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Neonatal Outcomes and Anomalies in Mothers with Hypothyroidism

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Abstract **Original Research Article**

Background: Maternal thyroid hormone is the main source of thyroxine for the fetus during the first half of pregnancy and its deficiency has been linked to preterm birth, low birth weight and adverse neurodevelopment. Data on neonatal outcomes among treated hypothyroid mothers in Bangladesh are scarce. Local data are therefore needed to guide antenatal thyroid care. ***Objective:*** To detect neonatal outcomes and congenital anomalies among infants born to mothers diagnosed with hypothyroidism at the Maternal and Child Health Training Institute (MCHTI), Dhaka, Bangladesh. ***Methods:*** This retrospective observational study, conducted from January 2022 to December 2024 at MCHTI and Ibn Sina Diagnostic & Consultation Center (Badda), Dhaka, reviewed records of 100 neonates of mothers with overt or subclinical hypothyroidism (TSH 2.5 to 10 mIU/L with normal free thyroxine) receiving levothyroxine. Mothers with chronic hypertension, pre-existing diabetes, autoimmune disease, high-risk pregnancy or fetal anomaly on ultrasound were excluded. Data were analysed descriptively using SPSS version 25.0. ***Results:*** Most mothers had subclinical hypothyroidism. TSH was measured before conception in 21%, in the first trimester in 36%, in the second in 30% and in the third in 13%. Neonatal jaundice was the most frequent outcome (80%), followed by low birth weight (29%), preterm birth (21%), respiratory distress syndrome (11%) and neonatal intensive care unit admission (10%). Hypoglycaemia occurred in 5% and congenital anomalies in 2%. Gestational hypertension (10%), postpartum haemorrhage (3%), preeclampsia (2%) and psychosis (1%) occurred among mothers. ***Conclusion:*** Maternal hypothyroidism was accompanied by frequent neonatal jaundice, low birth weight and preterm birth. Early diagnosis and regular trimester-wise thyroid monitoring are recommended.

Keywords: Maternal hypothyroidism; neonatal outcomes; low birth weight; preterm birth.

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INTRODUCTION

Thyroid dysfunction is among the commonest endocrine disorders of pregnancy and hypothyroidism in particular demands careful antenatal attention. Overt hypothyroidism is characterised by raised TSH with low free thyroxine, whereas subclinical hypothyroidism shows raised TSH with normal free thyroxine. Reported prevalence varies widely because diagnostic criteria, iodine status and gestational age at screening differ between studies [1]. Current guidance recommends trimester-specific reference ranges for thyroid-stimulating hormone (TSH) and levothyroxine treatment when indicated [2]. Pregnancy alters thyroid physiology considerably and approaches to diagnosis and management have changed substantially in recent years [3].

Thyroid hormones are indispensable for fetal development. The fetal thyroid gland is not fully functional until about 18 to 20 weeks of gestation, so early neuronal migration and other crucial stages of intrauterine brain development depend on maternal thyroxine [4]. In a population-based cohort, both low and high maternal free thyroxine concentrations were associated with lower child intelligence quotient and reduced cortical grey matter volume [4]. Meta-analytic evidence also links maternal subclinical hypothyroidism and hypothyroxinaemia with intellectual disability in offspring and maternal hypothyroidism with attention deficit hyperactivity disorder, autism spectrum disorder and epilepsy [5,6].

Maternal thyroid dysfunction also affects perinatal outcomes. An individual participant data meta-analysis of 19 cohorts showed that subclinical hypothyroidism was associated with a higher risk of

preterm birth [7]. Another meta-analysis of 48,145 mother and child pairs reported an inverse dose-response association between maternal TSH and birth weight, with subclinical hypothyroidism linked to lower birth weight and small-for-gestational-age infants [8]. A Chinese retrospective cohort of 8,985 mother and child dyads found a 2.01-fold higher risk of low birth weight when maternal TSH exceeded 4.0 mIU/L [9]. Because adverse birth outcomes influence both the short- and long-term health of children, these associations carry real clinical weight [9].

Registry data illustrate the influence of treatment. In a Finnish nationwide cohort of 16,364 hypothyroid mothers, adverse perinatal outcomes were more frequent, yet many associations disappeared among women who purchased levothyroxine consistently [10]. Hypothyroidism has also been linked with a modestly higher risk of major congenital malformations in offspring [11].

Regional evidence on neonatal outcomes remains limited. A tertiary centre study from Pakistan reported neonatal jaundice in 37.6% of 662 live births to hypothyroid mothers, with low birth weight and congenital anomalies significantly associated with a diagnosis made before pregnancy [12]. In Bangladesh, a hospital-based cross-sectional study of 252 women estimated the prevalence of overt and subclinical hypothyroidism at 3.2% and 5.2% and found low birth weight and neonatal hypothyroidism to be more common among affected women [13].

However, information on the full spectrum of neonatal outcomes, including congenital anomalies, among mothers diagnosed with hypothyroidism in Dhaka remains sparse and the pattern of thyroid function monitoring during pregnancy is rarely described. Documenting these outcomes can inform antenatal counselling, monitoring schedules and neonatal care planning. This study therefore aimed to detect neonatal outcomes and congenital anomalies among infants born to mothers diagnosed with hypothyroidism at MCHTI, Dhaka. Such local evidence is essential for refining antenatal thyroid care and counselling.

MATERIALS AND METHODS

This retrospective observational study was conducted at the Maternal and Child Health Training Institute (MCHTI) and Ibn Sina Diagnostic & Consultation Center (Badda), Dhaka, Bangladesh, from January 2022 to December 2024. It included neonates born to mothers with hypothyroidism, with a total sample size of 100.

Inclusion criteria

1. Overt or subclinical hypothyroidism (TSH 2.5 to 10 mIU/L with normal FT4), diagnosed before or during pregnancy
2. Levothyroxine therapy ongoing or newly started
3. Live-born neonates with available records

Exclusion criteria

1. Chronic hypertension
2. Pre-existing diabetes mellitus
3. Autoimmune disease
4. High-risk pregnancy
5. Fetal anomaly detected on ultrasound screening

Data collection procedure

Data were extracted retrospectively from maternal antenatal and delivery records and neonatal case files using a structured data collection form. Maternal variables included the type and timing of diagnosis, levothyroxine therapy and the timing of TSH measurement (preconception, first, second or third trimester). Neonatal variables included gestational age at birth, birth weight, neonatal jaundice, respiratory distress syndrome, neonatal intensive care unit (NICU) admission, hypoglycaemia and congenital anomalies identified at birth or on neonatal examination. Neonatal TSH values measured on the second or third day of life were recorded where available. Maternal outcomes, namely gestational hypertension, preeclampsia, postpartum haemorrhage, placental abruption, deep vein thrombosis, pulmonary embolism, psychosis and postpartum thyroiditis, were collected from the same records. Preterm birth was defined as delivery before 37 completed weeks and low birth weight as a birth weight below 2,500 g. Neonatal outcomes were not mutually exclusive. Only neonates meeting the selection criteria were analysed. Records were reviewed by the investigators after the study period and data were entered into a spreadsheet and checked for completeness before analysis. To promote accuracy and consistency, diagnoses and outcomes were taken from laboratory reports and clinical documentation, uniform definitions were applied to all records and entries with missing or conflicting information were verified against delivery registers and neonatal files. The study was carried out under the supervision of a consultant at MCHTI. Confidentiality was maintained by assigning each patient a code and removing identifying information at admission and the coded data were stored securely with access restricted to the research team.

Statistical analysis

Data were entered and analysed using the Statistical Package for the Social Sciences (SPSS) version 25.0. As the study aimed to describe outcomes, descriptive statistics were applied. Categorical variables, including timing of TSH measurement, neonatal outcomes and maternal outcomes, were summarised as frequencies and percentages and presented in tables. Missing data were not imputed and no inferential testing was performed.

RESULTS

A total of 100 mothers with hypothyroidism and their 100 live-born neonates were included. Most mothers had subclinical hypothyroidism and the diagnosis was commonly made before pregnancy; nearly two-thirds of the mothers presented during the first trimester. Neonatal jaundice (80%), low birth weight (29%) and preterm birth (21%) were the most frequent neonatal outcomes, whereas congenital anomalies were uncommon (2%). Gestational hypertension was the commonest maternal complication (10%).

Table 1 presents the timing of TSH measurement among the 100 mothers. TSH was recorded before conception in 21 mothers (21.0%) and in the first trimester in 36 (36.0%). It was recorded in the second trimester in 30 mothers (30.0%) and in the third trimester in 13 (13.0%).

Table 1: Timing of TSH measurement (n = 100)

Timing of TSH measurement	Frequency (n)	Percentage (%)
Preconception	21	21.0
First trimester	36	36.0
Second trimester	30	30.0
Third trimester	13	13.0
Total	100	100.0

Table 2 describes neonatal outcomes among the 100 live-born neonates. Neonatal jaundice was the most frequent outcome, occurring in 80 neonates (80.0%), followed by low birth weight in 29 (29.0%) and preterm birth in 21 (21.0%). Respiratory distress syndrome affected 11 neonates (11.0%) and 10 (10.0%) required NICU admission. Hypoglycaemia was reported in five neonates (5.0%) and congenital anomalies in two (2.0%). Outcomes were not mutually exclusive.

Table 2: Neonatal outcomes among live-born neonates (n = 100)

Neonatal outcome	Frequency (n)	Percentage (%)
Neonatal jaundice	80	80.0
Low birth weight	29	29.0
Preterm birth	21	21.0
Respiratory distress syndrome	11	11.0
NICU admission	10	10.0
Hypoglycaemia	5	5.0
Congenital anomalies	2	2.0

Note: Neonatal outcomes were not mutually exclusive; a neonate could have more than one outcome. NICU, neonatal intensive care unit.

Table 3 shows maternal outcomes. Gestational hypertension occurred in 10 mothers (10.0%), postpartum haemorrhage in three (3.0%), preeclampsia in two (2.0%) and psychosis in one (1.0%). No cases of placental abruption, deep vein thrombosis or pulmonary embolism were reported. The frequency of postpartum thyroiditis was not reported.

Table 3: Maternal outcomes (n = 100)

Maternal outcome	Frequency (n)	Percentage (%)
Gestational hypertension	10	10.0
Postpartum haemorrhage	3	3.0
Preeclampsia	2	2.0
Psychosis	1	1.0
Placental abruption	0	0.0
Deep vein thrombosis	0	0.0
Pulmonary embolism	0	0.0
Postpartum thyroiditis	Not reported	Not reported

DISCUSSION

In this retrospective study of 100 neonates born to mothers with hypothyroidism, neonatal jaundice, low birth weight and preterm birth were the most frequent adverse outcomes. Jaundice affected 80% of neonates, a considerably higher proportion than the 37.6% reported by Kiran *et al.,* among 662 live births to hypothyroid mothers in Pakistan [12]. Differences in bilirubin thresholds and the inclusion of mild jaundice may explain part of this gap. This high frequency supports

close postnatal bilirubin surveillance for neonates of hypothyroid mothers.

Low birth weight occurred in 29% of neonates, compared with 21.5% in the series of Kiran *et al.,*[12]. Goit *et al.,*similarly observed that low birth weight was more prevalent among Bangladeshi women with overt or subclinical hypothyroidism [13]. Chen *et al.,*reported a 2.01-fold higher risk of low birth weight when maternal TSH exceeded 4.0 mIU/L [9] and Derakhshan *et al.,*described an inverse dose-response association between maternal TSH and birth weight across 48,145 mother and child pairs [8], consistent with our finding.

Preterm birth was recorded in 21% of neonates, close to the roughly 20.5% obtained when the preterm categories of Kiran *et al.,*are combined [12], but higher than the 12.3% reported by Ferdousi and Baki among 130 hypothyroid mothers in Chattogram [14]. Korevaar *et al.,*showed that subclinical hypothyroidism was associated with a higher risk of preterm birth [7] and Turunen *et al.,*observed excess prematurity that was not evident among mothers who purchased levothyroxine consistently [10]. Ding *et al.,*likewise found a lower risk of preterm birth (odds ratio 0.63) with levothyroxine treatment in subclinical hypothyroidism [15], although Casey *et al.,*found no cognitive benefit in children at five years when treatment began between 8 and 20 weeks [16].

Respiratory distress syndrome occurred in 11% and NICU admission in 10% of neonates, whereas Kiran *et al.,*documented respiratory complications in 8.0% and NICU admission in nearly 15% [12]. Turunen *et al.,*found that NICU admission remained slightly more frequent (odds ratio 1.09) even with consistent levothyroxine use [10] and Maraka *et al.,*reported an association between subclinical hypothyroidism and neonatal death in a meta-analysis [17]. Comparable data on hypoglycaemia (5% here) were scarce.

Congenital anomalies were identified in 2% of neonates. Kiran *et al.,* found a significant association between anomalies and hypothyroidism diagnosed before pregnancy (odds ratio 2.39), with cardiovascular defects most common [12]. Turunen *et al.,* noted a slight excess of malformations in offspring of hypothyroid mothers [10] and Demir *et al.,* cited an adjusted odds ratio of 1.14 for major malformations [11]. The modest frequency here is likely influenced by the exclusion of fetuses with anomalies on screening ultrasound.

Among mothers, gestational hypertension (10%) was the most common complication, followed by postpartum haemorrhage (3%) and preeclampsia (2%). Ferdousi and Baki reported postpartum haemorrhage in 2.3% and preeclampsia in 3.1% [14], resembling our figures. Ding *et al.,* observed a lower risk of gestational hypertension (odds ratio 0.78) with levothyroxine [15], while Maraka *et al.,* found other adverse outcomes similar between the groups compared in 366 women with subclinical hypothyroidism [18]. The absolute frequencies are low, which may reflect the exclusion of mothers with chronic hypertension and high-risk pregnancy.

TSH was recorded before conception in 21% of mothers, in the first trimester in 36%, in the second in 30% and in the third in only 13%. The American Thyroid Association advises reassessment about every four weeks until midgestation and at least once near 30 weeks [2]. Korevaar argues that fixed TSH limits of 2.5 or 3.0 mU/L should give way to population- and trimester-specific ranges [19]. Chen *et al.,*later reported higher low birth weight among infants of thyroid peroxidase antibody positive women despite normal thyroid function [20], suggesting that antibody status may refine risk stratification. Late measurement in a small proportion of pregnancies suggests room to strengthen monitoring schedules.

Offspring may also face risks beyond the neonatal period. Korevaar *et al.,*linked both low and high maternal free thyroxine to lower child IQ [4], Thompson *et al.,*linked subclinical hypothyroidism and hypothyroxinaemia with intellectual disability [5] and Ge *et al.,*reported higher odds of attention deficit hyperactivity disorder, autism and epilepsy [6]. Careful neonatal documentation provides an early basis for follow-up.

LIMITATIONS AND RECOMMENDATIONS

This study has limitations. Its retrospective design, small sample drawn from two centres and absence of a euthyroid comparison group restrict causal inference and generalisability and levothyroxine dose, adherence, thyroid antibody status and long-term outcomes were not analysed. Larger prospective multicentre studies with comparison groups are recommended. Clinicians should ensure preconception counselling, early diagnosis, trimester-wise TSH monitoring, optimised levothyroxine dosing and heightened neonatal surveillance for jaundice, low birth weight and prematurity.

CONCLUSION

In this cohort of neonates born to mothers with hypothyroidism, neonatal jaundice, low birth weight and preterm birth were the most common adverse neonatal outcomes, while respiratory distress syndrome, NICU admission, hypoglycaemia and congenital anomalies occurred less often. Thyroid function was measured late in a notable proportion of pregnancies. Early detection, preconception counselling, regular trimester-wise thyroid monitoring and careful neonatal follow-up are recommended to reduce preventable neonatal morbidity in this setting. These findings support structured clinical thyroid care throughout pregnancy.

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