Original Article

The Spectrum of Thyroid Dysfunction During Pregnancy and Fetomaternal Outcome, A Study from the Premier Institute of Western India

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Abstract

Background: Thyroid dysfunction evaluation during pregnancy is important for the mother's health, obstetric outcomes, and the child's cognitive development. This study is conducted to know various thyroid disorders that can occur during antenatal and their impact on mother and fetus outcomes. **Materials and Methods:** This observational research was conducted over two years at a tertiary center in Western Rajasthan, India. Seven hundred and seventy-two low-risk singleton pregnant patients who met the inclusive criteria were recruited. The estimation of T3, T4, and TSH was done along with a routine investigation in antenatal women. Antenatal having abnormal thyroid profiles were then analyzed for mother and fetus problems. **Results:** The prevalence of thyroid dysfunction in antenatal women is 16.5%. Subclinical hypothyroidism (SCH) was seen in 12.5% of cases, overt hypothyroidism in 3.36%, and subclinical hyperthyroidism in only 0.51% of cases. Anti-TPO was positive in 46 (41.44%) women with hypothyroidism and 1 (25%) with hyperthyroidism. Compared to euthyroid women, women with overt hypothyroid (19.23% vs 3.1%, $P = 0.002$) and subclinical hypothyroid (9.27% vs 3.1%, $P = 0.003$) were found to be associated with a higher risk of hypertensive disease. Concerning fetal outcomes. There was a high risk for preterm (12.37% v/s 4.9%, $P = 0.004$) and fetal growth retardation (FGR) in patients with SCH (7.21% v/s 3.1%, $P = 0.04$). **Conclusion:** Considering the significant influence of thyroid disorders on mother and fetus outcomes, the screening for thyroid during pregnancy should be considered universally, particularly in developing countries with high prevalent rates, such as India.

Keywords: Hyperthyroidism, hypothyroidism, subclinical hypothyroidism, thyroid dysfunction in pregnancy

Introduction

The second frequent endocrine condition in antenatal women is thyroid disorder. Thyroid dysfunction evaluation during pregnancy is important for maternal/fetus outcomes and the development of the child. Hypothyroidism is the most common thyroid disorder seen during pregnancy among thyroid disorders. The incidence of hypothyroidism during pregnancy varies significantly throughout the country. It ranges from 2.5% in the west to 11% in India.[1] The maternal and fetal thyroid glands are intrinsically linked, and drugs that influence the mother's thyroid gland also affect the fetal gland. Thyroid autoantibodies have been linked to higher rates of abortion and uncontrolled thyrotoxicosis.[2] Both untreated hypothyroidism and uncontrolled thyrotoxicosis have been associated with poor pregnancy outcomes. Patients with elevated TSH and thyroid autoimmunity have a fourfold higher risk of diabetes in pregnancy (GDM) and a threefold higher risk of less weight at birth (LBW).[3]

Miscarriage, anemia, pre-eclampsia, gestational hypertension, placental abruption, premature birth, higher cesarean rate, and postpartum hemorrhage (PPH) are all mother complications associated with a thyroid disorder.[1] Thyroid dysfunction is linked to premature birth, respiratory distress syndrome, LBW, perinatal hazards, increased risk of hospitalization in neonatal ICU, and neurological and cognitive impairment in the newborn. Thyroid hormone is essential for a developing

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fetus's brain. If congenital hypothyroidism is not identified and managed early, it can cause severe cognitive, neurological, and developmental problems in children.[1]

Given the increased prevalence of thyroid dysfunction in antenatal women and the related danger to the women and their babies, this study seeks to determine the frequency of thyroid abnormalities in antenatal women and its impact on mother and fetal outcomes.

Material and Methods

This prospective observational study was conducted in the Department of Obstetrics and Gynecology of the tertiary care center of Western Rajasthan. With prior approval from the Institution's Scientific and Ethical Committee (AIIMS/IEC/2018/809-31/12/2018) and obtaining informed and written consent, 772 singleton pregnancies were recruited who visited our outpatient department(OPD). Multiple pregnancies and known cases of thyroid dysfunction or chronic diseases such as diabetes or heart or lung disorder and those delivered outside were excluded from the study. The blood sample was collected for routine hematological parameters and free T3, free T4, and serum TSH. The chemiluminescence method is used for the estimation of TSH. The anti-TPO antibody was sent to a patient with an abnormal thyroid function test (TFT).

As per regulation 14.2 of American Thyroid Association (ATA) guidelines (2017), the following references are recommended: TSH cut-off levels are as follows: 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. Normal levels of free T4 are 0.7 to 1.8 ng/dl, and the free levels of T3 are 1.7 to 4.2 pg/ml. The anti-TPO level is <35 IU/ml.[4]

Antenatal women with normal T4 and increased TSH were diagnosed with subclinical types of hypothyroidism (SCH); women with lower fT4 and increased TSH were diagnosed with overt hypothyroidism; those with normal fT4 and low TSH were diagnosed with SCH, and women with increased T4 and lower TSH diagnosed with overt hyperthyroidism. Anti-TPO is raised if the value is more than or equivalent to 35. Hypothyroidism and hyperthyroidism, both subclinical and overt, were treated. During pregnancy, thyroid profiles were performed six weeks, and medication doses were adjusted. Until termination, antenatal women were followed. The following pregnancy outcome characteristics were measured concerning thyroid disorders: pre-eclampsia, abruption placenta, premature birth, Fetal growth restriction(FGR), less weight at birth (LBW), stillbirth, abortion, GDM, anemia, cesarean section rate, and PPH are among the conditions that can occur during pregnancy. Weight at birth, Apgar at 1 and 5 minutes, hospitalization in the neonatal intensive care unit, premature birth, FGR, non-reassuring fetal heart rate, and stillbirth were all recorded as fetal outcomes. Hyperbilirubinemia, respiratory distress, septicemia, low sugar, hypothermia, intracranial bleeding, and necrotizing enterocolitis were documented in neonates.

Statistical analysis

The SPSS 23(Statistical Package for the Social Sciences) was utilized to maintain and analyze the data. The categorical variables were assessed using the Pearson Chi-square test. *P*-value less than 0.05 was considered significant.

Results

Seven hundred seventy-two antenatal women were recruited in this study. This study's mean age of the mother was 25.93 ± 4.16. The most patients were between the ages of 21 and 30. (n = 605; 78.4%). The prevalence of thyroid disorders rose as age groups increased. The majority of SCH and overt hypothyroidism was high at 31–40 years (n = 15/105; 14.2%) and (n = 8/105; 7.61%), respectively.

Among 772 patients, 333 (43.1%) patients were primigravida, 245 (31.7%) were multigravida with previous vaginal delivery, 134 (17.4%) were multigravida with last cesarean section, and 60 (7.8%) were multigravida with previous h/o abortion.

Among 772 patients, 645 (83.5%) were euthyroid, and the remaining 127 (16.5%) had thyroid disorders. Subclinical hypothyroidism was seen in 97 (12.5%) patients. 26 (3.36%) patients had overt hypothyroidism, and only four (0.51%) patients had hyperthyroidism during pregnancy. Among hyperthyroid patients, Graves' disease was present in one patient only. In all individuals with abnormal TSH levels, an anti-TPO Antibody was recommended. Antibodies for anti-TPO antibodies were seen in 46 hypothyroidism patients (41.44%) and one (25%) hyperthyroidism patient.

When compared to women with euthyroidism, patient with overt hypothyroid was found to have an increased risk of hypertensive disorder (GHTN and PE) [n = 5 (19.23%) vs n = 20 (3.1%), *P* = 0.002]. No significant increase in GDM [n = 5 (19.23%) vs 83 (12.8%), *P* = 0.369], anemia [n = 2 (7.69%) vs n = 49 (7.59%), *P* = 1.0], PPH [n = 1 (3.8%) vs n = 7 (1.08%), *P* = 0.27], and premature rupture of membrane [n = 1 (3.84%) vs n = 21 (3.25%) *P* = 0.58] [Figure 1].

Hypothyroidism in the subclinical state is also linked to a higher risk of hypertension in antenatal women [n = 9 (9.27%) vs n = 20 (3.1%), *P* = 0.003]. No statistical finding was seen in GDM [n = 16 (16.49%) vs n = 83 (12.8%), *P* = 0.327], placental abruption [n = 1 (1.0%) vs n = 1 (0.15%)], PPH [n = 1 (1.03%) vs n = 7 (1.08%) *P* = 1.0], anemia [n = 3 (3.09%) vs n = 49 (7.59%), *P* = 0.13], and premature rupture of membranes [n = 8 (6.18%) vs n = 21 (3.25%), *P* = 0.151] in subclinical hypothyroid patients when compared with euthyroid patients.

In this study, no complications related to hyperthyroidism, such as thyroid storm and myxedema, were seen [Figure 2].

There is an increased risk for preterm birth among SCH [n = 12 (12.37%) vs n = 32 (4.9%) *P* = 0.004] and also a significant risk for FGR in patients with SCH [n = 7 (7.21%) vs n = 20 (3.1%) *P* = 0.04]. No considerable risk association for low-birth weight [n = 9 (9.27%) v/s n = 39 (6.04%), *P* = 0.228]

and NICU admission [n = 3 (3.09%) v/s n = 32 (4.80%) $P = 0.607$] was found in SCH when compared to euthyroid patients. Only one patient out of four patients had a low-birth weight baby. No patient was in the group of preterm or FGR.

Overt hypothyroidism in antenatal women is significantly linked with a higher risk for preterm birth [n = 5 (19.23%) v/s n = 32 (4.9%) $P = 0.011$), low-birth weight [n = 5 (19.23%) v/s n = 39 (6.04%) $P = 0.02$], and FGR [n = 3 (11.53%) v/s n = 20 (3.1%) $P = 0.05$] No statistically significant finding for NICU admission was found in overt hypothyroidism [n = 1 (3.8%) v/s n = 32 (4.96%) $P = 1.0$) when compared to euthyroid patients [Figure 3].

As far as a route of delivery is concerned, there is no increase in cesarean section rate in overt hypothyroid [n = 9 (34.6%) v/s n = 245 (37.9%) $P = 0.728$) and SCH (44.33% v/s 37.9%, $P = 0.232$) patients when compared with euthyroid patients. Two out of three (66%) hyperthyroid patients underwent LSCS.

The most common indication for emergency cesarean section was fetal distress.

Compared to euthyroid, there is no increased risk for NICU admission in patients with overt hypothyroid (3.8% v/s 4.96%, $P = 0.797$) and subclinical hypothyroid patients (3.09% v/s 4.96%, $P = 0.607$).

The commonest indication of NICU admission was birth asphyxia and respiratory distress (50%), followed by low-birth weight and prematurity (36.1%).

Data on hyperthyroid patients was inconclusive as the sample size was relatively small. Among the hyperthyroid patients, only one patient had Graves' disease.

In this study, the rate of abortion was relatively low. One patient, each with euthyroid and SCH, had a spontaneous abortion. One patient in a euthyroid group with gestational hypertension had an unexplained IUD.

Discussion

One of the most prevalent endocrine problems in pregnant women is thyroid illness. In this research, the thyroid disorder prevalence encountered during pregnancy was 16.5%, which is relatively high compared to the Western literature; among the thyroid disorders, the majority of SCH is the highest at 12.5%, followed by overt hypothyroidism at 3.36%. The incidence of hyperthyroidism is comparatively small, 0.51%. This finding is similar to the research done by Dhanwal DK *et al.*,[5] who found that the prevalence of hypothyroidism in antenatal patients was 13.13%. Another research done in 2015[1] reported the increased prevalence of undetected thyroid disorder in the first trimester; the majority of SCH was 21.5%, 0.4% had overt, and 3.3% had subclinical stage.[1] A review of the Western literature by Al Shanqeeti *et al.*[6] reported 13% of SCH. Research by Ramachandran and Friends[7] reported a high prevalence of thyroid dysfunction in pregnant women, 22.39%, and subclinical (20.63%). The pooled prevalence of overall

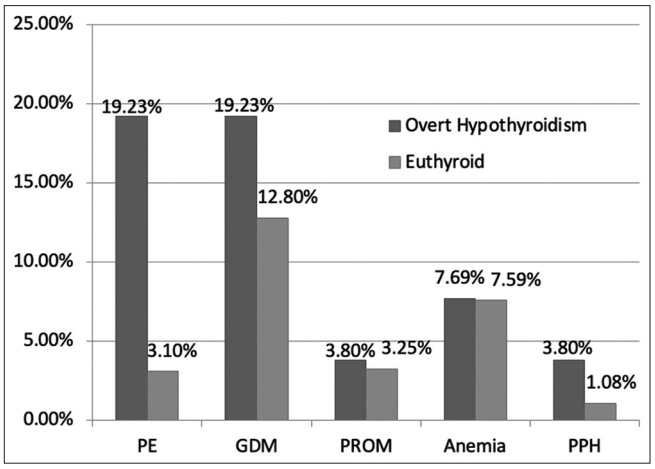

Figure 1: Adverse maternal outcomes in overt hypothyroidism

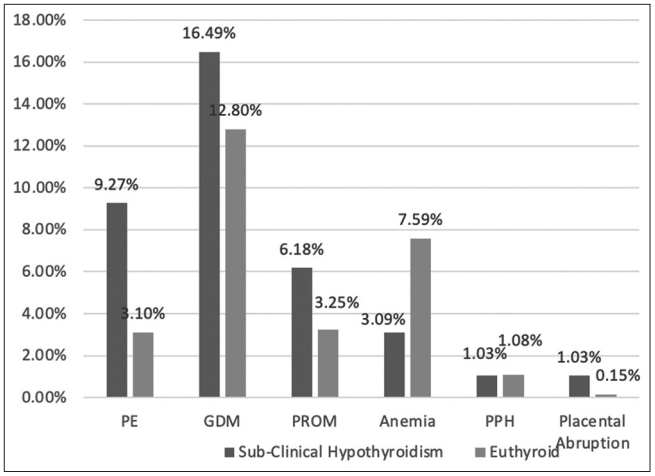

Figure 2: Adverse maternal outcomes in subclinical hypothyroidism

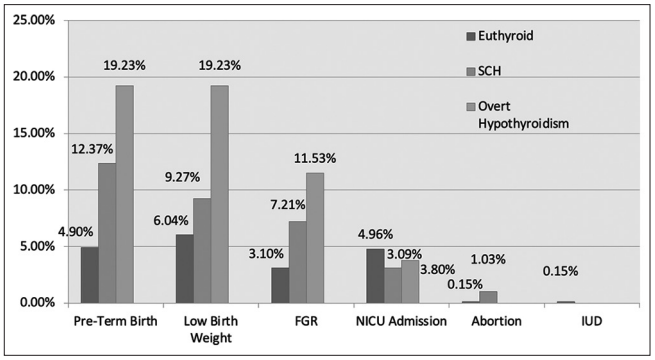

Figure 3: Adverse fetal outcomes in various thyroid dysfunctions

hypothyroidism in antenatal ladies was 11.07% in the research by Yadav V *et al.* (2021).[8] SCH and overt hypothyroidism prevalence rates were 9.51% and 2.74%, respectively. The results were comparable with the present study.

In this present study, a maternal complication such as hypertensive disorder in pregnancy (gestational HTN and pre-eclampsia) is significantly increased in patients with both SCH and overt hypothyroidism. The risk associated with

hypertensive disease (GHTN and PE) does not increase when anti-TPO is positive (17.39% v/s 6.15%, $P = 0.119$) compared to anti-TPO negative patients. This study found no significant increase in risk for GDM, anemia, PPH, placental abruption, and PROM compared to euthyroid patients. When the delivery route was compared, the cesarean section rate did not increase in patients with thyroid disorders. The commonest reason for an emergency section is non-reassuring fetal heart rate. Another research by Singh and Reddy[9] also reported the significant risk for pre-eclampsia in patients with hypothyroidism. Still, they didn't find any significant risk for IUGR, miscarriage, gestational diabetes, preterm labor and PPH.

Another study by Tuija Männistö *et al.*[10] 2013 reported that primary hypothyroidism and hyperthyroidism are associated with high risk for pre-eclampsia with OR = 1.47 and superimposed pre-eclampsia with OR = 2.25. However, their study also found the risk for gestational diabetes (OR = 1.57), preterm birth (OR = 1.34), placental abruption, and cesarean section rate in patients with primary hypothyroidism, which is inconsistent with this study. The incidence of anemia is 4.8 times greater in women with hypothyroidism than in women with euthyroid, according to Mahadik K *et al.*[11] 2020. There is also a considerably increased incidence of pre-eclampsia in women with hypothyroidism. They also reported the significant association between cesarean delivery rate and oligohydramnios in a patient with hypothyroidism in the considerable field. In one study by Pinar[12] and Saraladevi *et al.*,[13] the risk of hypertensive disorder in overt hypothyroidism was low compared to the present study. The risk of hypertensive disease in a survey conducted by Saraladevi *et al.*[13] and Jani *et al.*[14] was consistent with the present study.

Adverse fetal outcomes in this study in patients with SCH include preterm birth and FGR, which is significantly increased but not significantly increased risk for LWB and admission to neonatal ICU in women with SCH in comparison with euthyroid. Among pregnant patients with overt hypothyroidism, the adverse fetal outcomes include preterm birth ($P = 0.011$), LWB ($P = 0.022$), and FGR ($P = 0.05$), which are significantly increased when compared to normal patients. No significant increase in risk for abortion, IUD, and NICU admission is seen compared to euthyroid patients.

As per a study by Singh and Reddy,[9] the adverse fetus outcomes include miscarriages (16.6 vs. 1.7%), premature delivery (33.3 vs 5.8%), LWB (50 vs 12.11%), fetal growth retardation (FGR) (25 vs 4.9%), and intrauterine death (16.6 vs 1.7%) which are significantly increased in women with overt hypothyroidism as compared to the women with normal thyroid levels. In comparison with women with normal thyroid levels, patients having subclinical hypothyroidism had a substantially increased risk of adverse fetal outcomes such as miscarriages (5.5% vs 2.39%), premature birth (11.2% vs 5.8%), LWB (25% vs 12.11%), and FGR (8.4% vs 4.9%). According to research by Jani *et al.*,[14] there is a higher risk of abortion, preterm delivery, intrauterine death, and placenta abruption when hypothyroidism is overt or insufficiently treated. Hypothyroidism was strongly linked to an increased risk of IUGR, according to research by Singh and Reddy[9] ($P = 0.009$. In one research published by Dhabhai *et al.*[15] in 2023, pregnancy outcomes like LBW, preterm, and stillbirth were similar among euthyroid women and those with hypothyroidism. Still, in the present study, there is an increased risk for preterm birth among SCH vs in euthyroid [$P = 0.004$] and a significant risk for FGR in patients with SCH [$P = 0.04$]. There is no considerable risk association for Low-Birth Weight [P=0.228].

Limitation

Due to the heterogeneity in different TSH calculation methods, we cannot provide precise thyroid profile values in the third stage of pregnancy. Due to the small sample size, the data on hyperthyroidism needed to be more conclusive. Antibody levels of TPO were not tested in all antenatal women routinely.

Conclusion

One of the most typical, preventable endocrine diseases pregnant women experience is thyroid dysfunction. This study concludes that thyroid disorders are highly prevalent (16.5%) during pregnancy. Among thyroid disorders, the most common is subclinical hypothyroidism (SCH), followed by overt hypothyroidism. The most significant adverse maternal outcome is a hypertensive disorder PPH, anemia, and placental abruption. Adverse fetal effects associated with overt hypothyroidism include preterm birth, low-birth weight babies, and FGR, which are significantly increased compared to euthyroid patients. Early thyroid dysfunction detection and treatment initiation are essential due to the major impact of thyroid issues on the mother and fetal outcomes in pregnancy. Thus, widespread prenatal screening for undetected thyroid dysfunction should be explored, particularly in developing countries such as India, where the prevalence rate is high.

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Conflicts of interest

There are no conflicts of interest.

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