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Relationship Neonatal Hyper Bilirubinaemia with TSH -An Observational Study

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ABSTRACT

Background: Neonatal hyperbilirubinemia is a frequent clinical condition in the early neonatal period and remains a major cause of hospital readmission. While most cases are physiological, prolonged or severe jaundice may indicate underlying systemic disorders, including congenital hypothyroidism, which affects bilirubin metabolism through delayed hepatic maturation. **Objective:** To evaluate the relationship between neonatal serum total bilirubin levels and thyroid function parameters, specifically thyroid-stimulating hormone (TSH) and free thyroxine (FT4), in full-term neonates with hyperbilirubinemia. **Methodology:** This observational study was conducted in the Department of Pediatrics, Dhaka Shishu (Children) Hospital and Institute (DSH&I). A total of 120 full-term neonates with clinical features of hyperbilirubinemia were enrolled. Serum total bilirubin was measured using the Grot–Jendrassik method, while FT4 and TSH levels were assessed by chemiluminescence immunoassay. Data were analyzed using SPSS version 25. Pearson's correlation coefficient was used to assess the relationship between bilirubin and thyroid hormone levels, with $p < 0.05$ considered statistically significant. **Results:** The mean serum bilirubin level was 11.21 ± 3.08 mg/dL, mean TSH was 3.38 ± 3.57 μIU/mL, and mean FT4 was 1.27 ± 1.11 ng/dL. Serum bilirubin showed a significant positive correlation with TSH ($r = 0.626$, $p < 0.001$) and a significant negative correlation with FT4 ($r = -0.594$, $p < 0.001$). **Conclusion:** The study demonstrates a significant association between thyroid dysfunction and neonatal hyperbilirubinemia, highlighting the importance of thyroid function evaluation in jaundiced neonates for early diagnosis and management.

Keywords: Neonatal Hyperbilirubinemia, TSH, FT4, Congenital Hypothyroidism, Neonatal Jaundice.

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INTRODUCTION

Neonatal hyperbilirubinemia is a common clinical condition observed during the early neonatal period, affecting approximately 60–80% of newborns within the first week of life [1, 2]. Clinically, hyperbilirubinemia manifests as jaundice when serum bilirubin levels exceed 5 mg/dL, resulting in yellow discoloration of the skin, sclera, and mucous membranes [3, 4]. Although neonatal jaundice is often physiological and self-limiting, severe or prolonged hyperbilirubinemia may lead to serious complications, including bilirubin-induced neurological dysfunction and kernicterus, which can cause irreversible

neurodevelopmental impairment [5]. Hyperbilirubinemia is the leading cause of hospital readmission among term neonates and imposes a significant global healthcare burden [1]. While well-recognized causes include hemolytic disease, prematurity, breastfeeding jaundice, and infections, nearly half of pathological cases lack a clearly identifiable etiology, complicating prevention and early intervention strategies [6]. These unexplained cases contribute to increased healthcare costs, parental anxiety, and neonatal morbidity. Consequently, identifying underlying systemic and endocrine contributors to neonatal hyperbilirubinemia remains a clinical priority. Thyroid hormones play a critical role in hepatic maturation and bilirubin metabolism. Congenital hypothyroidism (CH), resulting from inadequate thyroid hormone production at birth, has been recognized as an important but often overlooked cause of prolonged neonatal hyperbilirubinemia Dwijayanti *et al.*, [7]. Thyroxine deficiency delays the maturation of hepatic uridine diphosphate glucuronyl transferase (UDPGT), the key enzyme responsible for bilirubin conjugation, leading to impaired bilirubin clearance and prolonged unconjugated hyperbilirubinemia [2]. Although the incidence of congenital hypothyroidism is estimated to be approximately 1 in 2,000–4,000 live births globally, clinical manifestations such as prolonged jaundice may precede definitive diagnosis in the absence of early screening [8]. In neonates, unconjugated hyperbilirubinemia may arise from increased red blood cell breakdown, reduced hepatic uptake, or defective bilirubin conjugation [9, 10]. Conditions such as hemolytic disorders, glucose-6-phosphate dehydrogenase deficiency, urinary tract infections, and genetic syndromes—including Crigler-Najjar and Gilbert syndromes—must be differentiated from endocrine causes such as congenital hypothyroidism [8]. Early identification of hypothyroidism-related hyperbilirubinemia is particularly important, as timely thyroid hormone replacement can prevent long-term neurodevelopmental consequences. Given the physiological relationship between thyroid hormones and bilirubin metabolism, evaluation of thyroid function parameters—namely thyroxine (T4) and thyroid-stimulating hormone (TSH)—in neonates with hyperbilirubinemia may provide valuable diagnostic insight. Therefore, the present study was designed to investigate the relationship between neonatal total serum bilirubin levels and thyroid function parameters (T4 and TSH), aiming to clarify the role of congenital hypothyroidism in neonatal hyperbilirubinemia and support earlier diagnosis and targeted management.

METHODOLOGY

This observational study was conducted in the Department of Pediatrics, Dhaka Shishu (Children) Hospital and Institute (DSH&I), after obtaining approval from the Institutional Ethical Committee. A total of 120 full-term neonates with normal birth weight who presented with clinical features of hyperbilirubinemia were enrolled. Blood samples were collected to estimate serum total bilirubin, free thyroxine (FT4), and thyroid-stimulating hormone (TSH) levels. Total serum bilirubin was measured using the Grot–Jendrassik method on a BS-400 autoanalyzer, while FT4 and TSH were analyzed by the chemiluminescence immunoassay method. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 25. Data were expressed as mean ± standard deviation, and the relationship between serum bilirubin and thyroid hormone levels was assessed using Pearson's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1: Demographic Characteristics of The Study Subject (n = 120)

Variable	Frequency (n)	Percentage (%)
Age (days)		
2–4 days	74	62.0
5–7 days	46	38.0
Gender		
Male	67	56.0
Female	53	44.0
Blood Group		

A	28	23.0
B	31	26.0
O	47	39.0
AB	14	12.0
Rhesus Factor		
Positive	119	99.0
Negative	1	1.0
TSH Level		
Normal	99	82.5
Borderline	0	0.0
Hypothyroid	21	17.5
Total Bilirubin		
Normal	62	52.0
High	58	48.0

Among the 120 study subjects, most were aged 2–4 days (62%) and were male (56%). Blood group O (39%) was the most common, and 99% were Rh positive. The majority had normal TSH levels (82.5%), while 17.5% were hypothyroid. Elevated total bilirubin was observed in 48% of the subjects.

Table 2: Descriptive Statistics of Biochemical Parameters among The Study Subjects (n = 120)

	Mean ±SD	Range (min-max)
TSH	3.38 (±3.57)	0.10-12.88
Bilirubin	11.21 (±3.08)	6.44-17.90
FT4	1.27 (±1.11)	0.15-4.50

The mean serum TSH level of the study subjects was 3.38 ± 3.57 µIU/mL, with values ranging from 0.10 to 12.88 µIU/mL. Mean total serum bilirubin was 11.21 ± 3.08 mg/dL, and the observed range was 6.44–17.90 mg/dL. The mean FT4 level was 1.27 ± 1.11 ng/dL, with a minimum value of 0.15 ng/dL and a maximum of 4.50 ng/dL.

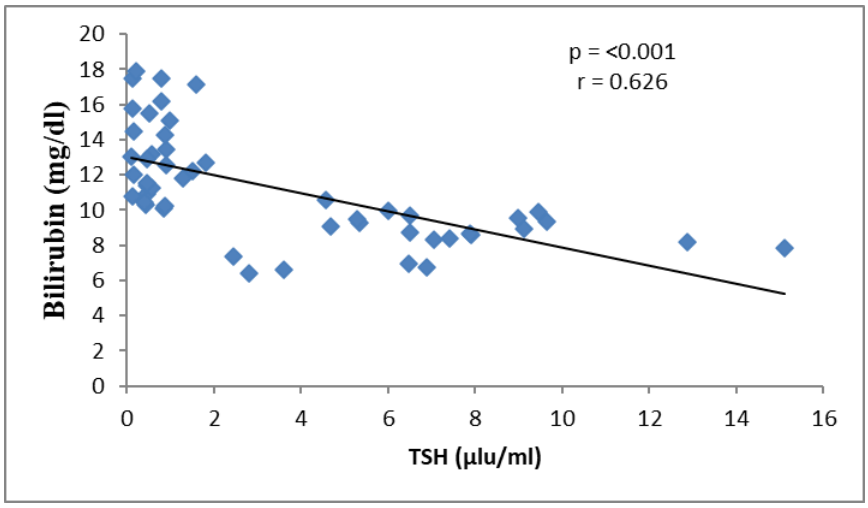

Figure 1: Correlation Between TSH and Serum Bilirubin

The scatter plot illustrates the relationship between serum TSH (µIU/ml) and serum bilirubin levels (mg/dl). A statistically significant correlation is observed between the two variables ($r = 0.626$, $p < 0.001$). The

regression line demonstrates a clear linear association, indicating that variations in TSH levels are significantly associated with corresponding changes in serum bilirubin levels. This finding suggests a meaningful relationship between thyroid function and bilirubin metabolism in the studied population (Figure 1).

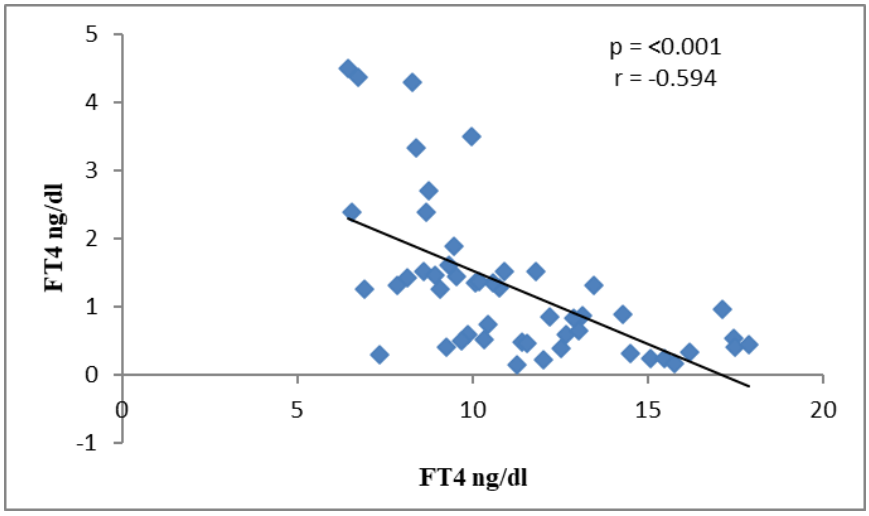

Figure 2: Correlation Between Serum Bilirubin and FT4

Serum bilirubin showed a moderate to strong negative correlation with FT4 levels ($r = -0.594$, $p < 0.001$). This result indicates that higher FT4 levels are significantly associated with lower serum bilirubin concentrations. The correlation was statistically significant at the 0.01 level (2-tailed) Figure 2.

DISCUSSION

The present observational study evaluated the relationship between neonatal hyperbilirubinemia and thyroid function parameters among 120 full-term newborns. Most neonates were aged 2–4 days (62%), with a male predominance (56%), findings that are consistent with previously published studies. Alizah *et al*., reported a similar age distribution, with 62% of neonates presenting between 2–4 days of life and a comparable male predominance (56%) [11]. Arshad *et al*., also observed that the majority of both diseased and control neonates were within the first week of life, supporting the notion that early neonatal days are critical for the manifestation of hyperbilirubinemia [12]. Male predominance observed in this study aligns with findings by Alizah *et al*., and Nurani *et al*., who reported that male neonates have a higher likelihood of developing hyperbilirubinemia [9, 11]. Gender has been considered a potential risk factor, possibly due to differences in hepatic enzyme maturity and bilirubin metabolism between male and female neonates [9]

Regarding thyroid status, the majority of neonates in the present study had normal TSH levels, while 21 cases were hypothyroid, with no borderline cases observed. In contrast, Alizah *et al*., reported only one borderline TSH case among 100 neonates, with the remaining 99% showing normal TSH levels [11]. This variation may be attributed to differences in sample size, population characteristics, and timing of thyroid function assessment. Physiological postnatal TSH surge shortly after birth is well documented and may lead to transient elevations, which usually normalize within one to two weeks [13, 14]. In the present study, mean serum TSH was 3.38 ± 3.57 μIU/mL, mean total bilirubin was 11.21 ± 3.08 mg/dL, and mean FT4 was 1.27 ± 1.11 ng/dL. Comparable biochemical profiles have been reported by Sivakumar et al., who demonstrated higher bilirubin levels in neonates with altered thyroid parameters [2]. Kayıran *et al*., also reported similar mean bilirubin and thyroid hormone levels, though their study demonstrated a weaker correlation between TSH and bilirubin [15]. A key finding of this study is the significant positive correlation between serum TSH and total bilirubin levels ($r = 0.626$, $p < 0.001$), suggesting that higher TSH levels are associated with increased bilirubin concentrations. This observation is consistent with findings by Arshad *et al*., who

demonstrated a significant positive relationship between TSH and total as well as indirect bilirubin levels in hypothyroid neonates [12]. Similarly, Sivakumar *et al*., reported a significant association between bilirubin and TSH levels, reinforcing the role of thyroid hormones in bilirubin metabolism [2].

Additionally, the present study demonstrated a moderate to strong negative correlation between serum bilirubin and FT4 levels ($r = –0.594$, $p < 0.001$), indicating that lower FT4 levels are associated with higher bilirubin concentrations. This finding supports the hypothesis that reduced thyroid hormone activity impairs hepatic glucuronyl transferase activity, leading to decreased bilirubin conjugation and increased unconjugated hyperbilirubinemia [7, 16]. Arshad *et al*., further emphasized that thyroid dysfunction primarily affects unconjugated bilirubin metabolism due to impaired hepatic conjugation, a mechanism that explains the persistence or severity of neonatal jaundice in hypothyroid states [12]. These findings highlight the importance of early thyroid screening in neonates presenting with significant or prolonged hyperbilirubinemia. Overall, the findings of the present study are in agreement with existing literature and support a meaningful association between thyroid function and neonatal bilirubin metabolism. Early recognition of thyroid dysfunction in jaundiced neonates may facilitate timely intervention, potentially reducing jaundice-related morbidity, unnecessary phototherapy, and prolonged hospitalization.

CONCLUSION

This study demonstrates a significant association between neonatal hyperbilirubinemia and thyroid function abnormalities. A positive correlation between serum bilirubin and TSH levels, along with a negative correlation between bilirubin and FT4 levels, indicates that reduced thyroid hormone activity contributes to impaired bilirubin metabolism in neonates. These findings emphasize the importance of routine evaluation of thyroid function in newborns presenting with significant or prolonged jaundice. Early identification and timely management of underlying thyroid dysfunction may help prevent unnecessary interventions, reduce jaundice-related morbidity, and improve long-term neurodevelopmental outcomes.

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