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Original Research Article

Observational Research to Assess the Prevalence and Impact of Thyroid Disorders on Maternal and Fetal Outcome

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Abstract

Aim: To determine the prevalence of thyroid dysfunction in pregnancy and its impact on obstetrical outcome.

Material & Methods: This observational study was carried out by the department of Biochemistry in collaboration with department of Obstetrics and Gynecology Venkateshwara Institute of Medical Sciences, Gajraula, Uttar Pradesh, India. A total of 360 pregnant women were selected over a period of one year, between 13 and 26 weeks of gestation were included in the study.

Results: The prevalence of hypothyroidism was 5%, out of which 2.7% had overt hypothyroidism and 3.1% had subclinical hyperthyroidism in the present study. The maternal complications in different groups were adverse maternal effects in overt hypothyroidism included preeclampsia (18.1 versus 9.09%) and placental abruption (18.1 versus 2.00%, P = 0.005).

Conclusion: The prevalence of thyroid disorders was high in our study with associated adverse maternal and fetal outcomes. Routine screening of thyroid dysfunction is recommended to prevent adverse fetal and maternal outcome.

Keywords: Maternal and fetal outcome, pregnant women, Thyroid disorders

Introduction

Pregnancy can be viewed as a state in which a combination of events concurs to modify the thyroidal economy. There is change in the level of thyroxine-binding globulin, total thyroid hormone level and change in the level of thyroid stimulating hormone (TSH) during normal pregnancy [1].

Thyroid dysfunction (TD) may be overlooked in pregnancy because of the nonspecific symptoms and hypermetabolic state of normal pregnancy. Thyroid dysfunction has varied impact on pregnancy outcome. The risk of miscarriage is increased in autoimmune thyroid disease. Severe maternal hypothyroidism can result in irreversible neurological deficit in the offspring. Graves' disease (GD) can lead to pregnancy loss as well as fetal thyroid dysfunction. The prevalence of hypothyroidism in pregnancy is around 2.5% according to the Western literature [2]. The prevalence of GD is around 0.1–

0.4% and that of thyroid autoimmunity (TAI) is around 5–10% [3].

Hypothyroidism is widely prevalent in pregnant women and the rate of detection, especially in a developing country like India, has not kept pace with the magnitude of the problem. Since hypothyroidism is easily treated, timely detection and treatment of the dysfunction could reduce the burden of adverse fetal and maternal outcomes in pregnancy which is commonly encountered. Prevalence of overt thyroid dysfunction is 2–3% in pregnant women; subclinical dysfunction is 10%, while rate of autoimmunity is 5–10% [4, 5].

Maternal complications include miscarriage, anemia, preeclampsia, gestational hypertension, placental abruption, preterm delivery, increased rate of caesarean section, and postpartum hemorrhage. The mode of delivery may have adverse impacts on fetal-pituitary-thyroid axis. Fetal outcomes resulting from thyroid dysfunction are preterm birth, neonatal respiratory distress syndrome, low birth weight (LBW), perinatal morbidity and mortality, increased NICU admission; and neuropsychological and cognitive impairment. Thyroid hormone is critical for brain development in the developing fetus. Children born with congenital hypothyroidism have severe cognitive, neurological and development abnormalities if the condition is not recognized and treated promptly. A study demonstrated that children born to pregnant women with hypothyroidism had lower intelligence quotient (IQ) scores compared to children born to pregnant women without hypothyroidism [6].

As the harmful effects of thyroid diseases for both mother and baby have started to come into prominence, the need for screening thyroid during pregnancy has also been discussed. Although literature shows that screening for subclinical hypothyroidism is cost-effective, the number of studies showing the results and benefits of screening has not yet reached a sufficient level [7-11].

Hence, we aim to determine the prevalence of thyroid dysfunction in pregnancy and its impact on obstetrical outcome.

Material & Methods:

This observational study was carried out by the department of Biochemistry in collaboration with department of Obstetrics and Gynecology Venkateshwara Institute of Medical Sciences, Gajraula, Uttar Pradesh, India

Prior permission from ethical committee of the hospital was taken. An informed consent was taken from all the study subjects. All patients were subjected to the usual history taking, clinical examination and ante-natal profile of investigations.

Methodology

A total of 360 pregnant women were selected over a period of one year, between 13 and 26 weeks of gestation were included in the study. All healthy pregnant women with no other medical disorder, with singleton pregnancy were included in the study. Patients with multifetal gestation, known thyroid and metabolic disorders like diabetes, hypertension, and a history of pregnancy loss were excluded from the study.

In addition to these tests, serum T3, T4, TSH and anti TPO antibody were done samples were collected at the same time as other investigations. The reference ranges of the test values used in this study were as per the 2011 Guidelines of American Thyroid Association for the Diagnosis (ATA) and Management of Thyroid Disease (MTD) during pregnancy.[12] As per Regulation 14.2 of ATA Guidelines, if trimester-specific ranges for TSH are not available in the laboratory, the following normal reference ranges are recommended: 1st trimester - 0.1 to 2.5 m IU/L, 2nd trimester - 0.2 to 3.0m IU/L and 3rd trimester - 0.3 to 3.0 m IU/L. In pregnancy, serum total T4 measurement is

recommended over direct immunoassay of free T4. Because of alterations in serum proteins in pregnancy free T4 assay may yield lower values based on reference ranges established with normal non-pregnant sera.[13] Also method-specific and trimester specific reference ranges for direct immunoassays of free T4 have not been generally established. By contrast, total T4 increase during the 1st trimester and the reference range throughout pregnancy is 1.5-fold that of the non-pregnant range. [14]

Statistical analyses:

All statistical analyses were performed using the Statistical Package of Social Sciences and

Problem Solutions (SPSS-20). Bilateral Fischer's exact test was used to compare two different rates if the number of measures in any one group was <5. Continuous variables were presented as mean±SD and analyzed using unpaired, two-tailed student's t test. Analysis was done of the data obtained.

Results:

All the patients were divided according to thyroid function. Out of 360 patients, 76 (21.1%) had deranged thyroid function, making the prevalence of thyroid dysfunction 19%. Prevalence of hypothyroidism was 17%, out of which in 2% had overt hypothyroidism and 9% had subclinical hypothyroidism.

The prevalence of hyperthyroidism was 5%, out of which 2.7% had overt hyperthyroidism and 3.1% had subclinical hyperthyroidism in the present study. Anti-TPO antibody was done in patients with deranged TSH levels. Anti TPO antibody was found positive in 55% of hypothyroid patients. No anti-TPO antibody was found in hyperthyroid patients.

The maternal age was high in the overt hypothyroid and overt hyperthyroid. In the present study, the mean BMI was 21.63 ± 3.7 for euthyroid patients, 23.82 ± 2.7 for subclinical hypothyroid, 25.92 ± 1.4for overt hypothyroid, 20.22 ± 0.11 for subclinical hyperthyroid, and 21.57 ± 1.6for overt hyperthyroid [Table 1].

Table 2 shows the maternal complications in different groups were adverse maternal effects in overt hypothyroidism included preeclampsia (18.1 versus 9.09%) and placental abruption (18.1 versus 2.00%, P = 0.005). No significant increase in anemia (18.1 versus 17.7%), gestational diabetes mellitus (GDM) (9.0 versus 1.7%), and postpartum hemorrhage (PPH) (9.0 versus 1.0%) was seen in the overt hypothyroid group. Subclinical hypothyroidism was significantly associated with preeclampsia (P = 0.03) as compared to the euthyroid patients. No significant increase in anemia, placental abruption (P = 0.09), GDM, and PPH was seen in the subclinical hypothyroid patients. There were no maternal deaths in any of the groups.

The rate of cesarean section was significantly higher in patients with overt hypothyroidism (P = 0.0020) as compared to the euthyroid controls. No significant increase was seen in the subclinical hypothyroid and hyperthyroid groups. Among the various indications of cesarean section, the most common was cesarean section for fetal distress.

Fetal outcome in different groups are adverse fetal outcomes in overt hypothyroidism included spontaneous abortion (P = 0.040), preterm birth (P = 0.02), low birth weight (LBW), intrauterine growth retardation (IUGR) (P = 0.01), and fetal death (P = 0.020) as compared to the euthyroid women. All of them were found to be highly significant. Adverse fetal outcomes in subclinical hypothyroidism included spontaneous abortion, preterm delivery, LBW, and IUGR as compared to the euthyroid women. Preterm birth was found to be statistically significant (P = 0.01)

Table 1: Obstetrical variable in the antenatal period

Type	Age Mean±SD	BMI Mean ±SD
Euthyroid (N=293)	24.32 ± 4.72	21.63 ± 3.7
Subclinical hypothyroidism (N=41)	26.71 ± 3.74	23.82 ± 2.7
Overt hypothyroidism (N=11)	29.06 ± 5.69*	25.92 ± 1.4*
Subclinical hyperthyroidism (N=9)	26.33 ± 2.85	20.22 ± 0.11
Overt hyperthyroidism (N=6)	30.74 ± 1.30*	21.57 ± 1.6*

*P ≤0.05

Table 2: Maternal complications in different groups

	Euthyroid N% = 293	Subclinical hypothyroidism N%= 41	Overt hypothyroidism N%= 9	Subclinical hyperthyroidism N%= 9	Overt hyperthyroidism N%= 6
		Maternal Complications			
Anemia	**52** (17.75)	**6** (14.63)	**2** (18.18)	**1** (11.11)	**1** (16.67)
Preeclampsia	**34** (11.6)	**13** (31.71)*	**2** (18.18)	**0**	**0**
Abruption	**9** (3.072)	**1** (2.439)	**2** (18.18)*	**0**	**0**
GDM	**5** (1.706)	**1** (2.439)	**1** (9.091)	**0**	**3** (50)*
PPH	**3** (1.024)	**4** (9.756)	**1** (9.091)	**0**	**0**
		Mode of Delivery			
Preeclampsia	**31** (10.58)	**12** (29.27)*	**3** (27.27)	**0**	**0**
Abruption	**7** (2.389)	**1** (2.439)	**2** (18.18)	**0**	**0**
GDM	**2** (0.683)	**1** (2.439)	**1** (9.091)	**0**	**7** (33.33)*
PPH	**29** (9.898)	**3** (7.317)	**1** (9.091)	**0**	**0**
		Fetal Outcomes			
Preterm birth	**16** (5.461)	**15** (36.59)*	**6** (54.55)*	0	**0**
IUGR	**10** (3.413	**4** (9.756)	**4** (36.36)*	**0**	**0**
LBW	**36** (12.29)	**11** (26.83)*	**9** (81.82)*	**0**	**0**
Abortions	**8** (2.73)	**1** (2.439)	**2** (18.18)*	**2 (**22.22)	**1** (16.67)
Still Births	**3** (1.024)	**0**	**1** (9.091)*	0	**0**
		Neonatal Outcomes			
Respiratory distress syndrome	**14** (4.778)	**5** (12.2)	**3** (27.27)*	**0**	**0**
Sepsis	**7** (2.389)	**1** (2.439)	**1** (9.091)*	**0**	**0**
Hypoglycemia	**2** (0.683)	**1** (2.439)	**0**	**0**	**0**
Hypothermias	**2** (0.683)	**1** (2.439)	**0**	**0**	**0**
Intracranial bleed	**2** (0.683)	**0**	**0**	**0**	**0**
Necrotizing enterocolitis	**1** (0.341)	**0**	**0**	**0**	**0**
Early neonatal death	**5** (1.706)	**1** (2.439)	**1** (9.091)	**0**	**0**

***P≤0.05**

Discussion:

Thyroid disorders are one of the most common endocrine disorders in women during pregnancy and are associated with adverse maternal and fetal outcomes in pregnancy. However, an early detection of

thyroid dysfunctions and treatment of mother during gestation improves the outcome. [15]

Early detection of thyroid during pregnancy is possible if the patient is suggested thyroid function test during her first prenatal visit or soon after the pregnancy is confirmed.[16] There has been a debate for a long time about the upper limit of normal TSH during pregnancy.

Recent guidelines by ATA and the National Association of Clinical Biochemists (NACB) have reduced this to 2.5 m IU/L in 1st trimester and 3.0 m IU/L in 2nd or 3rd trimesters. This was done because it was seen that in more than 95% of rigorously screened euthyroid volunteers, the normal range was from 0.4 to 2.5 m IU/L.[17] This of course increases the disease frequency of hypothyroidism in pregnancy up-to 5-fold. There is a wide variation in the prevalence of hypothyroidism in pregnancy 2.5% in the West to 11% in India. [18]

The miscarriage rate was 3 times more common in subjects with TAI (7.35 versus 26.5%) in our cohort (Table 3). The association has previously been established by various studies [19-22]. TAI may be viewed as a marker of generalized immune imbalance that will explain the rejection of fetal graft [23]. Presence of TAI could be associated with a subtle thyroid hormone deficiency, due to the reduced functional reserve characteristic of chronic thyroiditis [23]. Women with thyroid antibodies tend to become pregnant at an average 3-4 years later and are, therefore, more prone to pregnancy loss. In our cohort, the relatively higher age in the patients with miscarriage might also have contributed to pregnancy loss.

Hypothyroidism causes vascular smooth muscle contraction both in systemic and renal vessels, which leads to increased diastolic pressure, peripheral vascular resistance, and decreased tissue perfusion, which could be the pathophysiology of preeclampsia in hypothyroidism [24-25]. Thyroid dysfunction can be associated with proteinuria, which is known to result in increased excretion of thyroxine and thyroid-binding globulins. Rare cases have been reported in which proteinuria is severe enough to result in losses of thyroid-binding globulins and thyroxine that cannot be compensated by the body [26-28].

Low birth weight is associated with hypothyroidism due to its association with preeclampsia. Reduced fetal thyroxine may cause disruption to the development of the pituitary-thyroid axis of the newborn, fetal pituitary growth hormone secretion, vascular responsiveness and maturation, and cardiovascular homeostasis in utero [29-30]. These factors are causative for the observation of reduced neonatal birth weight of offspring born to mothers with inadequately controlled hypothyroidism at initial presentation or at third trimester. In this study LBW was observed in

31.6% of women with hypothyroidism, as compared to 20% observed in another study. [31,32]

Conclusion:

The prevalence of thyroid disorders was high in our study with associated adverse maternal and fetal outcomes. Routine screening of thyroid dysfunction is recommended to prevent adverse fetal and maternal outcome.

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