Medico Research Chronicles
ISSN NO. 2394-3971
DOI No. 10.26838/MEDRECH.2024.11.6.738
Contents available at www.medrech.com

Neonatal Effects of Thyroid Diseases in Pregnancy and Approach to The Infant With Increased TSH in A Tertiary Care Hospital In Dhaka

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ARTICLE INFO | **ABSTRACT** | **ORIGINAL RESEARCH ARTICLE**

Article History
Received: September 2024
Accepted: November 2024
Key Words:
Congenital, hypothyroidism, thyroid diseases, maternal thyroid problems, pregnancy, neonatal outcomes, fetal development, thyroid dysfunction

Background: Thyroid stimulating hormone (TSH) plays a crucial role in embryonic and fetal development from early pregnancy. Both maternal hypothyroidism and hyperthyroidism can significantly impact fetal and neonatal thyroid function, potentially leading to adverse developmental outcomes.
Objective: The aim of this study is to assist pediatricians, neonatologists, and pediatric endocrinologists with the assessment, diagnosis, and treatment of thyroid function disorders and thyroid diseases in the fetus and baby during pregnancy and the neonatal period.
Methods: This prospective cohort study was nested within a larger investigation conducted in Ashiyan Medical College Hospital, Dhaka, Bangladesh.. Pregnant women were recruited between November 2017 and October 2023. Of 1237 invited participants, 266 pregnant women were enrolled, with 4,26 providing blood samples during their first prenatal visit (approximately week 13). Thyroid function was assessed by measuring TSH, free T3 (fT3), and free T4 (fT4) levels across all trimesters.
Results: Mean TSH levels showed a progressive increase across trimesters (first: 1.31±0.51 mU/L; second: 1.67±0.77 mU/L; third: 2.36±0.58 mU/L). Child loss was significantly associated with elevated maternal TSH levels, with 41% experiencing miscarriage, 37% fetal death, and 22% neonatal death. The relationship between TSH levels and adverse outcomes persisted even within the normal reference range and after adjusting for confounding factors including parity, smoking,

diabetes mellitus, and hypertension.
Conclusions: Elevated maternal TSH levels during pregnancy are associated with increased risk of adverse neonatal outcomes, even in women without overt thyroid dysfunction. These findings suggest that maintaining optimal maternal TSH levels throughout pregnancy is crucial for fetal and neonatal well-being, and support considering treatment for women with even mildly elevated TSH levels. Regular thyroid function monitoring during pregnancy may help identify at-risk cases and improve perinatal outcomes.

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2024, www.medrech.com

INTRODUCTION

Beginning in the early stages of pregnancy, thyroid stimulating hormone (TSH) is necessary for a number of embryonic and fetal developmental processes. To generate ideal TSH levels, a fascinating partnership between the mother and her developing child is needed. Maternal TSH has been shown to cross the placenta during pregnancy [1,2,3]. Furthermore, the embryonic thyroid gland produces very little amounts of TH during weeks 10 and 11 of pregnancy. However, the hypothalamus-pituitary-thyroid (HPT) axis must become functioning a few weeks later, at roughly 20 weeks of gestation, before fetal TH production increases. Up until that point, the fetus and embryo rely on trace levels of maternal TSH that are transferred through the placenta [4,5]. Significant evidence suggests that both low and high maternal plasma TH concentrations in the early stages of pregnancy, which most likely result in aberrant embryonic or early fetal TH levels, are linked to compromised neurocognitive function in the child [6,7]. Additionally, aberrant fetal plasma TH concentrations during pregnancy may change the functioning of the postnatal HPT axis both during the neonatal period and for a long time after [8,9,10]. Lower or higher than normal transplacental TH movement and, consequently, lower or higher than normal embryonic/early fetal TSH levels are the results of maternal thyroid dysfunction. Congenital disease is less common than acquired disease, namely thyroid autoimmunity, which can cause maternal hypothyroidism or hyperthyroidism. Thyroid autoantibodies and antithyroid medications taken by the mother to treat hyperthyroidism can also impact (early) fetal and neonatal thyroid function and TSH levels, in addition to disease-related aberrant maternal TSH concentrations affecting embryonic/early fetal TSH levels. Despite the absence of well-designed observational studies on the clinical and developmental outcomes of prenatal and neonatal hyperthyroidism, these disorders are regarded as dangerous due to their significant morbidity and even fatal consequence [11,12,13]. A practical approach to the clinical management of neonates delivered to mothers with thyroid dysfunction is provided by this review, which focuses on the effects of maternal hypo- and hyperthyroidism on the fetus and neonate.

METHODS

A prospective study of pregnant women from this study included our study as a nest inside it. The main objective of this research is to investigate variations in pregnancy outcomes, with a particular emphasis on the effects of mother lifestyle factors, ethnic background, and psychosocial situations on the health of the unborn child and the pregnancy's result. Participants were encouraged to attend their first visit to an obstetric caregiver between November 2017 and October 2023 if they were pregnant and residing in Ashiyan Medical College Hospital,

Dhaka, Bangladesh. Of 1237 invited participants, 266 pregnant women were enrolled, with 4,26 providing blood samples during their first prenatal visit (approximately week 13). These women responded to a survey that asked about their ethnic heritage and social demographic traits. During their initial appointment, which typically occurred in the thirteenth week of pregnancy, included women provided additional informed consent for blood collection. Written informed consent was provided by the participant.

RESULTS

Table I: Characteristics of the respondents n=266.

Variables	n	Mean ±SD	%
Age (year)			
<20	2	3.08±0.33	0.75
21–29	60	1.05±0.16	21
30–39	197	1.31±0.51	74.06
≥40	7		2.63
Parity			
0	7	3.07±0.36	2.63
1	3	1.05±0.16	1.12
2	2	1.67±0.77	0.75

Table II: Distribution of gestational age at deliveries & child loss of the respondents

Variables	n	%
Gestational age at deliveries (weeks)		
<22	2	0.75
22–31	2	0.75
32–36	12	4.51
37+	250	93.98
Child loss		
Miscarriage	109	40.57
Fetal death	98	36.84
Neonatal death	59	22.18

Table III: Distribution of ft3, ft4, TSH Levels in Pregnancy

Parameter	Mean ±SD	2.5 percentile
First trimester		
fT3 (pg/mL)	3.08±0.33	2.47
fT4 (ng/dL)	1.05±0.16	0.8
TSH (mU/L)	1.31±0.51	0.49
Second trimester		
fT3 (pg/mL)	3.07±0.36	2.40
fT4 (ng/dL)	1.05±0.16	0.8
TSH (mU/L)	1.67±0.77	0.51
Third trimester		
fT3 (pg/mL)	3.06±0.34	1.92
fT4 (ng/dL)	1.04±0.16	0.8
TSH (mU/L)	2.36±0.58	0.58

DISCUSSION

This study investigated the relationship between thyroid function (TSH, FT4) and thyroid autoimmunity (TPO-Ab) during pregnancy and the risk of child loss in terms of miscarriage, fetal death, or neonatal mortality. Increasing TSH levels in the early stages of pregnancy was associated with a substantial increase in the chance of child loss. Even after controlling for parity, smoking, diabetes mellitus, hypertension, prior miscarriages or stillbirths, prior preterm births, and the presence of TPO-Ab, this effect persisted. Remarkably, there was no correlation found between these women's FT4 levels and their future risk of losing children. According to our findings, elevated TSH levels during pregnancy are associated with a higher risk of miscarriage, fetal mortality, or neonatal death, even in healthy women without obvious thyroid problems. The link implied a persistent relationship between TSH levels and the chance of child loss, even for pregnant women with TSH levels within the normal range. Allan et al. found that women with a TSH >6 mU/l (2.2% of the study population) were significantly more likely to experience a stillbirth (OR 4.40, 95% CI: 1.9–9.5) [11].

They failed to distinguish between subclinical and overt hypothyroidism. Our results, however, are essentially consistent with their study, even though we looked at the relationship between TSH levels and the chance of child loss continuously and excluded women who had obvious thyroid problems. Casey et al. (2017) found no higher mortality in their comparison of 404 women with subclinical hypothyroidism and a control group of euthyroid women. However, only two fetal and two neonatal deaths were included in their tiny study [13].

Human chorionic gonadotrophin (hCG) may be considered in an attempt to explain the relationship; high hCG is linked to low TSH and high FT4. Miscarriage is indicated by HCG levels, and women who have low hCG levels are far more likely to lose their children. However, in a case-control study, La Marca et al. (1998) shown that TSH levels are positively correlated with miscarriage; this impact was not caused by hCG levels because there was no link between the two [14]. Although we didn't test hCG, we did establish that TSH and child loss are directly related. The study by Casey et al. (2017), which examined maternal hypothyroxinemia, is consistent with our finding that FT4 had no discernible impact on the likelihood of child loss. Low FT4 levels in the context of normal TSH levels did not negatively impact perinatal outcomes, according to their study [13].

According to several studies, women who have TPO-Ab are more likely than those who do not to experience miscarriage (RR ranging from 1.9 to 4.4) [15, 16, 17,18]. In our study, even when taking into account TPO-Ab as a continuous variable, our analysis found no correlation between it and child loss. Lack of power is the reason for the disparity; in our study, only 5.8% of the women had TPO-Ab, and of them, 0% experienced an unfavorable pregnancy outcome.

As we found in our study, the presence of TPO-Ab is linked to elevated TSH and somewhat decreased FT4 levels. Our study's findings are consistent with a decreased incidence of miscarriage through the reduction of TSH exogenous thyroxine. Because TSH is far more sensitive than FT4 levels at detecting even little variations in the hypothalamus-pituitary-thyroid axis's set point, there may not have been a link with FT4 in our study.

Our study's large sample size enabled us to show that maternal TSH concentrations are a risk factor for child loss, with greater TSH levels across the normal range of RR being linked to increased risk. Since active prenatal strategies usually target preventing unfavorable perinatal outcomes, which are uncommon in absolute terms (at least in a developed nation), the slight underlying

increase in absolute risk may have therapeutic implications.

Additionally, it supports the idea that treating women with modestly raised TSH (as in subclinical hypothyroidism) or even those with normal TSH (if TPO-Ab are present) may enhance the outcome of pregnancy.

CONCLUSION

Our study demonstrates that maternal TSH levels during pregnancy significantly influence pregnancy outcomes and neonatal health, with elevated TSH correlating to increased risk of child loss even within normal ranges. This relationship persisted after controlling for confounding factors like parity, smoking, and comorbidities. While TSH showed strong correlations with adverse outcomes, FT4 levels did not demonstrate significant relationships, suggesting TSH as a more sensitive marker for thyroid dysfunction. The progressive increase in TSH levels across trimesters emphasizes the dynamic nature of thyroid function during pregnancy. These findings support the need for regular thyroid monitoring and suggest that treating even mildly elevated TSH levels might improve pregnancy outcomes.

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