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STUDY OF THYROID DISORDERS IN PREGNANCY AND ITS EFFECT ON MATERNAL AND FETAL OUTCOME

Gynecology

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ABSTRACT

Thyroid hormones have profound variation during the life span and are associated with
severe adverse health impacts. Pregnancy, as an important reproductive event, has a profound but reversible effect on the thyroid gland and its functions.

Diagnosing thyroid diseases

during pregnancy can be difficult as the clinical signs and symptoms mimic those of pregnancy. Hypothyroidism is associated with weight gain, fatigue and constipation while hyperthyroidism causes nausea and increased appetite.

Given the high prevalence of thyroid disturbances in pregnancy and associated risk to mother and fetus, this study was aimed to screen subclinical thyroid during pregnancy, to determine the incidence of thyroid disorders in pregnancy and to study the effects of thyroid disorders on maternal and fetal outcome of pregnancy. Hundred randomly selected Pregnant women coming for routine antenatal checkups were included in the study.

It is concluded from the present study that proportion of Thyroid abnormalities found were 11%. Proportion of Hypothyroidism was 10% while hyperthyroidism was 1%.

Preterm deliveries, miscarriage, Abruptio placenta, IUGR, Pre-eclampsia, still birth were the maternal outcomes while low birthweight was the most common fetal outcome. Our study concludes that there is a high prevalence of thyroid dysfunction in pregnancy in India, majority being subclinical hypothyroidism, and Universal screening for hypothyroidism is highly desirable in our country.

KEYWORDS:

Thyroid disorder, Subclinical hypothyroid, Pregnancy

Introduction

Thyroid hormones have imminent role during the life span and are associated with severe adverse health impacts. Pregnancy induces major but reversible changes in the thyroid gland and its functions.[1]

The concentrations of thyroid binding globulins increase up to mid pregnancy due to high estrogen levels; serum thyrotropin (TSH) levels decrease in early pregnancy due to direct thyroidal stimulation by human chorionic gonadotropin; thyroid size and thyroid hormone production increase throughout pregnancy and iodine requirements increase due to increased renal clearance and losses to the feto-placental unit. Pregnancy can be considered as a stress test of maternal thyroid function where womenwith limited thyroid reserve may develop hypothyroidism.[2]

Pregnancy is actually a state of excessive thyroid stimulation leading to an increase in thyroid size by 10% in iodide sufficient areas and 20-40% in iodide deficient regions.3 Furthermore following the physiological and hormonal changes caused by pregnancy and human chorionic gonadotropin (HCG) the production of thyroxin (T4) and triiodothyronine (T3) increase up to 50% leading to 50% increase in a woman's daily iodide need, while Thyroid-stimulating hormone (TSH) levels are decreased, especially in first trimester.4 In an iodide sufficient area, these thyroid adaptations during pregnancy are well tolerated, as stored inner thyroid iodide is enough; however in iodide deficient areas, these physiological adaptations lead to significant changes during pregnancy.[5]

Furthermore in women who suffered from thyroid dysfunction prior to pregnancy, the hormonal changes mentioned are magnified, leading to possibly adverse pregnancy outcomes if not been treated appropriately. The prevalence of thyroid dysfunction in pregnant women is relatively high so that overt thyroid dysfunction occurs in 2-3% of pregnancies, and subclinical dysfunction in 10% of pregnancies4 and thyroid autoimmunity is even more prevalent.[5]

Current recommendations suggest targeted TSH screening for women at high risk for thyroid disease before or during early pregnancy, with other thyroid function tests used to confirm the diagnoses and disease severity. However, reference ranges of TSH or free thyroxine (fT4) obtained from non-pregnant populations do not reflect normal values in pregnant women because of their physiologic changes in thyroid function.[5]

AIMS

- To determine the incidence of thyroid disorder in pregnancy.
- To know the maternal and fetal outcome in pregnancy.
- To screen subclinical thyroid during pregnancy.
- To determine whether universal screening is required or not.

Materials And Methods :

The "To Study Incidence of Thyroid Disorder in Pregnancy to Know Its Effect on Maternal and Fetal Outcome" is the descriptive longitudinal study. Hundred randomly selected Pregnant women coming for routine antenatal checkups who attend the Outdoor Patient Department (OPD) were included in the study.

Inclusion criteria

- Singleton Pregnancy
- Primigravida / Multigravida

Exclusion criteria

- Patient with twin pregnancy
- Patient with known thyroid disorder before pregnancy

A predesigned semi-structured questionnaire was prepared based on the review of literature of thyroid disorders during pregnancy. The questionnaire included the information regarding age, gender, education, height, weight and BMI. It also included information regarding clinical symptoms like weakness, tiredness, intolerance to cold, constipation, disturbed sleep, hoarseness of voice, sweating, heat intolerance, tremor, frequent bowel movements. The information regarding family and personal history of thyroid disorders, diabetes, menstrual history, history of infertility, history of miscarriage, blood pressure measurement and PIH presence were also recorded. The information regarding laboratory parameters like Hemoglobin, TSH, T3, T4 and TPO antibody were also noted. The diagnosis of thyroid disorders was done according to the national guidelines, and mode of delivery, Maternal and Fetal outcome were also recorded. Scientific Ethical Committee approval taken.

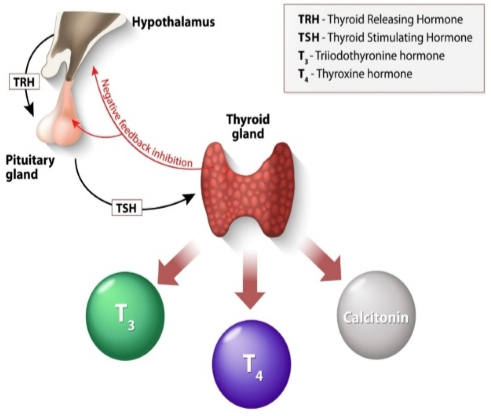

Figure 1: Mechanism of Thyroid Hormone Secretion and Regulation

Results :

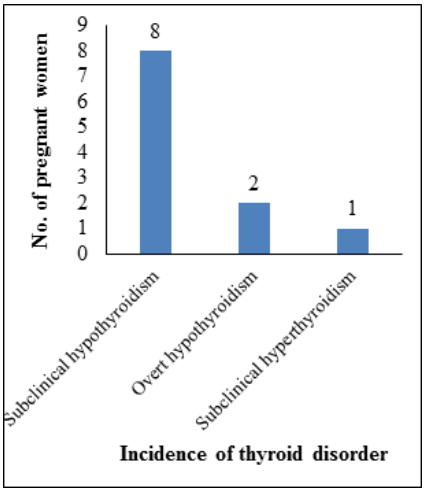

Figure 2: Incidence of thyroid disorder in pregnancy

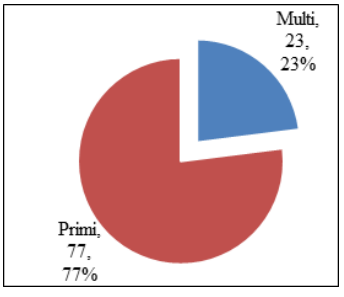

Figure 3: Distribution of study participants according to parity

Table 1: Mean age of study participants

Thyroid status	Frequency	Mean (years)	SD (years)
Normal	89	24.04	2.66
Hypothyroidism	10	24.40	1.42
Hyperthyroidism	1	26.0	-
Total	100	24.10	2.56

Table 2: Symptoms of thyroid disease among study participants

Symptoms	Frequency	Percent
Weakness	54	54.0
Tiredness	88	88
Intolerance to cold	58	58
Constipation	66	66
Disturbed sleep	65	65
Hoarseness	49	49
Sweating	50	50
Heat intolerance	50	50
Tremor	47	47
Frequent bowel movements	51	51

Table 3: Mean BMI of study participants

Thyroid status	Frequency	Mean BMI (kg/m2)	SD (kg/m2)
Normal	89	28.64	2.17
Hypothyroidism	10	28.85	2.05
Hyperthyroidism	1	28.30	-
Total	100	28.66	2.14

Table 4: Family history of thyroid disorders among study participants

Family history of thyroid disorders	Frequency	Percent
Present	18	18.0
Absent	82	82.0
Total	100	100.0

Table 5: Past history of miscarriage among study participants

Past history of miscarriage	Frequency	Percent
Yes	11	11.0
No	89	89.0
Total	100	100.0

Table 6: History of infertility among study participants

History of infertility	Frequency	Percent
Yes	12	12.0
No	88	88.0
Total	100	100.0

Table 7 : Mean TSH levels among study participants

Thyroid status	Frequency	Mean TSH µU/ml	SD
Normal	89	1.63	0.45
Hypothyroidism	10	7.0	2.81
Hyperthyroidism	1	0.8	-
Total	100	2.16	1.88

Table 8: Mean fT4 levels among study participants

Thyroid status	Frequency	Mean T4 level (µg/dl)	SD
Normal	89	1.382	0.243
Hypothyroidism	10	1.150	0.437
Hyperthyroidism	1	2.400	-
Total	100	1.369	0.292

Table 9: Maternal outcome of delivery among study participants

Maternal Outcome	Frequency	Percent
Abruptio placenta	1	1.0
IUGR	1	1.0
Miscarriage	2	2.0
Pre-eclampsia	1	1.0
Preterm	2	2.0
Stillbirth	1	1.0
Normal	92	92.0
Total	100	100.0

Table 10: Mean TPO Ab levels among study participants

Thyroid status	Frequency	Mean TPO Ab level (IU/mL)	SD
Normal	89	13.35	5.05
Hypothyroidism	10	18.00	5.98
Hyperthyroidism	1	39.0	-
Total	100	14.08	5.85

Table 11: Fetal outcome among study participants

Fetal Outcome	Frequency	Percent
Miscarriage	2	2.0
Stillbirth	1	1.0
Low Birth Weight	23	23.0
Normal	74	74.0
Total	100	100.0

Table 12: Mean birthweight of Neonates

Thyroid status	Frequency	Birth weight Mean (kg)	SD
Normal	89	2.759	0.264
Hypothyroidism	10	1.885	0.219
Hyperthyroidism	1	2.70	-
Total	100	2.695	0.344

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 treat¬ment of mother during gestation improves the outcome.[3] 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.[6] Thyroid dysfunction during pregnancy had been an important research area in clinical endocrinology due to the fact that thyroid dysfunction has immense impact on maternal and fetal outcomes.[7] More importantly, children born to hypothyroid mothers have poor intellectual function during later part of their life. [8] Therefore, majority of the developed countries have national neonatal screening program. The question whether to screen all pregnant women for hypothyroidism is still not resolved. There has been a wide geographic variation in prevalence of hypothyroidism during pregnancy. It varies from 2.5% from the West to 11% from India. It seems that prevalence of hypothyroidism is more in Asian countries compared with the West. [9]

In this study, we have reported the highest prevalence of hypothyr oidism predominantly subclinical from India compared with previous studies.[4,10] Incidence of subclinical hypothyroidism during pregnancy was found 8.0% and that of overt hypothyroidism and Subclinical hyperthyroidism were 2.0% and 1.0% respectively, which is compar able with indian study.

Various reasons have been proposed for increased prevalence of hypothyroidism in pregnancy. Increased iodine intake in diet, prese nce of goitrogens in diet as reported from studies in India, deficiency of micronutrients like selenium and iodine, rise in the number of autoimmune hypothyroidism in general population are some of the reasons ascribed to high Hypothyroidism prevalence in India. An inter-relation of this high prevalence of thyroid disorders with a high prevalence of the other major endocrinopathy - diabetes mellitus, has to be explored further.

The mean age of patients with hypothyroidism and hyperthyroidism was 24.40 ± 1.42 years and 26.0 years respectively in our study comparable with other indian study10. Pregnancy can imitate some of the signs that are observed in hypothyroidism, including fatigue, anxiety, constipation, muscle cramps, and weight gain; as a result, the clinical diagnosis of hypothyroidism during pregnancy may be difficult.[11] Moreover, most signs of hypothyroidism can be hidden by a woman's status following the increase in metabolism in pregnancy. Furthermore the thyroid hormonal profile in normal pregnancy can be mis-interoperated as hypothyroidism and as a result the interpretation of thyroid function tests needs trimester-specific reference intervals for a specific population.[12]

In our study, 18 percent had family history of thyroid disease comparable with study conducted by Weiwei Wang et al.[14]

In the present study, 11 % women had past history of miscarriage. The association has previously been established by various studies.

In the present study, mean BMI of women with normal thyroid function and hypothyroid women was 28.64 ± 2.17 and 28.85 ± 2.05 kg/m^2 respectively. One woman with hyperthyroid function had BMI of 28.30 kg/m^2, which is comparable with literature.

The mean serum T4 levels among hypothyroid women was 1.15 ± 0.437µg/dl. In comparison, mean serum T4 levels among normal thyroid women was 1.382 ± 0.243µg/dl; mean TSH levels among hypothyroid women was 7.0 ± 2.81µU/ml. In comparison, mean TSH levels among normal thyroid women was 1.63 ± 0.45 µU/ml.

In the present study, mean serum TPO Ab levels among hypothyroid women was 18.00 ± 5.98IU/mL. In comparison, mean serum TPO Ab levels among normal thyroid women was 13.35 ± 5.05IU/mL. similar findings depicted in previous studies[9].

Anti-thyroid antibodies are relatively common among women during their reproductive ages, 6-20% of all euthyroid women are positive for anti-thyroid antibodies[8] . The presence of anti-thyroid antibodies during a woman's reproductive age is not necessarily followed by a thyroid dysfunction and 10-20% of all pregnant women who are TPO antibody positive remain euthyroid in first trimester[3]. Despite the high prevalence of TPO antibody positive among reproductive age women, there is no consensus on the feto-maternal complications of euthyroid pregnant women who are TPO antibody positive. As a result, routine screening of pregnant women for thyroid antibodies is controversia[1,2]
The rate of cesarean section was high in cases with hypothyroidism when compared with controls with euthyroidism (39.28% vs. 23.3%, p = 0.046). In addition, hypothyroidism increased the risk of fetal distress, which is in agreement with the study done by Goel et al., in 2005. 13 It has been suggested that hypothyroidism may exert irreversible effects on the fetus and placenta in early pregnancy, which impair their ability to tolerate the stress of a normal delivery, thereby increasing the incidence of fetal distress in labor.

In the present study, maternal outcome was normal among 92 (92.0%) pregnant women, while 2 women had preterm delivery and 2 had miscarriage. Abruptio placenta, IUGR, Pre-eclampsia, still birth were seen in one women each. When compared with euthyroid cases, hypothyroidism was significantly associated with preeclampsia (33.3% vs. 7.3%; p = 0.0001) and IUGR (16.6% vs. 5.7%; p = 0.009). No significant increase in miscarriage (3.2% vs. 6.66%), anemia (9.2% vs. 10%), gestational diabetes (4.9% vs. 3.33%), preterm labor (4.6% vs. 3.33%), still birth (0.05% vs. 0%) and PPH (5% vs 3.31%) was noted in patients with hypothyroidism[14].

In the present study, out of 100 women, 74 women had normal weight babies, 23 had low birth weight babies, 1 woman had stillbirth and 2 women had miscarriage.

There is no consensus on adverse impacts of subclinical hypoth yroidism on pregnancy outcomes; while some studies demonstrated higher chance of placental abruption, preterm birth, miscarriage, gestational hypertension, fetal distress, severe preeclampsia and neonatal distress and diabetes, the other study have not reported and adverse effect .[14] The long term effect of overt hypothyroidism on cognitive function has been well documented; these children have lower IQ and more developmental dysfunction , however there is no consensus on the long term cognitive effects of subclinical hypoth yroidism[15].

Indications for screening of high-risk group includes history of thyroid dysfunction or prior thyroid surgery, age >30 years, symptoms of thyroid dysfunction or the presence of goiter, thyroid peroxidase antibody (TPOAb) positivity, type 1 diabetes or other autoimmune disorders, history of miscarriage or preterm delivery (RPL), history of head or neck radiation, family history of thyroid dysfunction, morbid obesity (body mass index [BMI] ≥40 kg/m^2), use of amiodarone or

lithium, or recent administration of iodinated radiologic contrast, history of infertility and residing in an area of known moderate-to-severe iodine sufficiency. In view of the wide variation in the results of FT4 assays, method-specific and trimester-specific reference ranges of serum FT4 are required. [2]

It is very difficult to distinguish the symptoms of SCH from that of normal pregnancy as these are not always classical. There may be no signs and symptoms or mild general signs and symptoms of hypothyroidism, like depression, weight gain, dry or flaky skin, body weakness or feeling cold easily, slow pulse, low body temperature and increased need for sleep.

Diagnosis can be best done by serum TSH and FT4. Free T3, total T3 and T4 are to be done when there is disturbed TSH level to know the secondary reason for hypothyroidism. Next step is antithyroid antibodies (maternal thyroid peroxidase) should be done in all cases where serum TSH is out of range. Other least important tests includes red cell selenium, urinary T3 (recent studies show that symptoms of hypothyroidism correlate best with 24-hour urinary Ft3), urinary iodine concentration, thyroid ultrasound, serum cholesterol, which may be elevated in hypothyroidism, prolactin as a widely available test of pituitary function, testing for anemia and basal body temperature.

These tests are important because the risk complications arising from hypothyroidism either overt or subclinical is very high. These includes a three-fold increase in risk of placental abruption and a two-fold risk of preterm delivery; reported in mothers with SCH. [13]

However, even when hypothyroid pregnant women were insufficiently treated with levothyroxine (Lt4), the intelligence quotient (IQ) scores of their offspring were not different from those of controls. Pregnant women with SCH have higher incidence of neonatal morbidity and mortality, although contradictory results have also been reported. Two-fold risk increase in neonate intensive care nursery admission (RR 1.8; 95% CI 1.1- 2.9%) and incidence of respiratory distress syndrome defined as ventilator assistance >24 hours.

The goal of treatment is to normalize maternal serum TSH values within the trimester-specific pregnancy reference range. If trimester-specific reference ranges for TSH are not available in the laboratory, the following reference ranges are recommended by USPSTF; first trimester (0.1-2.5 mIU/L) second trimester (0.2-3.0 mIU/L) third trimester (0.3-3.0 mIU/L).

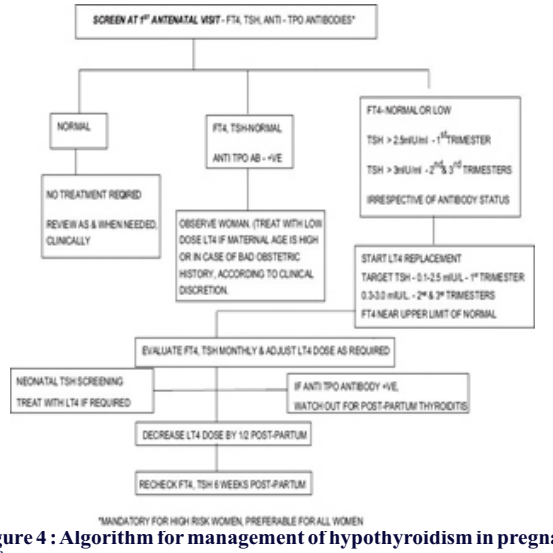

Figure 4 : Algorithm for management of hypothyroidism in pregnancy[10]

Recent guidelines proposed by the Antithyroid Association (ATA) and National Association of Clinical Biochemistry have stated that it is likely that in the future the upper limit of the serum TSH euthyroid reference range will be reduced to 2.5 mIU/L for all adults, because more than 95% of rigorously screened normal euthyroid volunteers have serum TSH values between 0.4 and 2.5 mIU/L. [15]

SCH has been associated with adverse maternal and fetal outcomes. The 2010 Cochrane review of such potential interventions concluded that it may be useful to treat women with SCH that are also antithyroid antibody positive with exogenous thyroid hormone in an attempt to improve pregnancy outcomes. In light of the safety in pregnancy of levothyroxine (pregnancy category A drug), the AACE recommends treatment of all pregnant women, even those with SCH or positive TPO-Ab. [16]

When treatment with levothyroxine was inadequate, the outcome of pregnancy was abortion (60% vs 71.4%), premature delivery (20% vs 7.2%) and term delivery (20% vs 21.4%) in overtly hypothyroid patients and subclinically hypothyroid patients, respectively. When treatment was adequate, term delivery (100% vs 90.5%) in overtly hypothyroid and subclinically hypothyroid patients respectively; there were no abortions in any of the groups. Abortions, premature and term deliveries in patients who were euthyroid on levothyroxine at the time of conception were 4%, 11.1% and 84.9%, respectively. So, they concluded that the evolution of pregnancies did not depend on whether the hypothyroidism was overt or subclinical but mainly on the treatment received. The adequate treatment of hypothyroidism during gestation minimizes risks and generally, makes it possible for pregnancies to be carried to term without complications.

Conclusion

It is concluded from the present study that proportion of Thyroid abnormalities found were 11%. Proportion of Hypothyroidism was 10% while hyperthyroidism was 1%. Tired, constipation and intolerance to cold were common features among hypothyroidism cases. Normal vaginal delivery was the most common mode of delivery. Preterm deliveries, miscarriage, Abruptio placenta, IUGR, Pre-eclampsia, still birth were the maternal outcomes while low birthweight was the most common fetal outcome. Our study concludes that there is a high prevalence of thyroid dysfunction in pregnancy in India, majority being subclinical hypothyroidism, and Universal screening for hypothyroidism is highly desirable in our country.

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