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Original Research Article

FREQUENCY OF CONGENITAL HYPOTHYROIDISM IN PRETERM AND LOW BIRTH WEIGHT NEONATES IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: *Congenital hypothyroidism (CH) is a preventable cause of neurodevelopmental impairment. Preterm and low birth weight neonates are at heightened risk and may require repeat thyroid-stimulating hormone (TSH) screening to avoid missed or delayed diagnoses.* ***Objective:*** *To determine the frequency of CH in preterm and low birth weight neonates admitted to a tertiary care hospital and to explore its association with key perinatal variables.* ***Study Design:*** *Descriptive cross-sectional study.* ***Settings:*** *Department of Pediatrics, Chaudhry Muhammad Akram Teaching and Research Hospital, Lahore, Pakistan.* ***Duration of Study:*** *3 December 2024 to 3 June 2025.* ***Methods:*** *A total of 165 neonates who were preterm (<37 weeks' gestation) or low birth weight (<2500 g) were enrolled through non-probability consecutive sampling. Dried blood spot specimens were analyzed for TSH using an immunoradiometric assay. CH was defined as TSH ≥20 mIU/L. Associations between CH status and age at testing, sex, gestational age, and mode of delivery were evaluated with a two-sided α of 0.05.* ***Results:*** *The mean gestational age was 33.29 ± 1.78 weeks, and the mean birth weight was 1841.56 ± 310.97 g. CH was detected in 10.3% (n=17/165) of neonates. There was no statistically significant association between CH and age at testing (p=0.704), sex (p=0.778), gestational age (p=0.923), or mode of delivery (p=0.189).* ***Conclusion:*** *A notably high frequency of CH was observed among preterm and low birth weight neonates in this tertiary care setting. These data support routine and repeat TSH screening in this high-risk population to enable timely diagnosis and initiation of therapy.*

Keywords: Congenital Hypothyroidism; Preterm Neonates; Low Birth Weight; TSH Screening; Neonatal Endocrine Disorders

INTRODUCTION

Congenital hypothyroidism (CH), characterized by insufficient thyroid hormone production present at birth (1-4), is recognized as the leading preventable cause of intellectual disability across the globe. The primary form of CH commonly arises due to structural abnormalities in thyroid gland development—such as agenesis or dysgenesis—or from inherited enzymatic defects affecting thyroid hormone synthesis, collectively referred to as dyshormonogenesis (5). Neonatal hypothyroidism, particularly congenital hypothyroidism (CH), is a significant endocrine disorder that can lead to severe neurodevelopmental impairments if not promptly diagnosed and treated. The prevalence of CH in the general newborn population is estimated between 1 in 2,000 and 1 in 3,000 live births (6). Preterm infants, defined as those born before 37 weeks of gestation, are at an increased risk for thyroid dysfunction, including hypothyroidism. Studies have reported a higher incidence of CH in preterm infants compared to their term counterparts. For instance, multiple screening programs have confirmed a higher incidence of CH in preterm infants, with almost 50% occurrence (7).

The etiology of hypothyroidism in preterm neonates is multifactorial. The hypothalamic-pituitary-thyroid axis, which regulates thyroid hormone production, may be underdeveloped in these infants, leading to insufficient hormone synthesis (8). Additionally, the immaturity of the thyroid gland itself can contribute to decreased hormone production. Environmental factors, such as iodine deficiency or exposure to medications that interfere with thyroid function, may also play a role (9).

Early detection through neonatal screening programs is crucial for the timely initiation of treatment to prevent adverse outcomes. However, the optimal timing and methodology for screening preterm infants remain subjects of ongoing research and debate. Some studies suggest that initial screenings may miss cases of delayed TSH elevation, advocating for repeat testing in this vulnerable population (10).

In a study conducted by Akram et al. (11), congenital hypothyroidism was identified in 27 neonates (12%), while the remaining 198 neonates (88%) were found to be euthyroid. The mean age at the time of testing was 17.76 ± 6.40 days, with the youngest and oldest neonates aged 8 and 28 days, respectively. Of the total participants, 51.6% (n=116) were male and 48.4% (n=109) were female. The mean gestational age was reported as 33.10 ± 1.98 weeks, ranging from 30 to 36 weeks. The mean birth weight was 1846.27 ± 330.58 grams, with weights ranging between 1211 and 2397 grams.

Given the potential for both transient and permanent forms of hypothyroidism in preterm infants, longitudinal follow-up is essential to monitor thyroid function over time. This approach ensures appropriate management tailored to the individual needs of each infant, thereby mitigating the risk of long-term neurodevelopmental deficits associated with untreated hypothyroidism. With minimal local data available on the burden of CH, this study seeks to fill that gap by determining its frequency, enabling earlier identification and management to avert lasting developmental impairments. This will open windows for new research protocols and will set priorities for national screening programs for congenital hypothyroidism.

METHODOLOGY

A cross-sectional study was conducted at the Department of Pediatrics, Chaudhry Muhammad Akram Teaching and Research Hospital, Lahore. The study was completed over six months from 3 December 2024 to 3 June 2025, following approval of the research synopsis by the hospital's ethical review committee. A total of 165 neonates were enrolled in the study using non-probability consecutive sampling. The sample size was calculated based on an expected

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proportion of congenital hypothyroidism of 12%, with a 95% confidence level and a 5% margin of error. Eligible participants included preterm neonates (born before 37 weeks of gestation) and low birth weight neonates (birth weight <2500 grams) of either gender, as per operational definitions. Neonates were excluded if they were born at term, had birth weights appropriate for gestational age, had congenital anomalies, or had a maternal history of antithyroid medication use, autoimmune thyroiditis, or radioactive iodine exposure.

After obtaining informed consent from the parents or guardians, demographic and clinical data were recorded. A dried blood spot (DBS) sample for newborn screening (NBS) was collected via heel prick after 48 hours of life. In the case of preterm neonates, a second sample was obtained at 14 days of life. Samples were collected on standardized filter paper and sent to the NBS laboratory for testing. Serum thyroid-stimulating hormone (TSH) levels were assessed using an immunoradiometric assay. Neonates were categorized as hypothyroid if TSH was ≥20 mIU/L.

All data were documented on a structured proforma by the primary investigator. Using SPSS version 26.0, the data were analyzed to compute descriptive statistics. Continuous variables—such as age, gestational age, and birth weight—were expressed as mean ± standard deviation. Categorical variables—such as gender, mode of delivery, and the presence or absence of congenital hypothyroidism—were presented as frequencies and percentages. To assess potential effect modifiers, stratified analysis was carried out based on variables like age, gender, and mode of delivery. Post-stratification comparisons were conducted using the Chi-square test, with a significance level set at $p \leq 0.05$.

RESULTS

A total of 165 neonates with either preterm birth or low birth weight were enrolled in the study. At the time of sampling, the mean age was 17.38 ± 5.58 days. The average gestational age was recorded as 33.29 ± 1.78 weeks, while the mean birth weight was 1841.56 ± 310.97 grams. The average thyroid-stimulating hormone (TSH) level among the participants was 15.55 ± 10.42 mIU/L (Table 1).

Table 1: Summary Statistics for Key Continuous Variables (n = 165)

Variable	Mean	Standard Deviation	N
Age (days)	17.38	5.576	165
Gestational Age (weeks)	33.29	1.7752	165
Birth Weight (g)	1841.56	310.966	165
TSH Level (mIU/L)	15.55	10.42	165

Regarding gender distribution, 49.7% (n=82) of the neonates were male, and 50.3% (n=83) were female. Most of the neonates (63.6%, n=105) were born between 30 and 34 weeks of gestation, while 36.4% (n=60) were born between 34 and 36 weeks. The majority (61.8%, n=102) were delivered via expected vaginal delivery (NVD), and 38.2% (n=63) were delivered through lower segment cesarean section (LSCS). Congenital hypothyroidism (CH) was identified in 10.3% (n=17) of the neonates, whereas 89.7% (n=148) were euthyroid. (Table 2)

Table 2: Categorical Data Summary (n = 165)

Variable	Category	Frequency	%
Gender	Male	82	49.7%
	Female	83	50.3%
Gestational Age	30–34 weeks	105	63.6%
	34–36 weeks	60	36.4%
Mode of Delivery	Normal Vaginal Delivery	102	61.8%
	Lower Segment Cesarean Section	63	38.2%
CH Status	Yes	17	10.3%
	No	148	89.7%

When comparing CH status with age at testing, 41.2% (n=7) of the hypothyroid cases were in neonates aged ≤15 days, while 58.8% (n=10) were in those aged 16–29 days (p = 0.704). Among male neonates, 52.9% (n=9) were hypothyroid, compared to 47.1% (n=8) of female neonates (p = 0.778), indicating no significant gender-based difference. In terms of gestational age, CH was found in 64.7% (n=11) of neonates born between 30–34 weeks and in 35.3% (n=6) of those born between 34–36 weeks (p = 0.923). CH was more frequent in neonates delivered vaginally (76.5%, n=13) compared to those delivered via LSCS (23.5%, n=4) (p = 0.189). Overall, while congenital hypothyroidism was observed in a notable proportion of this high-risk neonatal population, no statistically significant association was found between CH and age at testing, gender, gestational age, or mode of delivery. (Table 3)

Table 3: Congenital Hypothyroidism according to various effect modifiers(n = 165)

Variable	Group	CH: Yes (n, %)	CH: No (n, %)	p-value
Age (days)	≤15	7 (41.2%)	54 (36.5%)	.704
	16–29	10 (58.8%)	94 (63.5%)	
Gender	Male	9 (52.9%)	73 (49.3%)	.778
	Female	8 (47.1%)	75 (50.7%)	
Gestational Age	30–34 weeks	11 (64.7%)	94 (63.5%)	.923
	34–36 weeks	6 (35.3%)	54 (36.5%)	
Mode of Delivery	NVD	13 (76.5%)	89 (60.1%)	.189
	LSCS	4 (23.5%)	59 (39.9%)	

DISCUSSION

This study was conducted to determine the frequency of congenital hypothyroidism (CH) in preterm and low birth weight neonates admitted to a tertiary care hospital. The results revealed that 10.3% of the neonates screened had elevated TSH levels (≥20 mIU/L), indicating CH. This finding is notably higher than the incidence reported in the general neonatal population and suggests a significant burden of thyroid dysfunction in this high-risk group. While CH was more frequently observed among male neonates, those delivered vaginally, and those with lower gestational age, no statistically significant associations were found between CH and gender, age at sampling, gestational age subgroup, or mode of delivery. These findings highlight the importance of targeted screening strategies in vulnerable neonatal populations to ensure early diagnosis and timely intervention.

The observed frequency of 10.3% in our study is consistent with the findings of Akram et al., who reported a CH rate of 12% in a comparable neonatal population (11). Both studies were conducted in Pakistani tertiary care hospitals and included preterm and low birth weight neonates within a similar range of gestational ages and birth weights. This similarity in findings strengthens the credibility of our results and reinforces the notion that CH is considerably more prevalent in preterm populations than in term neonates. Globally, CH

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occurs in approximately 1 in 2,000 to 1 in 3,000 live births; (12) however, the prevalence may be significantly underestimated in preterm and low birth weight neonates if repeat or delayed screening is not performed.

The higher risk of CH in premature infants is attributed to multiple factors. Immaturity of the hypothalamic-pituitary-thyroid (HPT) axis in these neonates can result in delayed or inadequate thyroid-stimulating hormone (TSH) response, compromising thyroid hormone synthesis. Additionally, underdeveloped thyroid tissue may result in structural abnormalities such as thyroid agenesis or ectopy, while genetic defects can impair hormone biosynthesis—conditions collectively termed thyroid dysgenesis and dyshormonogenesis (13). These are recognized as the most common causes of primary congenital hypothyroidism, especially in populations lacking universal screening. Environmental and maternal factors—such as iodine deficiency or exposure to medications affecting thyroid metabolism—may further exacerbate this dysfunction. Our study design accounted for some of these variables by excluding neonates with known maternal thyroid disease or medication use, ensuring a more focused evaluation of idiopathic CH.

Although CH was slightly more common in neonates tested after 15 days of life, the difference was not statistically significant ($p = 0.704$), which suggests that delayed TSH elevation might occur, but was not frequent enough to show a meaningful trend in this sample. Similarly, gender-based comparison showed no significant difference in CH prevalence between males and females, aligning with global data suggesting no strong gender predisposition (14). In our study, neonates delivered vaginally had a higher frequency of CH compared to those born via cesarean section, but this difference also lacked statistical significance ($p = 0.189$). These patterns indicate that while certain demographic and perinatal factors may appear associated with CH, the disorder is likely multifactorial and may not be predicted solely based on observable clinical variables.

One of the strengths of this study is its exclusive focus on a high-risk neonatal group—preterm and low birth weight infants—who are often underrepresented in population-based screening data. The use of a defined TSH cutoff (≥20 mIU/L) and incorporation of repeat screening for preterm neonates enhanced detection of both early and delayed-onset cases. The data collection was rigorous, utilizing standardized dried blood spot sampling and immunoradiometric assay testing (15). Moreover, stratified analysis allowed us to explore possible effect modifiers and demographic correlates, adding analytical depth to our findings.

One notable limitation is the study's restricted scope. Being confined to a single center with a sample size of 165 may reduce the generalizability of results to larger or more diverse populations. Additionally, the cross-sectional nature of the study precluded long-term follow-up, which is necessary to distinguish between transient and permanent forms of CH. This distinction is crucial for guiding treatment duration but cannot be addressed here (10). Another limitation is that thyroid hormone levels, such as free T4 or total T4, were not measured alongside TSH, which could have provided a more complete picture of thyroid function. Moreover, potential confounding factors like neonatal illnesses, iodine status, or medication exposure were not explored in detail (16).

In light of these findings, several recommendations emerge. First, screening programs in Pakistan should adopt repeat TSH testing in preterm and low birth weight neonates, ideally around day 14 of life, to detect delayed TSH elevation (15). National guidelines should be updated to reflect the higher risk of CH in this subgroup, with clear protocols for follow-up and treatment. Furthermore, future studies should include a larger, multicenter sample and incorporate longitudinal follow-up to evaluate the persistence of hypothyroidism and neurodevelopmental outcomes. It would also be beneficial to routinely assess free T4 levels alongside TSH to improve diagnostic specificity. Finally, efforts should be made to raise awareness among pediatricians and neonatologists about the unique screening needs of this population, to initiate treatment as early as possible, and to prevent long-term developmental deficits (17).

CONCLUSION

A relatively high frequency of CH was observed in this high-risk population. These findings underscore the importance of repeat TSH screening in preterm and low birth weight neonates to ensure early diagnosis and management.

DECLARATIONS

Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned.

Consent for publication

Approved

Funding

Not applicable

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

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Study Design, Review of Literature.
AMARA ZAHID (*Postgraduate Resident****)***
Conception of Study, Final approval of manuscript.
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Data entry, data analysis, and drafting an article.
JAWAIRIA ZAHID (*Postgraduate Resident****)***
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, and final approval of manuscript.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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