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Original Research Article

Prevalence of congenital hypothyroidism in preterm neonates: a NICU-based study

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ABSTRACT

Introduction: Congenital hypothyroidism (CH) is a common endocrine disorder in neonates. Early diagnosis of CH plays a key role in preventing neurodevelopmental impairment in future. Preterm neonates are at higher risk due to their immature hypothalamic-pituitary-thyroid axis. This study aimed to assess the prevalence of congenital hypothyroidism in preterm neonates admitted to the Neonatal Intensive Care Unit (NICU).
Methods: This cross-sectional study was conducted in the Department of Neonatology, Combined Military Hospital, Dhaka, Bangladesh, from July 2016 to December 2016. In this study, we included 50 preterm neonates with gestational ages ranging from 28 to 37 weeks admitted to the Department of Neonatology of our study institution.
Result: The mean age of neonates at sample collection was 5.38±2.66 days. The mean gestational age was 34.06±1.81 weeks. Of the 50 neonates, 27 (54%) were male and 23 (46%) were female, with a male-to-female ratio of 1:0.85. Only 4 (8%) neonates had a maternal history of thyroid disorders. The majority of neonates (50%) were between 32–34 weeks of gestation. Serum TSH and FT4 levels were within normal ranges across all gestational age groups. Only one neonate had a borderline elevated TSH level (10.70 mU/l) with a normal FT4 level, indicating no confirmed cases of congenital hypothyroidism.
Conclusion: This study showed that thyroid function was within normal limits in nearly all preterm neonates, with no confirmed cases of congenital hypothyroidism. Given the potential consequences of undiagnosed thyroid dysfunction, routine screening for thyroid disorders in preterm neonates remains essential for early detection and intervention.

Keywords: Preterm neonates, Congenital hypothyroidism, Thyroid function, TSH, FT4

INTRODUCTION

Congenital hypothyroidism (CH) is defined as a deficiency of thyroid hormones present at birth.[1] It is one of the most common endocrine disorders in newborns, with an incidence that varies by geography and ethnicity, ranging from 1 in 3,500 to 1 in 5,000 live births.[1,2] CH affects all populations but is more frequently seen in females, with studies generally reporting a female-to-male ratio of approximately 2.3:1.[3] The early detection of congenital hypothyroidism through newborn screening stands as a major success in preventive medicine. Before the implementation of routine screening in the 1970s, about one-third of children with CH were not diagnosed until after three months of age, by which time irreversible intellectual disability had often already occurred.[1,4,5] To prevent irreversible brain damage and growth retardation, neonatal screening for CH has become standard practice worldwide.[6] A comprehensive understanding of prenatal thyroid development and hormone requirements is important, especially when considering preterm infants. Since preterm thyroid function reflects both fetal and neonatal physiology, it differs significantly from full-term infants. Before the fetal thyroid gland becomes functional, thyroid hormones, primarily FT4, are transferred from the mother to the fetus and can be detected in embryonic tissues.[7] Preterm infants, especially those born before 32 weeks of gestation, are at

a significantly increased risk of developing hypothyroidism. They often exhibit blunted TSH surges and lower serum FT4 levels, a condition known as hypothyroxinemia of prematurity. Repeated thyroid function testing is crucial in these infants, even when initial results appear normal. This higher risk of thyroid dysfunction may be related to both iodine deficiency and excess.[8] In the United States, all newborns are screened for CH through state-sponsored programs. Traditionally, screening begins with an FT4 measurement followed by TSH testing in infants with low FT4. However, this approach or alternatives that rely solely on TSH may miss some cases. A combined assay measuring both FT4 and TSH would improve diagnostic sensitivity.[9] Typically, neonates with a capillary blood spot TSH of ≥20 mU/l are recalled for confirmatory serum testing. A diagnosis of true hypothyroidism is made in infants with elevated TSH and low free FT4.[6]

Most infants with CH show no symptoms at birth, likely due to maternal transfer of thyroid hormone across the placenta. However, infants born to mothers with hypothyroidism can still experience significant neurodevelopmental delays, even when treated early.[10] Around 12% of affected infants may have other congenital abnormalities.[11] CH is one of the most common and preventable causes of intellectual disability.[12] Early diagnosis and prompt treatment are essential to prevent delays in both mental and physical development.[13] Although CH leads to physical and mental retardation, neurological problems can be avoided with early detection and treatment.

A study conducted in Bangladesh found the incidence of CH to be 1.5 per 1,000 live births higher than global averages, suggesting a pressing public health concern.[11] Although this may not reflect the national average, it highlights the urgent need for a national neonatal screening program to prevent avoidable cases of mental retardation and ensure timely intervention for affected infants. Therefore, in this study, we aimed to assess the prevalence of congenital hypothyroidism in preterm neonates admitted to the Neonatal Intensive Care Unit (NICU) at our study institution.

METHODS

This cross-sectional study was conducted in the Department of Neonatology, Combined Military Hospital, Dhaka, Bangladesh, from July 2016 to December 2016. In this study, we included 50 preterm neonates with gestational ages ranging from 28 to 37 weeks admitted in the Department of Neonatology of our study institution.

Inclusion criteria

Preterm neonates with gestational age between 28 and 37 weeks; neonates aged between Day 5 and Day 20 of life at the time of sample collection, neonates whose parents or guardians consented to participate in the study. Neonates admitted to the Neonatal Intensive Care Unit (NICU) during the study period;

Exclusion criteria

Neonates with congenital anomalies or known chromosomal disorders, Neonates with terminal illness, neonates receiving medications that could affect thyroid function (e.g., dopamine, steroids, amiodarone), neonates with active infection/sepsis during the study period.

Data collection procedure

The legal guardians or parents of neonates were invited to participate in the current study. Written consent was obtained after explaining the study procedure. This cross-sectional study used a structured questionnaire to gather relevant data. The questionnaire included variables such as age, sex, clinical presentation, and laboratory findings (serum FT4 and TSH levels). Gestational age was assessed using the Ballard scoring system. Data were collected through face-to-face interviews with mothers of preterm neonates. Clinical and demographic information was recorded on a pre-designed data sheet, which was securely stored and maintained throughout the study.

Sample collection

Approximately 2 ml of venous blood was drawn from the antecubital vein of each preterm neonate between days 5 and 20 of life. Blood samples were collected without the use of anticoagulants and were sent to the Microbiology Department of the Armed Forces Institute of Pathology for analysis.

Serum FT4 and TSH levels were measured using direct chemiluminometric technology. A TSH level ≥10 µIU/mL was considered elevated. The normal reference ranges for serum FT4 were defined based on gestational age as GA 28–31 weeks: 6.3±2.0 mcg/dl. GA 32–34 weeks: 7.6±2.3 mcg/dl. GA 35–37 weeks: 9.2±1.9 mcg/dl.

Statistical analysis

All data were recorded systematically in a pre-formatted data collection form. Quantitative data was expressed as mean and standard deviation, and qualitative data was expressed as frequency distribution and percentage. The data were analyzed using SPSS 15 (Statistical Package for Social Sciences) for Windows version 10. This study was ethically approved by the Institutional Review Committee of Combined Military Hospital, Dhaka, Bangladesh.

RESULTS

Table 1 demonstrates the mean age of the neonates at the time of sample collection was 5.38±2.66 days, with a

range from 5 to 20 days. The average body length was 43.12±2.77 cm, ranging from 34.0 to 47.0 cm. The mean birth weight was 1932±284 grams, with values ranging between 1300 and 2400 grams. The mean occipitofrontal circumference (OFC) was 31.42±2.70 cm, ranging from 20.0 to 34.0 cm. The mean gestational age of the neonates was 34.06±1.81 weeks, with a minimum of 28 weeks and a maximum of 36 weeks.

Of the total 50 neonates, 27 (54.0%) were males and 23 (46.0%) were females. The male-to-female ratio was 1:0.85 in this study (Figure 1). Figure 2 illustrates the distribution of neonates based on the maternal history of thyroid disorders. Among the 50 neonates studied, 4 (8.0%) had mothers with a known history of thyroid disorder, while 46 (92.0%) had no such maternal history.

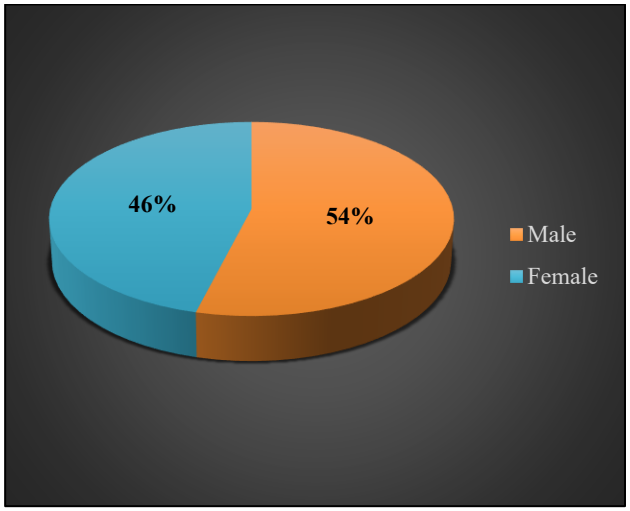

Figure 1: Distribution of neonates by sex.

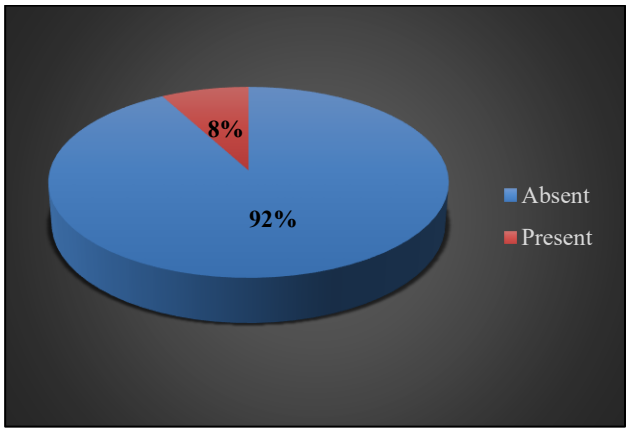

Figure 2: Neonates with maternal history of thyroid disorder.

Table 2 shows that among the 50 preterm neonates included in the study, the majority were within the gestational age range of 32 to 34 weeks, accounting for 25 cases (50%). This was followed by 23 neonates (46%) in the 35 to 37 weeks group. The smallest group consisted of neonates between 28 to 31 weeks, comprising only 2 cases (4%).

This distribution indicates that most of the preterm neonates in this study were of moderate to late preterm gestational age. Table 3 presents the mean±standard deviation (SD) of serum TSH and FT4 levels among preterm neonates, categorized by gestational age. For neonates born between 28 to 31 weeks, the mean serum TSH level was 6.95±2.04 mU/l (range: 5.51–8.40 mU/l), and the mean serum FT4 level was 8.20±0.00 mcg/dl (range: 8.20–8.20 mcg/dl).

Among those born between 32 to 34 weeks, the mean TSH was 4.77±2.88 mU/l (range: 2.20–10.00 mU/l), and the mean FT4 was 8.34±1.16 mcg/dl (range: 6.80–10.50 mcg/dl). In neonates of 35 to 37 weeks gestation, the mean TSH was 4.81±2.63 mU/l (range: 1.63–10.70 mU/l), and the mean FT4 was 8.49±0.83 mcg/dl (range: 7.27–9.90 mcg/dl).

Table 1: Baseline characteristics of our study neonates (n=50).

Baseline characteristics	Mean±SD	Range
Age (days)	05.38±2.66	5-20
Length (cm)	43.12±2.77	34.00-47.00
Weight (gm)	1932±284	1300-2400
OFC (cm)	31.42±2.70	20.00-34.00
Gestational age (Weeks)	34.06±1.81	28-36

Table 2: Distribution of study participants by gestational age (GA).

GA (weeks)	Frequency	%
28-31	2	4
32-34	25	50
35-37	23	46

Table 3: Mean±SD of serum TSH and FT4 levels of the preterm neonates.

GA group in weeks	S. TSH level (mU/l)	S. FT4 Level (mcg/dl)
	Mean±SD (Min-Max)	**Mean±SD (Min-Max)**
28-31	6.95±2.04 (5.51-8.40)	8.20±0.00 (8.20-8.20)
32-34	4.77±2.88 (2.20-10.00)	8.34±1.16 (6.80-10.50)
35-37	4.81±2.63 (1.36-10.70)	8.49±0.83 (7.27 - 9.90)

DISCUSSION

Preterm birth remains a significant public health issue in Bangladesh, with a high incidence rate contributing to various short and long-term health complications.

Premature neonates are particularly vulnerable to a range of developmental disorders, including cognitive impairments, behavioral issues, cerebral palsy, and sensory deficits such as vision and hearing loss. Some studies have even linked preterm birth to an increased risk of autism spectrum disorder later in life.[14] Survival rates among preterm neonates can vary widely depending on several factors, including birth weight, sex, antenatal corticosteroid administration, and whether the birth was singleton or multiple.[15] Furthermore, emerging evidence indicates that those born very prematurely may face an increased risk of chronic adult conditions such as diabetes, hypertension, and cardiovascular diseases.[16] In the current study, 50 preterm neonates were evaluated to assess the prevalence of congenital hypothyroidism. The sample comprised 27 males (54%) and 23 females (46%), resulting in a male-to-female ratio of 1:0.85, which aligns with findings from similar studies on neonatal thyroid screening. For example, a study involving 300 healthy, full-term neonates reported a nearly equal male-to-female ratio of 1.1:1 in their study.[17]

The mean gestational age of neonates in our study was 34.06±1.81 weeks, with an average birth weight of 1932±284 grams. The mean age at the time of sample collection was 5.38±2.66 days. Of the 50 neonates, only 4 (8%) had a maternal history of thyroid disorder, suggesting that most cases were not directly associated with maternal thyroid dysfunction. Thyroid hormone levels were stratified by gestational age. The mean serum TSH and FT4 levels remained within normal reference ranges across all groups. The highest mean TSH level (6.95±2.04 mU/l) was observed in neonates between 28 to 31 weeks of gestation, while the lowest (4.77±2.88 mU/l) was in those aged 32 to 34 weeks. Only one neonate had a TSH level slightly above the cutoff point (10.70 mU/l), yet with a normal FT4 level, and did not meet the criteria for congenital hypothyroidism.

These findings are consistent with previous research suggesting that the current TSH cutoff threshold plays a critical role in diagnosing CH. A prospective study of 311,390 newborns conducted by Mengreli et al highlighted the impact of lowering the TSH screening cutoff from 20 to 10 mU/l for detecting CH. They found that 28% of CH cases had TSH levels between 10 and 20 mU/l. Among 47 infants who underwent reevaluation, 40 (85.1%) were found to have persistent congenital hypothyroidism.[18] Freire et al conducted a longitudinal study on 178 children in Spain to assess whether neonatal TSH levels are linked to later cognitive outcomes. Higher cord blood TSH levels were associated with lower scores in general cognition and executive function at age 4, even after adjusting for maternal and environmental factors. Children with the highest TSH levels had an increased risk of poor memory performance, suggesting that even subtle thyroid dysfunction at birth may affect neurodevelopment.[19] Hertzberg et al analyzed data from U.S. newborn screening programs between 1991 and 2000 and found that TSH-based screening detected 24% more cases of congenital hypothyroidism than FT4-based screening. Changes in assay methods, especially a shift from RIA to EIA or FIA, also influenced CH detection rates. However, even after accounting for screening changes, CH incidence continued to rise, indicating other unidentified contributing factors.[20]

A study by Kramer et al evaluated the risk of false negatives in TSH-based CH screening. Among 190 newborns with borderline TSH levels (15–20 IU/l), four were later diagnosed with CH, including three with thyroid dysgenesis. The study concluded that repeating TSH testing around 30 days of age for borderline cases can reduce false negatives without significantly increasing costs.[21] Another study found that in some preterm infants, TSH concentrations fluctuated between the initial sample (around day 5 of life) and a follow-up sample taken at around 36 weeks corrected gestational age. While some TSH values dropped below the screening threshold over time, others rose, emphasizing the complexity of thyroid hormone dynamics in preterm neonates. Their findings also suggest that repeat testing may not be necessary in all cases if a lower TSH threshold (e.g., 6 mU/l) is adopted, although this must be balanced against the increase in recall rates and associated healthcare costs.[2]

Furthermore, research evaluating the relationship between gestational age and thyroid function in preterm neonates found no significant difference in FT4 levels between healthy and ill neonates under 32 weeks. However, neonates with bronchopulmonary dysplasia (BPD) had significantly lower FT4 levels than controls ($p<0.01$). The reported reference range of FT4 for neonates aged 32 to 36 weeks was 5.56 to 15.58 mcg/dl, with a mean of 9.82±0.40 mcg/d.[14] Overall, these findings underscore the importance of adjusting TSH thresholds and considering repeat screening protocols in preterm populations to ensure timely diagnosis and management of congenital hypothyroidism.

The study was a single-center study, so it may not be representative of the whole country. We took a small sample size due to the short study period. After evaluating those neonates, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these neonate patients.

CONCLUSION

In this NICU-based study, our findings indicate no confirmed cases of congenital hypothyroidism among the preterm neonates studied, though the presence of a borderline elevated TSH in one case highlights the need for careful follow-up. Given the developmental importance of thyroid hormones, especially in the early neonatal period, routine screening and possibly lowering the TSH threshold could help identify and manage CH earlier, particularly in preterm populations at higher risk.

Early diagnosis and timely treatment of thyroid dysfunction in preterm infants are crucial for ensuring normal linear growth and cognitive development. As delayed intervention can reduce intelligence, making speech delays, and other developmental challenges, so routine thyroid screening for all preterm newborns should be strongly recommended.

Recommendations

Further multicentre studies with larger sample sizes need to be done for the early detection of congenital hypothyroidism and to improve long-term neurodevelopmental outcomes in preterm neonates.

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