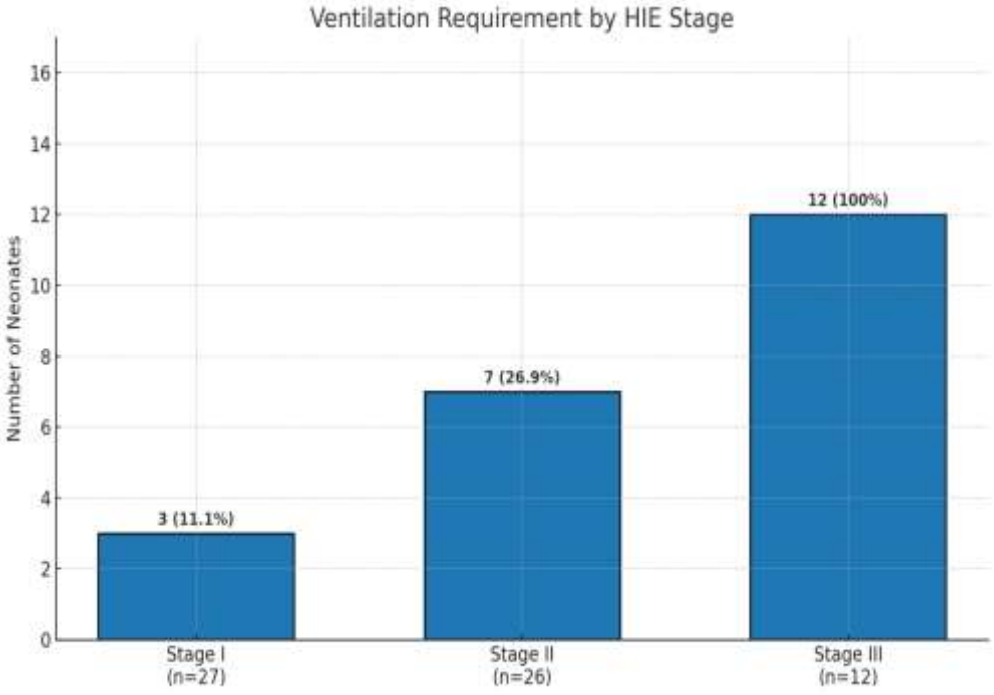


**Figure 2: Ventilation Requirement by HIE Stage**

Low birth weight neonates (2.5–3.0 kg) had significantly higher rates of abnormal T3, T4, and TSH values, suggesting birth weight as a predictor of thyroid dysfunction in asphyxiated neonates ($p<0.005$ for all). (See Table 5)

**Table 5: Birth Weight vs Thyroid Levels**

| Birth Weight Category | Low T3 Present (n,%) Abnormal | Low T3 Absent (n,%) Normal | Low T4 Present (n,%) Abnormal | Low T4 Absent (n,%) Normal | TSH Present (n,%) Abnormal | TSH Absent (n,%) Normal |
|---|---|---|---|---|---|---|
| **2.5–3.0 kg** | 10 (50.0%) | 10 (50.0%) | 12 (60.0%) | 8 (40.0%) | 11 (55.0%) | 9 (45.0%) |
| **3.0–3.5 kg** | 7 (28.0%) | 18 (72.0%) | 9 (36.0%) | 16 (64.0%) | 8 (32.0%) | 17 (68.0%) |
| **> 3.5 kg** | 3 (15.0%) | 17 (85.0%) | 4 (20.0%) | 16 (80.0%) | 5 (25.0%) | 15 (75.0%) |
| **p-value** | T3: 0.001* | | T4: 0.002* | | TSH: 0.001* | |

Out of all the participants, 66.2% of asphyxiated neonates had Apgar ≤3, and none had Apgar ≥7, whereas all controls had Apgar ≥7. This was highly significant ($p=0.001$) and confirms poor neonatal adaptation in the asphyxiated group. (See Table 6)

**Table 6: Apgar Scores at 5 Minutes**

| Apgar Score Category | Asphyxiated (n=65) | Controls (n=65) | p-value |
|---|---|---|---|
| **≤ 3** | 43 (66.2%) | 0 (0%) | 0.001* |
| **4–6** | 22 (33.8%) | 0 (0%) | |
| **≥ 7** | 0 (0%) | 65 (100%) | |

Figure 3 shows that Stage III HIE (OR: 6.5), low T3 (<80 ng/dL; OR: 4.2), and low socioeconomic status (OR: 3.1) were independently associated with increased mortality, highlighting these as significant predictors of poor neonatal outcomes.

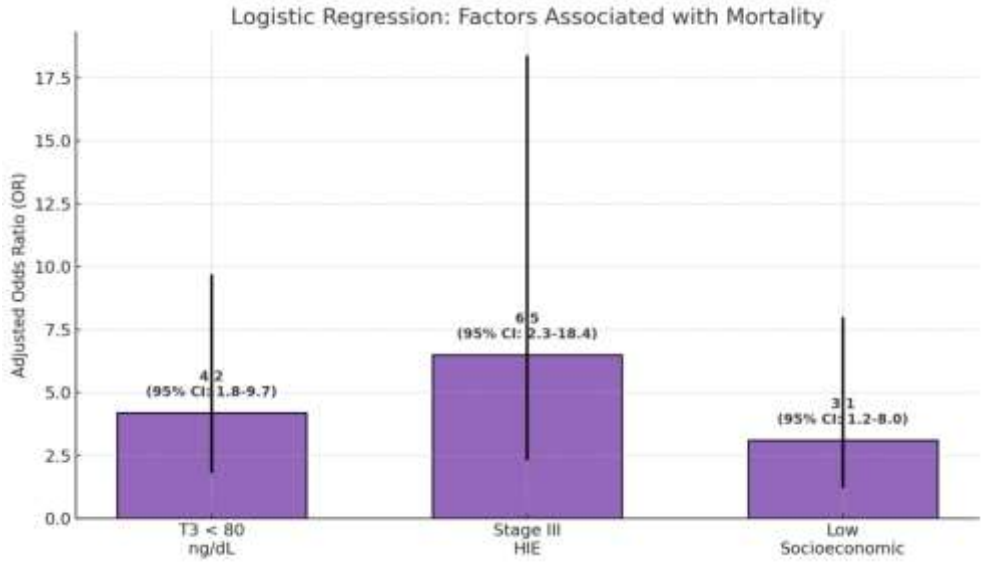


**Figure 3: Logistic Regression for Mortality**

## Discussion

The study assessed and compared thyroid hormone profiles—T3, T4, and TSH—among term neonates with and without perinatal asphyxia. A significant association was observed between perinatal asphyxia and altered thyroid function, with lower T3 and T4 levels and elevated TSH in the asphyxiated group, indicating central hypothyroidism. These findings align with recent literature, including Gutta et al. (2023)[14] and Haris et al. (2022)[6], who also reported significant thyroid hormone dysregulation in asphyxiated neonates.

A marked decline in T3 and T4 levels with increasing hypoxic-ischemic encephalopathy (HIE) severity was noted, with Stage III HIE neonates showing the most profound hormonal abnormalities. This trend matches the results of Tam et al. (2022)[13] and Gutta et al.[14], reinforcing the prognostic value of thyroid hormone monitoring. Moreover, low birth weight was associated with higher rates of thyroid dysfunction, echoing findings by Sadeghi et al. (2022)[19].

The study also demonstrated a strong correlation between thyroid dysfunction and multi-organ impairment. Renal, hepatic, and cardiac dysfunctions were more prevalent in asphyxiated neonates, particularly those with low T3 levels. A significant portion required ventilatory or inotropic support. These complications were consistent with recent evidence from Haris et al.[6] and Fikri et al. (2021)[9]. Furthermore, logistic regression revealed low T3 (<80 ng/dL), Stage III HIE, and lower socioeconomic status as independent predictors of mortality, reaffirming the multifactorial impact of asphyxia on neonatal outcomes.

Maternal education emerged as another critical determinant, with neonates born to illiterate mothers showing significantly higher mortality. This observation is supported by recent studies like Gutta et al.[14], which emphasized maternal literacy's role in neonatal health.

## Conclusion

Perinatal asphyxia significantly alters thyroid hormone levels in neonates, with a clear association between low T3 and increased severity of HIE and multi-organ dysfunction. These hormonal disturbances correlated with adverse clinical outcomes, including higher mortality. Early identification of thyroid dysfunction through routine screening in asphyxiated neonates may serve as a valuable prognostic tool and guide timely therapeutic interventions to improve survival and neurodevelopmental outcomes in affected infants.

**Conflict of Interest:** None.

**Funding:** None.

**Ethical Approval:** Obtained.

**Consent:** Written consent secured.

**References**

1. Morales P, Bustamante D, Espina-Marchant P, Neira-Peña T, Gutiérrez-Hernández MA, Allende-Castro C, Rojas-Mancilla E. Pathophysiology of perinatal asphyxia: can we predict and improve individual outcomes?. EPMA Journal. 2011 Jun;2(2):211-30.
2. UNICEF. Neonatal mortality - UNICEF DATA. UNICEF DATA. 2023. Available from: https://data.unicef.org/topic/child-survival/neonatal-mortality/
3. Lee AC, Cousens S, Wall SN, Niermeyer S, Darmstadt GL, Carlo WA, Keenan WJ, Bhutta ZA, Gill C, Lawn JE. Neonatal resuscitation and immediate newborn assessment and stimulation for the prevention of neonatal deaths: a systematic review, meta-analysis and Delphi estimation of mortality effect. BMC public health. 2011 Apr 13;11(Suppl 3):S12.
4. Lawn JE, Kerber K, Enweronu-Laryea C, Massee Bateman O. Newborn survival in low resource settings—are we delivering?. BJOG: An International Journal of Obstetrics & Gynaecology. 2009 Oct;116:49-59.
5. Yazici A, Kadioglu Simsek G, Elbayiyev S, Canpolat FE, Kanmaz Kutman HG. Thyroid function in neonates with hypoxic ischemic encephalopathy. Therapeutic Hypothermia and Temperature Management. 2023 Mar 1;13(1):11-5.
6. Haris M, Gul H, Hayat AK, Asma B, ur Rehman S. Neonatal Blood Gases and Outcomes Following Perinatal Asphyxia. Pak-Euro Journal of Medical and Life Sciences. 2024 Dec 28;7(Special 2):S331-6.
7. Bernal J. Thyroid hormone receptors in brain development and function. Nature clinical practice Endocrinology & metabolism. 2007 Mar;3(3):249-59.
8. Yamada M, Mori M. Mechanisms related to the pathophysiology and management of central hypothyroidism. Nature clinical practice Endocrinology & metabolism. 2008 Dec;4(12):683-94.
9. Fikri AB, Zafrullah A, Ibrahim NR, Van Rostenberghe HA, Cheng KY. Effect Of Birth Asphyxia on The Thyroid Hormone in Term Newborns Delivered In Hospital Universiti Sains Malaysia (Hospital USM). Malaysian Journal of Medicine & Health Sciences. 2024 May 2;20.
10. Bagnolı F, Farmeschı L, Peruzzı L, Paffettı P, Badıı S, Casuccı M, Pasquı L, Lacoponı F. Altered thyroid function in small for gestational age newborns: study based on screening test for congenital hypothyroidism. Journal of Pediatric Sciences. 2010 Sep 22;2(4).
11. Hingorani M, Spitzweg C, Vassaux G, Newbold K, Melcher A, Pandha H, Vile R, Harrington K. The biology of the sodium iodide symporter and its potential for targeted gene delivery. Current cancer drug targets. 2010 Mar 1;10(2):242-67.
12. Shivprasad Kachrulal Mundada, Nitin Narayan Ambekar. A comparative study of thyroid function tests in children with and without birth asphyxia. MedPulse International Journal of Pediatrics. June 2021; 18(3): 65-68.
13. Tam EW, Haeusslein LA, Bonifacio SL, Glass HC, Rogers EE, Jeremy RJ, Barkovich AJ, Ferriero DM. Hypoglycemia is associated with increased risk for brain injury and adverse neurodevelopmental outcome in neonates at risk for encephalopathy. The Journal of pediatrics. 2012 Jul 1;161(1):88-93.
14. Gutta LM. A Systematic Review of Cloud Architectural Approaches for Optimizing Total Cost of Ownership and Resource Utilization While Enabling High Service Availability and Rapid Elasticity. International Journal of Statistical Computation and Simulation. 2024 Mar;16(1):1-20.
15. Anand KJ, Scalzo FM. Can adverse neonatal experiences alter brain development and subsequent behavior?. Neonatology. 2000 Feb 7;77(2):69-82.
16. Kilby MD, Verhaeg J, Gittoes N, Somerset DA, Clark PM, Franklyn JA. Circulating thyroid hormone concentrations and placental thyroid hormone receptor expression in normal human

pregnancy and pregnancy complicated by intrauterine growth restriction (IUGR). The Journal of Clinical Endocrinology & Metabolism. 1998 Aug 1;83(8):2964-71.
17. Bagnoli F, Laura F, Sara N, Salvatore G. Thyroid function in small for gestational age newborns: a review. Journal of clinical research in pediatric endocrinology. 2013 Mar 1;5(Suppl 1):2.
18. Dilli D, Oğuz ŞS, Andıran N, Dilmen U, Büyükkağnıcı Ü. Serum thyroid hormone levels in preterm infants born before 33 weeks of gestation and association of transient hypothyroxinemia with postnatal characteristics.
19. Sadeghi N, Mousavi S, Mirmohammadkhani M, Rahmanian M. Cross-sectional analysis of maternal and neonatal factors influencing cord blood TSH and free T4 levels in congenital hypothyroidism screening. Discover Medicine. 2024 Jul 18;1(1):13.
20. Frank JE, Faix JE, Hermos RJ, Mullaney DM, Rojan DA, Mitchell ML, Klein RZ. Thyroid function in very low birth weight infants: effects on neonatal hypothyroidism screening. The Journal of pediatrics. 1996 Apr 1;128(4):548-54.