Impact of maternal thyroid disorders on maternal and neonatal outcomes in women delivering after 34 weeks of gestation

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ABSTRACT

Introduction: The association of altered thyroid regulation during pregnancy can lead to the development of hypothyroidism or hyperthyroidism, and the resultant thyroid dysfunction ultimately leads to pregnancy-related complications. **Objective:** The objective of this study was to determine the impact of maternal thyroid disorders on maternal and neonatal outcomes in women delivering at/after 34 weeks of gestation. **Methods:** The current study was a prospective observational case–control study done over 6 months. Comparisons were made between the pregnancy-related complications and the neonatal outcomes in 100 dysthyroid mothers with those of 100 euthyroid mothers, delivering at/after 34 weeks of gestation. **Results:** Enrollment of 200 mother-infant dyads, 100 in each group were done. The need for cesarean delivery was higher in hypothyroid patients as they failed induction of labor (36.1%). Among the neonatal outcomes, the hypothyroid patients had a significantly higher incidence of late preterm delivery (31%) and had a higher incidence of small for gestational age infants (32%). Infants of such dysthyroid mothers did not show any significant abnormalities in their thyroid function tests. **Conclusion:** Abnormalities in thyroid function tests remain uncommon in infants born to dysthyroid mothers. Early screening and optimum treatment of thyroid disorders are extremely vital for optimum maternal and neonatal health outcomes. Knowledge of the associated comorbidities such as gestational diabetes, prematurity, growth retardation, and greater need for cesarean births can help to provide better medical care.

Key words: *Dysthyroid, Hyperthyroid, Hypothyroid, Neonatal thyroid function, Preterm*

Thyroid disorders constitute one of the most common endocrine disorders in pregnancy. Pregnancy is associated with profound modifications in the regulation of thyroid function. The modifications driving unstable regulation of thyroid function are increased thyroxine-binding globulin levels due to elevated levels of estrogen and human chorionic gonadotropin, increase in renal losses of iodine is secondary to increased glomerular filtration rate, peripheral metabolism of maternal thyroid hormones, and modification in iodine transfer to the placenta also undergoes alternations in their regulations [1]. In normal pregnant women, the thyroid gland maintains euthyroidism with only minor fluctuations in serum thyroxine (T4) and thyroid-stimulating hormone (TSH). However, in women with limited thyroid reserve, secondary to thyroid autoimmunity, or iodine deficiency, there are significant chances of the development of hypothyroidism.

It is estimated that 10–13% of Indian women are hypothyroid during the course of pregnancy, whereas the occurrence of unconcealed hyperthyroidism is estimated to be around 0.4–1.7% [2]. Thyroid dysfunction in pregnant women at both overt and subclinical levels significantly increases the risks of pregnancy-related complications. Maternal complications include threatened abortion, pre-eclampsia, preterm labor, placental abruption, and postpartum hemorrhage.

Fetal complications include the first-trimester spontaneous abortions, preterm delivery, low birth weight babies, fetal or neonatal hyperthyroidism, intrauterine growth retardation, high rates of stillbirth and neonatal deaths, neonatal hyperbilirubinemia, higher incidence of neonatal hypothyroidism, and an increased perinatal mortality [3]. Hence, understanding the role of maternal thyroid dysfunctions to prevent further maternal and neonatal complications is crucial. The present study aims to study the impact of maternal thyroid dysfunction on maternal and neonatal outcomes in late preterm and term deliveries at a tertiary level hospital in India.

METHODS

The present study was a prospective case–control study done in a tertiary care public hospital in Western India from July 2017 to December 2017. Approval was taken from the ethics review committee of the hospital along with written informed consent from the patients enrolled in the study. The prevalence of thyroid disorders in pregnant women delivering at the current facility was around 10% as this was a tertiary referral hospital. Sampling was done on the principle of convenience sampling as 100 dysthyroid mothers following up at the current antenatal clinic at 34 weeks

of gestation were enrolled. Hundred euthyroid pregnant mothers of the same gestation period were also enrolled in the present study. They were followed up biweekly till they delivered, and the pregnancy outcome and neonatal outcomes were recorded.

Maternal demographic characteristics, medical, reproductive, prenatal history, pregnancy complications such as anemia, abortions, pre-eclampsia, postpartum hemorrhage, and need for cesarean section were recorded. High-risk pregnant women underwent thyroid screening as recommended in the national guidelines and the diagnosis of maternal thyroid disease was established using TSH levels measured during their first antenatal visit for thyroid function test. Classification was done as euthyroid, hypothyroid, and hyperthyroid [4]. The reference range used in the present study was based on the guidelines of the American Thyroid Association (2011) for the diagnosis and management of thyroid disease during pregnancy and postpartum [3]. The trimester specific normal ranges for TSH are 0.1–2.5 mIU/L in the first trimester, 0.2–3 mIU/L in the second trimester, and 0.3–3 mIU/L in the third trimester [1,3].

Baseline neonatal variables were defined using standard definitions and were recorded. The variables included gestational age at delivery, sex, small for gestational age (SGA) status, and neonatal morbidities such as hyperbilirubinemia, respiratory distress syndrome, early-onset sepsis, hypoglycemia, hypocalcemia, perinatal asphyxia, necrotizing enterocolitis (NEC), and intraventricular hemorrhage were recorded.

Neonatal thyroid function (free T4, TSH) was checked after 48 h of life as the center did not have facilities for universal newborn screening. Neonates were classified as euthyroid, hypothyroid, and hyperthyroid based on following gestational age and postnatal days. The specific normal values as under were 1.2–4.4 ng/dl for free T4 and 1.2–21.5 mIU/L at <37 weeks of GA whereas for ≥37 weeks of GA, 5.6 ng/dl for free T4, and 1–10 mIU/L for TSH [5,6].

Infants with abnormal values of TSH underwent a rechecking for thyroid status by 2 weeks of life and were finally classified as euthyroid, hypothyroid, and hyperthyroid as per the American Academy of Pediatricians guidelines [5]. All infants received standard nursing care as per unit protocol. They were followed up daily till death/discharge from unit whichever was earlier, which was proposed as the endpoint of the study.

Obtained information was entered into SPSS version 25 (SPSS Inc., Chicago, Illinois, United States of America). Relevant statistical analysis such as the mean, standard deviation, and frequency tables was calculated for the quantitative and qualitative variables, respectively. Chi-square test was used to compare categorical variables. Continuous variables were analyzed using the ANOVA test. p=0.05 was considered statistically significant.

RESULTS

Four thousand seven hundred and eighty-nine mothers visited the antenatal clinic in the facility for over 6 months of the study period. Enrollment of 100 consecutive dysthyroid mothers at 34 weeks in the study group was done and 100 euthyroid mothers were enrolled at 34 weeks in the control group. Three of these mothers were on pre-existing hypothyroid treatment with levothyroxine while the remaining was diagnosed in the first-trimester screening. Their infants were enrolled in the study after delivery. Mothers were categorized into three groups according to thyroid function test results: 97 were hypothyroid and three were hyperthyroid. Maternal demographic characteristics and morbidities are shown in Table 1.

The mean maternal age was comparable in all three groups (26.64±5.42 years for euthyroid, 27.15±4.33 years for hypothyroid, and 30.33±1.53 years for hyperthyroid mothers, respectively). The mean maternal weight was 48.77±7.32 kg in euthyroid, 50.16±6.96 kg in hypothyroid, and 46.67±6.66 kg in hyperthyroid group, respectively. There was no significant difference in age and weight parameters in the three groups.

Associated maternal morbidities in the hypothyroid group included pre-eclampsia (7.2% vs. 3%; p=0.121) and GDM (11.3% vs. 2%; p=0.026). The need for cesarean delivery was significantly higher in the hypothyroid group (36.1% vs. 19%; p=0.025). The most common indication for cesarean section was the failure of induction of labor. There was no significant difference in the incidence of anemia (53.6% vs. 43%; p=0.279), PPH (3.1% vs. 0%; p=0.198), abortions (17.5% vs. 14%; p=0.559), and MSAF (8.2% vs. 5%; p=0.133). The number of hyperthyroid mothers was very small for any valid comparisons. Mean TSH values were 1.3910±0.290 mIU/L for euthyroid, 4.131±1.455 for hypothyroid, and 0.833±0.208 for hyperthyroid mothers, as shown in Table 1.

Neonatal outcomes in different groups are shown in Table 2. Hypothyroid mothers delivered more often in between 34 and 37 weeks than euthyroid mothers (31% vs. 21%; p=0.03). Hypothyroid mothers also delivered smaller babies: SGA (32% vs. 15%; p=0.01). There was no significant difference in neonatal morbidities such as RDS (4.1% vs. 2%; p=0.651), sepsis (3.1% vs. 2%; p=0.852), hypoglycemia (1% vs. 0%; p=0.586), NEC (1% vs. 0%; p=0.586), TTNB (1% vs. 0%; p=0.586), need for resuscitation (4.1% vs. 4%; p=0.938), perinatal asphyxia (5.2% vs. 1%; p=0.221), and neonatal hyperbilirubinemia (23.7% vs. 19%; p=0.480).

Mean TSH values were 3.437±1.387 mIU/L, 3.949±2.379 mIU/L, and 4.076±1.246 mIU/L for infants of euthyroid, hypothyroid, and hyperthyroid mothers, respectively. Mean T4 values were 1.778±0.079 ng/dl for infants of euthyroid mothers, 1.530±0.535 ng/dl for the baby of hypothyroid mothers, and 1.306±0.1 ng/dl for infants of hyperthyroid mothers. There was no significant difference in the TSH (p=0.17). However, free T4 values did show a significant variation (p=0.015) in the infants born to mothers belonging to the various groups; although none of the babies were rescreened or treated as their individual TSH and free T4 values were within normal ranges.

DISCUSSION

Thyroid disorders are the most common endocrine disorders seen in pregnancy. It is recommended to screen women early in the pregnancy for thyroid dysfunction as these disorders are

Table 1: Maternal demographics, morbidity, and TSH values

Maternal variables	Euthyroid (n=100)	Hypothyroid (n=97)	Hyperthyroid (n=3)	p-value
Age (Mean±SD)	26.64±5.417	27.15±4.333	30.33±1.528	0.368
Weight (Mean±SD)	48.77±7.314	50.16±6.961	46.67±6.658	0.515
Pre-eclampsia	3 (3%)	7 (7.2%)	0	0.121
GDM	2 (2%)	11 (11.3%)	0	0.026
Anemia	14 (14%)	17 (17.5%)	0	0.599
PPH	0	3 (3.1%)	0	0.198
Abortions	14 (14%)	17 (17.5%)	0	0.599
MSAF	5 (5%)	8 (8.2)	1 (33.3%)	0.133
Bad obstetric history	8 (8%)	7 (7.2%)	1 (33.3%)	0.260
Mode of delivery				
ND	81 (81%)	60 (61.9)	3 (100%)	0.025
LSCS	19 (19%)	35 (36.1)	0	
Instrumental delivery	0	2 (2.1%)	0	
TSH (mIU/l)	1.3910±0.290	4.1312±1.455	0.8333±0.208	

GDM: Gestational diabetes mellitus, PPH: Postpartum hemorrhage, MSAF: Meconium-stained amniotic fluid, ND: Normal delivery, LSCS: Lower segment cesarean section, TSH: Thyroid-stimulating hormone

Table 2: Neonatal morbidities and TSH values

Neonatal variables	Euthyroid (n=100)	Hypothyroid (n=97)	Hyperthyroid (n=3)	p-value
Late preterm	21 (21%)	30 (31%)	0	0.03
SGA	15 (15%)	31 (32%)	0	0.01
RDS	2 (2%)	4 (4.1%)	0	0.651
Sepsis	2 (2%)	3 (3.1%)	0	0.852
Hypocalcemia	0	0	0	
Hypoglycemia	0	1 (1%)	0	0.586
NEC	0	1 (1%)	0	0.586
TTNB	0	1 (1%)	0	0.586
Required resuscitation	4 (4%)	4 (4.1%)	0	0.938
Asphyxia	1 (1%)	5 (5.2%)	0	0.221
Jaundice	19 (19%)	23 (23.7%)	0	0.480
TSH (mIU/L)	3.437±1.387	3.949±2.379	4.076±1.246	0.170
Free T4	1.778±0.709	1.530±0.535	1.306±0.100	0.015

SGA: Small for gestational age, RDS: Respiratory distress syndrome, NEC: Necrotizing enterocolitis, TTNB: Transitory tachypnea of newborn, TSH: Thyroid-stimulating hormone

common, treatable and pose a special risk for pregnancy and the developing fetus. Screening for thyroid dysfunction is not only important in pregnant women but also in women who wish to conceive because the status of the regulation of thyroid hormone is directly related to fetal brain development. Thyroid disorders may be overlooked in pregnancy due to non-specific symptoms and hypermetabolic state of pregnancy. Physiological changes occurring during pregnancy can mimic thyroid disease.

The prevalence of thyroid disorders during pregnancy has a wide geographic variation. There is a paucity of data on the prevalence of thyroid disorders in Indian pregnant women; few reports show a prevalence of 10–13% among Indian pregnant populations [2]. Sahu *et al*. have reported a prevalence of hypothyroidism as 6.47% in pregnant women [7]. Ajmani *et al*. reported a prevalence of 12% and 1.25%, respectively, for hypo- and hyper-thyroidism in the pregnant women in his study [8]. The most common cause of hypothyroidism in pregnancy in developing countries like India is iodine deficiency. Hashimoto's thyroiditis is the most common cause of hypothyroidism in iodine-sufficient areas [4].

There were several important observations in the present study. Gestational diabetes commonly coexisted with hypothyroidism (11%). The need for cesarean delivery was higher in hypothyroid patients as they failed induction of labor (36.1%). Among the neonatal outcomes, the hypothyroid patients had a significantly higher incidence of late preterm delivery (31%) and had a higher incidence of SGA in infants (32%). In the study by Ajmani *et al*., the incidences of comorbidities in pregnant women with hypothyroidism such as pre-eclampsia (22.3%), preterm births (33.3%), and SGA (25%) were reported which are non-significant in comparison to the present study [8]. The need for cesarean section (41%) was higher than that found in the present study. Similarly, in the study by Sahu *et al*., the comorbidities in hypothyroid mothers and their infants like pre-eclampsia (9.8%) were higher, but the incidence of preterm delivery (10.3%) and SGA (13.8%) was lower than the population from the present study [7]. Saraladevi *et al*. found that that pre-eclampsia was a common situation in hypothyroid mothers (14.28%), which was higher than the present study, but the incidence of SGA (6.25%) was much lower [9].

Thyroid dysfunction in newborns of dysthyroid mothers was negligible as all babies had normal thyroid hormone levels. Transient thyroid dysfunction up to 8 weeks of age was reported by Ozdemir *et al*. in their study. They also reported a greater incidence of prematurity, respiratory distress, and suspect sepsis in infants born to dysthyroid mothers [10]. Although hyperthyroidism in pregnancy is uncommon, the effects on both mother and child are critical. However, in the present study, authors were unable to derive any significant findings that might have further established the direct link between the regulation of maternal thyroid function and its maternal and neonatal outcomes. Hypothyroidism is a significant comorbidity in high-risk pregnant women which can have a significant impact on maternal and fetal outcomes. One of the major limitations of the present study was the number of hyperthyroid mothers enrolled, which was very small since the disease is comparatively infrequent.

CONCLUSION

Knowledge of the coexisting morbidities such as gestational diabetes, prematurity, growth retardation, and greater need for cesarean births can guide us in handling adverse maternal and neonatal outcomes; however, larger studies are needed for establishing an association between dysthyroidism. Abnormalities in thyroid function tests, however, remain uncommon in infants born to dysthyroid mothers. Early screening and optimum treatment of thyroid disorders are extremely vital for optimum maternal and neonatal health outcomes.

REFERENCES

1. Abalovich M, Amino N, Barbour LA, Cobin RH, De Groot LJ, Glinoer D, *et al.* Management of thyroid dysfunction during pregnancy and postpartum: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2007;92:S1-47.
2. Dhanwal DK, Bajaj S, Rajput R, Subramaniam KA, Chowdhury S, Bhandari R, *et al.* Prevalence of hypothyroidism in pregnancy: An epidemiological study from 11 cities in 9 states of India. Indian J Endocrinol Metab 2016;20:387-90.
3. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, *et al.* Guidelines of the American thyroid association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011;21:1081-125.
4. Arunabh R. National Guidelines for Screening of Hypothyroidism during Pregnancy. India: MoHFW; 2014.
5. Smith L. Practice guidelines: Updated AAP guidelines on newborn screening and therapy for congenital hypothyroidism. Am Fam Phys 2007;76:439-44.
6. Léger J, Olivieri A, Donaldson M, Torresani T, Krude H, van Vliet G, *et al.* European society for paediatric endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. Horm Res Paediatr 2014;81:80-103.
7. Sahu MT, Das V, Mittal S, Agarwal A, Sahu M. Overt and subclinical thyroid dysfunction among Indian pregnant women and its effect on maternal and fetal outcome. Arch Gynecol Obstet 2010;281:215-20.
8. Ajmani SN, Aggarwal D, Bhatia P, Sharma M, Sarabhai V, Paul M, *et al.* Prevalence of overt and subclinical thyroid dysfunction among pregnant women and its effect on maternal and fetal outcome. J Obstet Gynaecol India 2014;64:105-10.
9. Saraladevi R, NirmalaKumari T, Shreen B, Rani VU. Prevalence of thyroid disorder in pregnancy and pregnancy outcome. IAIM 2016;3:1-11.
10. Ozdemir H, Akman I, Coskun S, Demirel U, Turan S, Bereket A, *et al.* Maternal thyroid dysfunction and neonatal thyroid problems. Int J Endocrinol 2013;2013:987843.

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