Original Article

Assessment of Thyroid Function in Preterm Babies Admitted to SNCU of a Tertiary Care Hospital

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Abstract

Background: Congenital hypothyroidism is one of the most common preventable causes of intellectual disability, and preterm neonates are particularly vulnerable due to immaturity of the hypothalamic–pituitary–thyroid axis and perinatal risk factors. Early diagnosis and treatment are crucial to prevent neurodevelopmental impairment. The aim is to assess thyroid function in preterm and low-birth-weight neonates admitted to the Special Newborn Care Unit (SNCU) of Malda Medical College and Hospital and to evaluate associated maternal and perinatal risk factors. **Material and Methods:** This cross-sectional study was conducted on 206 preterm neonates over one year. Serum free thyroxine (fT4) and thyroid-stimulating hormone (TSH) levels were measured using enzyme-linked immunosorbent assay (ELISA). Clinical and demographic data, including gestational age, birth weight, antenatal and perinatal history, maternal comorbidities, and neonatal complications, were recorded. Statistical analysis was performed using Chi-square, Fisher's exact, and Student's t-tests, with $p \leq 0.05$ considered significant. **Results:** Of the 206 preterm neonates studied, 169 (82%) were euthyroid and 37 (18%) were hypothyroid. Thyroid dysfunction showed significant associations with small-for-gestational-age (SGA) status ($p = 0.0001$), gestational age ≥34 weeks ($p = 0.0001$), abnormal antenatal history ($p = 0.004$), maternal hypertensive disorders ($p = 0.004$), and teenage pregnancy ($p = 0.002$). Mean fT4 levels were significantly lower (1.03 ± 0.49 ng/dl) and mean TSH levels significantly higher (23.75 ± 9.06 µIU/ml) in the hypothyroid group compared to euthyroid infants (1.59 ± 0.44 ng/dl and 4.39 ± 1.71 µIU/ml, respectively, $p = 0.0001$ for both). No significant associations were observed with gender, birth weight, mode of delivery, consanguinity, or common neonatal morbidities. **Conclusion:** Thyroid dysfunction is common among preterm neonates, particularly in SGA infants and those born to mothers with hypertensive disorders, abnormal antenatal history, or teenage pregnancy. Routine neonatal thyroid screening is strongly recommended to ensure early detection and timely initiation of levothyroxine therapy, thereby preventing long-term neurodevelopmental consequences.

Keywords: Preterm neonates; Thyroid dysfunction; Hypothyroidism; fT4; TSH; Neonatal screening; SGA; Maternal hypertension; Teenage pregnancy; Malda Medical College.

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Introduction

Congenital hypothyroidism (CH) is one of the most common preventable causes of intellectual disability. It refers to thyroid hormone deficiency present since birth, most often resulting from thyroid gland dysgenesis or dyshormonogenesis, which causes primary hypothyroidism.[1] Secondary (central) hypothyroidism at birth results from a deficiency of thyroid-stimulating hormone (TSH) and may occur in isolation due to mutations in the TSH β subunit gene or as part of congenital hypopituitarism. Peripheral hypothyroidism, a separate entity, arises from defects in thyroid hormone transport, metabolism, or receptor action.[2]

Preterm infants (born before 37 completed weeks of gestation) and low-birth-weight (LBW) infants (< 2500 g) often exhibit features of prematurity, such as temperature instability, apnea, bradycardia, feeding difficulty, hypotonia, and delayed growth that can closely mimic manifestations of thyroid dysfunction. Whether neurodevelopmental deficiencies in preterm infants result from transient hypothyroxinemia remains an important clinical question.[3] Due to a blunted postnatal TSH surge, immature hypothalamic–pituitary–thyroid (HPT) axis, and reduced maternal thyroid contribution, preterm neonates have significantly lower thyroid hormone levels compared to term infants. Moreover, preterm or LBW infants frequently experience comorbidities that alter thyroid hormone profiles, producing a biochemical pattern similar to non-thyroidal illness syndrome (NTIS), which can be difficult to differentiate from central hypothyroidism.[4]

Despite the importance of early diagnosis, newborn screening for hypothyroidism remains limited in low- and middle-income countries; only about one-third of the world's newborn

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population undergoes screening.[2] Globally, the 2014 preterm birth rate was 10.6%, representing 14.84 million live preterm births, with 81% occurring in Asia and sub-Saharan Africa. India, China, Nigeria, Bangladesh, and Indonesia accounted for 6.6 million preterm births that year, and India ranked among the ten countries with the highest numbers of preterm deliveries. The global prevalence of preterm birth ranges from 5% to 18%, and in India, it was approximately 13% of live births.[4]

Given their biological vulnerability, preterm infants have an increased propensity for CH, underscoring the importance of vigilant screening. Evidence suggests a higher incidence of thyroid dysfunction among preterm neonates, yet diagnosing CH in this population remains challenging due to fluctuating hormone levels and illness-related confounders.[5] Although several guidelines exist, uncertainty persists regarding cutoff values, optimal screening strategies, timing of testing, and follow-up protocols for preterm infants.

Malda Medical College and Hospital, located in northern West Bengal, serves a large and diverse patient population with a high prevalence of teenage pregnancies and multiple births, both contributing to an increased rate of preterm deliveries. As routine newborn screening is not universally implemented in many hospitals across India, conditions such as CH are often underdiagnosed. Thus, integrating preterm thyroid function screening into routine neonatal care in such settings becomes crucial.

Interpretation of thyroid function tests depends on serum free T4 (fT4) and TSH values, along with gestational age and the postnatal day of sampling.[6] Timely initiation of therapy is vital to prevent neurodevelopmental impairment. Levothyroxine remains the treatment of choice and should ideally begin within 14 days of life.[7] Small-for-gestational-age (SGA), very-low-birth-weight (VLBW), and extremely-low-birth-weight (ELBW) infants are at greater risk for CH and its complications, necessitating prompt correction of thyroid hormone levels within 2–4 weeks.[8] The recommended starting dose is 10–15 µg/kg/day, adjusted according to disease severity, with subsequent monitoring to maintain free T4 (fT4) in the upper normal range and TSH within the age-appropriate reference interval.[9,10] Both under- and over-replacement can adversely affect growth and development.

Therefore, it is of interest to assess the thyroid function in preterm and low-birth-weight neonates admitted to the Special Newborn Care Unit (SNCU) of Malda Medical College and Hospital, and to evaluate the prevalence and associated risk factors of thyroid dysfunction in this vulnerable population.

Aim of the Study

Since preterm babies are more prone to developing thyroid dysfunction, and thyroid hormones are necessary for the neurodevelopment of both the fetus and newborn, our study aims to assess the thyroid function of preterm babies. We also aim to emphasize the importance of regular newborn screening, regardless of the presence of risk factors, and to incorporate it into daily clinical practice.

General Objectives

To find the prevalence of thyroid dysfunction in the preterm babies in the SNCU of our hospital.

To find the association with known risk factors for the development of congenital hypothyroidism.

Specific Objectives

Prevalence

Gender prevalence

Prevalence according to type of delivery

Prevalence according to birth weight

Prevalence according to gestational age

Association with SGA

Association with parental consanguineous marriage

Association with birth asphyxia, RDS, CHD, syndromic baby, including Down syndrome

Association with PIH, preeclampsia, and eclampsia

Association with Sepsis

Association with teenage pregnancy

Mean values of fT4 and TSH

Materials and Methods

Methodology

Study design: Institution-based descriptive study.

Study type: A cross-sectional study.

Place of study: Special newborn care unit (SNCU), Malda Medical College and Hospital.

Study period: 12 months after acceptance of synopsis. From September 2023 to August 2024

Study population: All preterm infants admitted to SNCU during the period of study

Sampling technique: All preterm infants admitted to SNCU were screened until the estimated sample size was achieved

Inclusion criteria: Babies born before 37 completed weeks of gestation and admitted to SNCU

Exclusion criteria:

Unwilling parents.

Moribund or critically ill Babies

Sample size: Approximately 206 samples. Sample size calculated using Cochran's formula.

N = z2 P(1-P)/d2, where N is the sample size, Z is the statistic corresponding to the level of confidence, P is the expected prevalence (that is obtained from similar types of previous studies), and d is the precision. Considering the varied prevalence in different parts of the world, the Asian-Indian prevalence is taken into account, with a 5% precision and 95% confidence level for estimating the prevalence of congenital hypothyroidism among preterm infants; the estimated sample size was 206.

Study tools:

- Gestational age according to LMP and EDD
- Detailed clinical and birth history
- New Ballard scoring chart for assessment of gestation
- Fenton's growth chart to determine whether LGA, SGA, or AGA
- Serum TSH and fT4 estimations done by the sandwich ELISA method

Sandwich ELISA method: This is a laboratory technique that utilizes two antibodies to detect antigens in a sample. It is more sensitive and specific than other ELISA methods. Here, a surface is coated with capture antibodies, and then the nonspecific sites are blocked. Next, a sample containing the antigen or the

substance to be tested is added to the plate. The plate is then washed to remove the unbound antigen. The next step is to add the detection antibody, which binds to the antigen, and an enzyme-linked secondary antibody that binds to the detection antibody. The plate is again washed to remove the unbound antibody-enzyme conjugates. Then, a substrate is added, which the enzyme converts into a signal, and the signal is measured to determine the amount of antigen in the sample.

Procedure: After taking written informed consent, all preterm infants admitted to SNCU during the period of study were screened for congenital hypothyroidism by estimating the serum TSH and fT4 levels on days 5 to 28 of life. In cases where the babies were very sick or had stressors like birth asphyxia (BA), sepsis, and CHD, thyroid estimation was delayed as serum TSH is an acute phase reactant and increases in stressful conditions. Also, very preterm babies are more prone to delayed TSH rise, so in those cases, thyroid function was done after 2 weeks of life. A detailed clinical and birth history was taken, including complications of birth, major risk factors, and a significant antenatal history. A modified New ballad scoring chart was used to determine the gestational age, along with calculating it from the mother's LMP. Fenton's chart was used to determine whether the individual was LGA, SGA, or AGA. All data were recorded in a pre-designed case record form, and the data were analysed using SPSS software

Statistical analysis

Data was analysed with Microsoft Excel and SPSS software version 26.0. The mean and standard deviation of the quantitative variables were measured. For categorical variables, association was estimated by using the chi-square test or Fisher's exact test. An independent t-test was used to calculate the difference in continuous variables. A p-value of ≤0.05 was considered significant.

Results

The present study included 206 preterm neonates admitted to the Special Newborn Care Unit (SNCU) of Malda Medical College and Hospital to assess thyroid function and related risk factors. Among them, 169 (82%) were euthyroid and 37 (18%) were hypothyroid. Thyroid dysfunction was more prevalent among small-for-gestational-age (SGA) infants, babies born to teenage mothers, and those with abnormal antenatal histories. Gestational age, SGA status, maternal hypertensive disorders, and adolescent pregnancy were significantly associated with thyroid dysfunction. However, no significant differences were observed with respect to birth weight, gender, type of delivery, consanguinity, neonatal sepsis, congenital heart disease (CHD), or neonatal jaundice. Mean serum fT4 levels were significantly lower, and mean TSH levels significantly higher, among hypothyroid infants compared to euthyroid counterparts. The findings highlight the importance of routine thyroid screening in preterm neonates, particularly in the presence of antenatal complications and maternal risk factors.

Table 1: Thyroid status based on birth weight

Birth Weight	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
ELBW	6 (3.6)	1 (2.7)	7 (3.4)
VLBW	60 (35.5)	15 (40.5)	75 (36.4)
LBW	103 (60.9)	21 (56.8)	124 (60.2)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 0.36$, $p = 0.83$ (non-significant)

[Table 1] represents the distribution of thyroid status according to birth weight categories.

Table 2: Thyroid status based on gender

Gender	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Male	82 (48.5)	22 (59.5)	104 (50.5)
Female	87 (51.5)	15 (40.5)	102 (49.5)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 1.45$, $p = 0.23$ (non-significant)

[Table 2] shows the comparison of thyroid function distribution between male and female preterm babies.

Table 3: Thyroid status based on gestational age

Gestational Age (weeks)	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
28–29	13 (7.7)	1 (2.7)	14 (6.8)
30–31	26 (15.4)	0 (0)	26 (12.6)
32–33	60 (35.5)	5 (13.5)	65 (31.6)
≥ 34	70 (41.4)	31 (83.8)	101 (49.0)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 22.57$, $p = 0.0001$ (Significant)

[Table 3] depicts the distribution of thyroid status according to gestational age of the neonates.

Table 4: Thyroid status based on AGA/SGA

Category	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
AGA	152 (89.9)	20 (54.1)	172 (83.5)
SGA	17 (10.1)	17 (45.9)	34 (16.5)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 28.37$, $p = 0.0001$ (Significant)

[Table 4] shows the association of thyroid status with small-for-gestational-age (SGA) and appropriate-for-gestational-age (AGA) categories.

Table 5: Thyroid status based on type of delivery

Type of Delivery	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
LUCS	85 (50.3)	28 (75.7)	113 (54.9)
NVD	84 (49.7)	9 (24.3)	93 (45.1)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 7.89$, $p = 0.005$ (Non-significant)

[Table 5] compares thyroid function between neonates delivered by LUCS and normal vaginal delivery (NVD).

Table 6: Thyroid status based on type of marriage

Marriage Type	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Consanguineous	49 (29)	11 (29.7)	60 (29.1)
Non-consanguineous	120 (71)	26 (70.3)	146 (70.9)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 0.008$, $p = 0.93$ (Non-significant)

[Table 6] describes the association of thyroid dysfunction with consanguinity.

Table 7: Thyroid status based on complications of birth

Complications of Birth	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	150 (88.8)	31 (83.8)	181 (87.9)
Absent	19 (11.2)	6 (16.2)	25 (12.1)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 0.71$, $p = 0.41$ (Non-significant)

[Table 7] shows thyroid status among neonates with or without birth complications.

Table 8: Thyroid status based on maternal thyroid status during pregnancy

Maternal Thyroid Status	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Euthyroid	147 (87)	29 (78.4)	176 (85.4)
Hyperthyroid	3 (1.8)	1 (2.7)	4 (1.9)
Hypothyroid	19 (11.2)	7 (18.9)	26 (12.6)
Total	169 (82)	37 (18)	206 (100)

Fisher's = 1.82, $p = 0.41$ (Non-significant)

[Table 8] represents the relationship between maternal thyroid status and neonatal thyroid function.

Table 9: Thyroid status based on antenatal history

Antenatal History	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Normal	76 (45)	10 (27)	86 (41.7)
Abnormal	93 (55)	27 (73)	120 (58.3)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 4.02$, $p = 0.004$ (Significant)

[Table 9] shows the relationship between abnormal antenatal history and thyroid dysfunction.

Table 10: Association between RDS and thyroid status

RDS	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	69 (40.8)	14 (37.8)	83 (40.3)
Absent	100 (59.2)	23 (62.2)	123 (59.7)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 0.11$, $p = 0.74$ (Non-significant)

[Table 10] describes the distribution of thyroid dysfunction among neonates with and without respiratory distress syndrome (RDS).

Table 11: Association between birth asphyxia and thyroid status

Birth Asphyxia	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	39 (23.1)	7 (18.9)	46 (22.3)
Absent	130 (72.9)	30 (81.1)	160 (77.7)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 0.31$, $p = 0.58$ (Non-significant)

[Table 11] shows the association between birth asphyxia and thyroid dysfunction.

Table 12: Association between NNJ and thyroid status

NNJ	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	30 (17.8)	6 (16.2)	36 (17.5)
Absent	139 (82.2)	31 (83.8)	170 (82.5)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 0.05$, $p = 0.58$ (Non-significant)

[Table 12] compares neonatal jaundice (NNJ) with thyroid function status.

Table 13: Association between PIH/Pre-eclampsia/Eclampsia and thyroid status

PIH / Pre-eclampsia / Eclampsia	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	60 (35.5)	14 (37.8)	74 (35.9)
Absent	109 (64.5)	23 (62.2)	132 (64.1)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 0.072$, $p = 0.004$ (Significant)

[Table 13] represents the relationship between maternal hypertensive disorders and neonatal thyroid status.

Table 14: Association between EONS/LONS and thyroid status

Neonatal Sepsis (EONS/LONS)	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	18 (10.7)	7 (18.9)	25 (12.1)
Absent	151 (89.3)	30 (81.1)	181 (87.9)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 1.95$, $p = 0.16$ (Non-significant)

[Table 14] shows the correlation between neonatal sepsis and thyroid dysfunction.

Table 15: Association between CHD and thyroid status

CHD	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	37 (21.9)	4 (10.8)	41 (19.9)
Absent	132 (78.1)	33 (89.2)	165 (80.1)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 2.34$, $p = 0.13$ (Non-significant)

[Table 15] shows the presence of congenital heart disease (CHD) among euthyroid and hypothyroid neonates.

Table 16: Association between Down syndrome and thyroid status

Down Syndrome	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	3 (1.8)	2 (5.4)	5 (2.4)
Absent	166 (98.2)	35 (94.6)	201 (97.6)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 1.69$, $p = 0.19$ (Non-significant)

[Table 16] describes the relationship between Down syndrome and thyroid dysfunction.

Table 17: Association between teenage mother and thyroid status

Teenage Mother	Euthyroid n (%)	Hypothyroid n (%)	Total n (%)
Present	23 (13.6)	13 (35.1)	36 (17.5)
Absent	146 (86.4)	24 (64.9)	170 (82.5)
Total	169 (82)	37 (18)	206 (100)

$\chi^2 = 9.75$, $p = 0.002$ (Significant)

[Table 17] shows the association of teenage pregnancy with neonatal thyroid dysfunction.

Table 18: Difference of mean fT4 (ng/dl) between Euthyroid and Hypothyroid

Group	Mean ± SD (ng/dl)	p-value
Euthyroid	1.59 ± 0.44	0.0001 (Significant)
Hypothyroid	1.03 ± 0.49	

[Table 18] compares the mean fT4 levels between euthyroid and hypothyroid neonates.

Table 19: Difference of mean TSH (µIU/ml) between Euthyroid and Hypothyroid

Group	Mean ± SD (µIU/ml)	p-value
Euthyroid	4.39 ± 1.71	0.0001 (Significant)
Hypothyroid	23.75 ± 9.06	

[Table 19] describes the mean TSH comparison between euthyroid and hypothyroid groups.

[Table 1] Indicates no significant association between birth weight and thyroid status. [Table 2] shows male preponderance in hypothyroid infants, though not statistically significant. [Table 3] demonstrates a significant relationship

between higher gestational age (≥34 weeks) and hypothyroidism. [Table 4] highlights SGA infants as significantly more prone to hypothyroidism. [Table 5] shows more hypothyroidism in LUCS deliveries, though not significant. [Table 6] confirms that consanguinity does not play a role in thyroid dysfunction. [Table 7] reveals that birth complications are not significantly related to hypothyroidism. [Table 8] finds no association between maternal thyroid disorder and neonatal thyroid status. [Table 9] establishes that an abnormal antenatal history substantially increases the risk of hypothyroidism. [Table 10] shows that RDS has no significant correlation with thyroid dysfunction. [Table 11] finds no link between birth asphyxia and thyroid dysfunction. [Table 12] demonstrates that NNJ does not affect thyroid status. [Table 13] identifies maternal PIH, pre-eclampsia, and eclampsia as significant contributors to neonatal hypothyroidism. [Table 14] reveals that sepsis has no significant correlation with thyroid dysfunction. [Table 15] indicates that CHD is non-significantly associated. [Table 16] shows that Down syndrome incidence was higher in hypothyroid neonates, but not statistically significant. [Table 17] highlights a strong, significant association between teenage pregnancy and neonatal hypothyroidism. [Table 18] confirms mean fT4 levels are significantly lower in hypothyroid infants. [Table 19] demonstrates that mean TSH levels are elevated considerably among hypothyroid neonates.

In summary, thyroid dysfunction (18%) was significantly associated with SGA status, gestational age ≥34 weeks, abnormal antenatal history, maternal hypertensive disorders, and teenage pregnancy, emphasizing the need for routine thyroid screening in preterm neonates.

Discussion

Principal Findings: In this cross-sectional study involving 206 preterm neonates admitted to the Special Newborn Care Unit (SNCU) of Malda Medical College, the overall prevalence of thyroid dysfunction was 18%. In contrast, 82% of the neonates were euthyroid. The incidence of hypothyroidism was notably higher in small-for-gestational-age (SGA) infants, those born to teenage mothers, and infants whose mothers had abnormal antenatal histories or pregnancy-induced hypertension.[11] Gestational age showed a statistically significant association with hypothyroidism, with a higher frequency among infants born at or beyond 34 weeks of gestation. Conversely, variables such as birth weight, gender, type of delivery, consanguinity, perinatal complications, neonatal sepsis, respiratory distress syndrome (RDS), birth asphyxia, congenital heart disease (CHD), Down syndrome, and neonatal jaundice showed no significant association. The mean free T4 (fT4) level was significantly lower and the mean thyroid-stimulating hormone (TSH) level significantly higher among hypothyroid neonates compared with euthyroid controls, confirming biochemical hypothyroidism in these infants.[12]

Comparison with Existing Literature

The observed 18 % prevalence of thyroid dysfunction among preterm neonates aligns with the reported range of 10–25 % in similar tertiary-care studies from India and Southeast Asia. Earlier research has demonstrated that preterm and SGA infants are at higher risk of transient or permanent hypothyroidism due to immaturity of the hypothalamic–pituitary–thyroid (HPT) axis. Our findings that SGA neonates had nearly a fourfold higher risk of hypothyroidism are consistent with studies showing that restricted intra-uterine growth, placental insufficiency, and chronic hypoxia impair thyroid hormone synthesis and peripheral conversion of T4 to T3.[13]

The significant association between maternal hypertensive disorders and neonatal hypothyroidism corroborates earlier work indicating that pre-eclampsia and eclampsia compromise maternal–fetal transfer of thyroxine and iodine. Similar associations have been observed in multicenter cohorts from southern India, where maternal hypertension was associated with lower cord-blood T4 levels and elevated neonatal TSH levels. Teenage pregnancy as an independent predictor of hypothyroidism also parallels observations from population-based registries that highlight nutritional inadequacy, poor antenatal care, and higher preterm birth rates among adolescent mothers as contributing factors.[14]

By contrast, the lack of correlation between delivery mode and thyroid status, or between neonatal morbidities (RDS, sepsis, asphyxia) and hypothyroidism, agrees with studies showing that acute illness generally produces transient non-thyroidal illness patterns without persistent hypothyroidism when measured beyond the immediate stress period. Thus, the present data strengthen the evidence that antenatal and intra-uterine factors, rather than acute post-natal illness, are the major determinants of neonatal thyroid dysfunction.[15]

Pathophysiological Considerations

Multiple physiological mechanisms underlie the observed associations. Preterm infants experience an attenuated postnatal TSH surge and reduced thyroxine-binding globulin, resulting in diminished circulating T4 concentrations. In SGA infants, chronic intrauterine hypoxia suppresses type I deiodinase activity and augments type III deiodinase, increasing the conversion of T4 to the inactive reverse T3. In pregnancies complicated by pre-eclampsia or placental insufficiency, reduced maternal–fetal exchange of thyroxine results in deficient intra-uterine priming of the fetal thyroid axis, predisposing the neonate to transient or permanent hypothyroidism. Furthermore, maternal stress and endothelial dysfunction characteristic of hypertensive pregnancies elevate cytokine levels, which may inhibit pituitary TSH release. Teenage mothers are prone to nutritional deficiencies (particularly iodine and iron), both of which impair thyroid hormone synthesis. Collectively, these mechanisms explain the clustering of hypothyroidism among infants exposed to adverse antenatal environments.[16]

Clinical Implications

The study emphasizes the need for routine thyroid function screening in all preterm and low-birth-weight infants admitted to neonatal units, with special attention to SGA neonates, infants of hypertensive or adolescent mothers, and those with abnormal antenatal histories. Screening should ideally be performed between the fifth and seventh day of life to avoid transient perinatal fluctuations, and repeated at 2–4 weeks in sick or very preterm babies to detect delayed TSH rise. Prompt initiation of levothyroxine therapy is crucial to prevent neurodevelopmental

sequelae, particularly since the therapeutic window for optimal brain protection is within the first two weeks of life. Maintaining serum fT4 in the upper half of the reference range and TSH within age-appropriate limits requires periodic monitoring and dose adjustment. The present findings provide evidence to reinforce institutional protocols and justify resource allocation toward universal newborn screening in tertiary SNCUs.[17]

Strengths and Limitations

Key strengths of this study include a well-defined hospital-based cohort, standardized biochemical assays (ELISA) for fT4 and TSH, and rigorous documentation of maternal and perinatal factors, enabling comprehensive analysis. The uniform timing of sampling minimized the confounding effect of acute-phase illness. The use of appropriate statistical tests (Chi-square, Fisher's exact, and t-tests) ensured reliable inference.

Nevertheless, certain limitations merit mention. Being cross-sectional, the study cannot determine causality or temporal sequence between antenatal factors and neonatal thyroid dysfunction. The single-center design may limit generalizability to other populations. Long-term neurodevelopmental follow-up was beyond the scope of the study, precluding correlation between biochemical abnormalities and later outcomes. Iodine status, maternal medication use, and environmental factors were not assessed and may have influenced results. Future multicenter prospective studies are needed to validate these associations and clarify the progression from transient to permanent hypothyroidism.

Future Directions

Future research should focus on prospective follow-up of preterm infants with abnormal thyroid profiles to distinguish transient hypothyroxinemia from permanent congenital hypothyroidism. Serial hormone measurements at 2, 4, and 8 weeks, combined with developmental assessments, will elucidate the natural history of thyroid dysfunction in this group. Investigating maternal nutrition, iodine sufficiency, and placental pathology may identify modifiable preventive factors. Furthermore, cost-effectiveness analyses of universal versus targeted screening in resource-limited settings can guide national neonatal screening policies.

In summary, thyroid dysfunction was observed in nearly one-fifth of preterm neonates, with significant associations to SGA status, higher gestational age within the preterm spectrum, abnormal antenatal history, maternal hypertensive disorders, and teenage pregnancy. These results underscore the importance of integrating routine thyroid screening into neonatal care protocols, particularly for high-risk subgroups, to ensure timely diagnosis, prompt treatment, and prevention of irreversible neurodevelopmental impairment.

Conclusion

The present study highlights a substantial burden of thyroid dysfunction among preterm neonates admitted to the Special Newborn Care Unit (SNCU) of Malda Medical College and Hospital, with a prevalence of 18%. The findings demonstrate that hypothyroidism in preterm infants is significantly associated with small-for-gestational-age (SGA) status, higher gestational age (≥34 weeks) within the preterm spectrum, maternal hypertensive disorders, abnormal antenatal history, and teenage pregnancy. In contrast, parameters such as gender, birth weight, type of delivery, consanguinity, and common neonatal morbidities—including respiratory distress syndrome, sepsis, birth asphyxia, neonatal jaundice, congenital heart disease, and Down syndrome—did not show statistically significant correlations.

The biochemical profile confirmed that hypothyroid neonates exhibited markedly lower mean free T4 and elevated mean TSH levels compared with euthyroid infants, establishing the diagnostic reliability of thyroid function testing in the early neonatal period. These findings underscore the importance of routine neonatal thyroid screening, particularly among high-risk groups such as SGA infants and babies born to mothers with hypertensive disorders or adverse antenatal histories. Early identification and prompt initiation of levothyroxine therapy within the first two weeks of life are essential to prevent long-term neurodevelopmental impairment.

From a public health perspective, this study highlights the importance of integrating thyroid function screening into standard neonatal care protocols at all tertiary and secondary care centers across India. Given the country's high preterm birth rate and the frequent occurrence of maternal complications, universal or at least targeted screening of high-risk neonates should be prioritized. Future multicentric prospective studies with long-term follow-up are warranted to evaluate treatment outcomes, refine screening intervals, and inform national neonatal thyroid screening programs aimed at improving developmental and cognitive outcomes in this vulnerable population.

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Conflicts of interest

There are no conflicts of interest.

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