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Original Research Article

Prevalence of Neonatal Subclinical Hypothyroidism and Its Clinical Correlation in a Tertiary Care Centre

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Abstract

Background: Subclinical hypothyroidism (SH) in neonates is increasingly identified via expanded newborn screening programs; however, its natural trajectory and precise clinical significance remain under active investigation. Early detection is critical because persistent hyperthyrotropinemia can adversely affect neurodevelopmental outcomes if left unmanaged.

Objective: To evaluate the prevalence of neonatal subclinical hypothyroidism, determine the proportion of neonates exhibiting persistent thyroid-stimulating hormone (TSH) elevation requiring levothyroxine therapy, and analyze potential associations between maternal thyroid disorders and neonatal SH.

Methods: A prospective observational investigation was conducted in the postnatal care unit of a major tertiary care teaching hospital over a four-month period (June to September 2025). Inborn neonates meeting inclusion criteria with informed parental consent were enrolled. Venous blood samples were collected after 72 hours of life and analyzed for TSH using chemiluminescence immunoassay (CLIA). Infants with TSH concentrations between 6–20 mIU/L underwent systematic follow-up and repeat testing at 14 days of life. Comprehensive maternal and neonatal clinical variables were recorded and analyzed.

Results: Among 218 eligible neonates screened, 58 (26.6%) were diagnosed with subclinical hypothyroidism, while 160 (73.4%) demonstrated normal thyroid function profiles. Upon serial follow-up, 22 out of 58 neonates (37.9%) exhibited persistently elevated TSH levels, 32 (55.2%) showed complete biochemical normalization, and 4 (6.9%) were lost to follow-up. Seven neonates ultimately met criteria and were initiated on levothyroxine replacement therapy. Among evaluated maternal comorbidities, maternal hypothyroidism demonstrated a statistically significant association with neonatal SH ($\chi^2 = 5.16$, $p = 0.02$).

Conclusion: Neonatal subclinical hypothyroidism is notably prevalent and frequently persists in a substantial subset of infants, necessitating structured therapeutic intervention. Serial biochemical surveillance is indispensable, particularly among neonates born to hypothyroid mothers.

Keywords: Neonatal subclinical hypothyroidism, Hyperthyrotropinemia, Newborn screening, maternal hypothyroidism, Chemiluminescence immunoassay.

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Introduction

Congenital hypothyroidism (CH) represents one of the foremost preventable causes of intellectual disability and neurodevelopmental delay in pediatric populations worldwide. With the widespread implementation and increasing sensitivity of neonatal screening programs, transient or mild thyroid hormone dysregulation—specifically neonatal subclinical hypothyroidism (SH)—is diagnosed with growing frequency [1, 2]. Subclinical hypothyroidism in the neonatal period is conventionally defined as serum thyroid-stimulating hormone (TSH) concentrations exceeding the upper reference threshold while maintaining normal free thyroxine (FT4) levels [3, 4]. Depending upon the degree of biochemical elevation, SH is frequently stratified into mild (TSH 4.5–10 mIU/L) or moderate-to-severe (TSH >10–20 mIU/L) categories [5]. The etiopathogenesis of neonatal SH is multifactorial, encompassing physiological adaptation mechanisms to extrauterine life, immaturity of the hypothalamic-pituitary-thyroid axis, maternal endocrine status, perinatal stressors, and intrauterine growth restriction [6, 7]. While a substantial proportion of neonates with mild hyperthyrotropinemia experience spontaneous

biochemical normalization within the first few weeks of life, a distinct subset exhibits persistent TSH elevation that, if undetected or unmanaged, carries potential risks for long-term cognitive and psychomotor deficits [8, 9].

Despite established consensus guidelines by international pediatric endocrine societies regarding overt congenital hypothyroidism, clinical management protocols for neonatal subclinical hypothyroidism remain variable due to uncertainties surrounding its long-term neurodevelopmental impact [10, 11]. Furthermore, the influence of maternal medical disorders—particularly treated or untreated maternal hypothyroidism—on neonatal thyroid indices requires continuous clinical scrutiny [12]. This prospective observational study was undertaken to determine the exact prevalence of neonatal subclinical hypothyroidism in a tertiary care setting, evaluate the proportion of infants demonstrating persistent hyperthyrotropinemia requiring hormonal therapy, and analyze the correlation between maternal comorbidities and neonatal thyroid function.

Materials and Methods

Study Design and Setting: This prospective observational investigation was conducted within the postnatal care ward of the Department of Pediatrics at a tertiary care teaching hospital in Mandya over a four-month duration from June to September 2025. Approval from the Institutional Ethics Committee was formally secured prior to patient enrollment, and written informed consent was obtained from all participating parents or legal guardians.

Study Population and Eligibility Criteria: All inborn neonates delivered during the study period whose parents consented to participation were evaluated for inclusion. Exclusion criteria were strictly defined to eliminate confounding pathologies and included extreme preterm neonates (<28 weeks gestation), neonates with major congenital malformations, and infants requiring prolonged intensive care unit (NICU) admission for severe asphyxia, congenital heart disease, or surgical emergencies.

Data Collection and Laboratory Analysis: Comprehensive baseline demographic data, including gestational age, birth weight, sex, mode of delivery, and maternal clinical history, were meticulously recorded using a standardized proforma. Venous blood samples (2 mL) were drawn from all enrolled neonates after 72 hours of life under strict aseptic precautions. Serum TSH concentrations were quantitatively estimated using automated Chemiluminescence Immunoassay (CLIA) technology adhering to strict quality control standards.

Follow-Up Protocol and Intervention Criteria

Neonates were stratified based on their initial venous TSH levels:

- Infants with TSH >20 mIU/L were immediately evaluated and managed in accordance with established international consensus guidelines for congenital hypothyroidism [13].
- Infants with TSH concentrations ranging between 6 mIU/L and 20 mIU/L were diagnosed with subclinical hypothyroidism and recalled for systematic repeat TSH estimation at 14 days of life.
- At the 14-day follow-up, infants whose repeat TSH remained >10 mIU/L underwent concomitant free T4 (FT4) estimation, and levothyroxine replacement therapy was initiated where indicated.
- Infants with repeat TSH values remaining between 6–10 mIU/L were placed under close clinical and biochemical surveillance.

Maternal comorbidities (hypothyroidism, gestational hypertension, gestational diabetes mellitus) and neonatal complications (neonatal hyperbilirubinemia, sepsis, respiratory distress) were documented for association analyses.

Statistical Analysis: Data were compiled, verified, and analyzed using statistical software (SPSS version 25.0). Continuous variables were summarized as means ± standard deviations, while categorical variables were expressed as frequencies and absolute percentages.

The Chi-square test (χ^2) was employed to assess associations between categorical risk factors (maternal and neonatal comorbidities) and the development of neonatal subclinical hypothyroidism. Statistical significance was defined a priori at a threshold of $p < 0.05$.

Results

A total of 218 eligible neonates were consecutively enrolled and evaluated during the study window. Among the screened cohort, 160 neonates (73.4%) demonstrated normal serum TSH levels, while 58 neonates (26.6%) were diagnosed with subclinical hypothyroidism based on initial venous TSH evaluations (>6 mIU/L).

Follow-Up Outcomes in Neonates with Subclinical Hypothyroidism: Of the 58 neonates diagnosed with subclinical hypothyroidism, comprehensive follow-up data revealed that 32 infants (55.2%) achieved spontaneous biochemical normalization of TSH levels without therapeutic intervention. However, 22 neonates (37.9%)

exhibited persistently elevated TSH concentrations on repeat testing, and 4 infants (6.9%) were lost to follow-up despite multiple tracking attempts. Among those with persistent hyperthyrotropinemia, 7 neonates met definitive endocrine criteria and were successfully initiated on levothyroxine replacement therapy in accordance with contemporary consensus guidelines.

Table 1: Baseline Demographic Characteristics of Neonates with Subclinical Hypothyroidism (n = 58)

Clinical Parameter	Category	Frequency (n = 58) / Percentage
Gestational Age	Term (≥ 37 weeks) Preterm (< 37 weeks)	48 (82.8%) 10 (17.2%)
Birth Weight	Normal Birth Weight (≥ 2.5 kg) Low Birth Weight (< 2.5 kg)	47 (81.0%) 11 (19.0%)
Gender Distribution	Male Female	32 (55.2%) 26 (44.8%)

As outlined in Table 1, the majority of neonates presenting with subclinical hypothyroidism were born at term gestation (82.8%) with normal birth weights (81.0%), and male infants accounted for 55.2% of the affected cohort.

Table 2: Neonatal Comorbidities and Statistical Association with Subclinical Hypothyroidism

Neonatal Comorbidity	SH Infants (n = 58)	p-value	Normal TSH Group (n = 160)
Neonatal Hyperbilirubinemia (NNHB)	32 (55.2%)	p = 0.11	82 (51.3%)
Neonatal Sepsis	4 (6.9%)	p = 0.06	2 (1.3%)
Respiratory Disorders	6 (10.3%)	p = 0.92	16 (10.0%)
Other Comorbidities	6 (10.3%)	p = 0.41	11 (6.9%)
No Comorbidity (Nil)	13 (22.4%)	p = 0.54	63 (39.4%)

Evaluation of neonatal comorbidities (Table 2) revealed that neonatal hyperbilirubinemia (NNHB) was the most frequent concurrent condition, occurring in 55.2% of SH infants. Although neonatal sepsis demonstrated a slight numerical elevation among SH cases (6.9% vs. 1.3%), statistical analysis indicated no significant association between evaluated neonatal comorbidities and subclinical hypothyroidism (all $p > 0.05$).

Table 3: Maternal Comorbidities and Their Association with Neonatal Subclinical Hypothyroidism

Maternal Comorbidity	SH Neonates (n = 58)	Statistical Significance	Normal Group (n = 160)
Maternal Hypothyroidism	10 (17.2%)	**p = 0.02 ***	17 (10.6%)
Gestational Hypertension	2 (3.4%)	p = 0.15	15 (9.4%)
Gestational Diabetes Mellitus (GDM)	1 (1.7%)	p = 0.58	5 (3.1%)
Other Maternal Conditions	4 (6.9%)	p = 0.73	9 (5.6%)

As detailed in Table 3, maternal hypothyroidism was present in 17.2% of mothers in the SH cohort compared to 10.6% in the normal group. This relationship demonstrated a statistically significant association ($\chi^2 = 5.16$, $p = 0.02$), highlighting maternal thyroid dysfunction as a critical risk factor influencing neonatal TSH dynamics. Conversely, gestational hypertension, gestational diabetes mellitus, and other maternal medical conditions showed no statistically significant correlation with neonatal SH ($p > 0.05$).

Discussion

The findings of this prospective observational study highlight a notable prevalence of neonatal subclinical hypothyroidism (26.6%) among screened inborn neonates in a tertiary care setting. This observed proportion aligns with broader epidemiological literature emphasizing that expanded newborn screening programs frequently identify mild, transient elevations in TSH that exceed traditional screening cut-offs [14, 15]. Variations in reported prevalence across global and regional studies are largely attributable to differing assay sensitivities, TSH reference cutoff thresholds, iodine nutritional status, and demographic characteristics of the studied cohorts [16, 17]. A critical clinical takeaway from our investigation is that more than one-third (37.9%) of neonates diagnosed with subclinical hypothyroidism exhibited persistent hyperthyrotropinemia upon follow-up evaluation at 14 days of life, with 7 infants ultimately requiring levothyroxine replacement therapy. This underscores the clinical imperative of structured serial monitoring rather than dismissing initial borderline TSH elevations as purely physiological phenomena [18, 19]. Untreated persistent thyroid dysfunction during

early infancy carries recognized risks of subtle neurodevelopmental, cognitive, and motor deficits, reinforcing the value of timely pediatric endocrine consultation and intervention [20, 21].

Furthermore, our analysis established a statistically significant association between maternal hypothyroidism and neonatal subclinical hypothyroidism ($p = 0.02$). Maternal thyroid hormone transport, placental iodide handling, and autoimmune antibody transfer significantly impact the developing fetal and neonatal hypothalamic-pituitary-thyroid axis [22, 23]. These findings emphasize that neonates born to mothers with known thyroid disorders represent a high-risk subgroup warranting prioritized screening, vigilant biochemical follow-up, and targeted pediatric surveillance [24, 25].

Conclusion

Neonatal subclinical hypothyroidism is a frequently encountered condition in contemporary neonatal practice. A substantial minority of affected infants demonstrate persistent TSH elevations that necessitate structured follow-up and targeted hormonal therapy to safeguard optimal neurodevelopmental outcomes.

The significant correlation identified between maternal hypothyroidism and neonatal SH underscores the clinical necessity of targeted surveillance in infants born to mothers with thyroid disorders. Future multi-center longitudinal studies incorporating extended neurodevelopmental assessments are warranted to refine evidence-based management algorithms and therapeutic thresholds for neonatal hyperthyrotropinemia.

Declarations

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