

DOI: <http://dx.doi.org/10.18203/2320-1770.ijrcog20191224>

Original Research Article

Comparison of maternal and perinatal outcome in pregnancy with altered thyroid profile and euthyroid patients: a prospective, observational and case control study in a tertiary care centre

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Received: 28 January 2019

Accepted: 05 March 2019

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ABSTRACT

Background: Thyroid disease is one of the commonest endocrine disorder affecting women of reproductive age, and when untreated during pregnancy is associated with an increased risk of complications. The objective of this review was to increase awareness and to provide a review on adverse effect of thyroid dysfunction on maternal and perinatal outcome.

Methods: This prospective, observational hospital-based case-control study carried on women coming for antenatal check-up in a Tertiary Care Hospital in INDORE from May 2018-December 2018. 50 known booked antenatal (case) patient with established thyroid disorder, more than 32 week of gestation, and 50-matched euthyroid patients (control) were taken.

Results: Women suffering from overt and subclinical hypothyroidism and hyperthyroidism are nulliparous in 72% cases as compared to 32% in euthyroid patient. Increased maternal age was associated with higher incidence of thyroid dysfunction. Normal vaginal delivery by spontaneous labour seen in 56% of euthyroid, while it is reduced with thyroid dysfunction. 38% of altered thyroid profile patient undergo induction of labour and 24% cases undergo caesarean section as compared to control (17%). Adverse fetal outcome like intrauterine growth retardation, preterm birth and ICU admission seen increased with thyroid dysfunction as compared to euthyroid patients.

Conclusions: Thyroid dysfunction in pregnancy, although has a low incidence, but is associated with adverse maternal and fetal implications. Thus, thyroid screening should be done in antenatal period to improve fetomaternal outcome.

Keywords: Antenatal outcome, Hyperthyroidism, Hypothyroidism, Perinatal outcome, Thyroid dysfunction

INTRODUCTION

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 function.¹⁻³ 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. Furthermore following the physiological and hormonal changes caused by pregnancy and human chorionic gonadotropin (HCG) the production of thyroxin (T4) and tri-iodothyronine (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.¹⁻³ Compared to hyperthyroidism, hypothyroidism is very common during pregnancy; 2-3% of pregnant women

suffer from hypothyroidism (0.3-0.5% overt hypothyroidism and 2-2.5% subclinical hypothyroidism).^{4,5} 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.^{6,7}

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-interpreted as hypothyroidism and as a result the interpretation of thyroid function tests needs trimester-specific reference intervals for a specific population.^{8,9,10}

Inadequately treated or subclinical hypothyroidism increases the risk for miscarriage and fetal death, anemia, postpartum haemorrhage, placental abruption, cardiac dysfunction, preeclampsia, gestational diabetes, and preterm births whereas adequately treated hypothyroidism only increases the risk for cesarean sections.¹¹⁻¹³

Overt hyperthyroidism during pregnancy was not prevalent and was reported in 2 out of 1000 pregnancies (0.2%), while subclinical hyperthyroidism was occurred in 1.7% of pregnancies.^{14,15} The most prevalent reason for hyperthyroidism during pregnancy was the transient hyperthyroidism resulting from hyperemesis gravidarum (THHG) due to the thyroid stimulation of beta-HCG.¹⁶

The natural physiological changes during pregnancy can mimic some of the signs observed in hyperthyroidism, including increased in basal metabolism, heart rate, fatigue, anxiety, palpitations, heat intolerance, warm and wet skin, hand tremors and systolic murmur.^{17,18,19} Poor control of hyperthyroidism during pregnancy is also associated with increased risk of miscarriage and stillbirth, hypertension in pregnancy, preterm births, and maternal heart failure.^{20,21}

Race/ethnicity may be important in modifying the potential risks thyroid diseases pose during pregnancy because the risk of hyperthyroidism and hypothyroidism in the population and predisposition to adverse outcomes in pregnancy varies by race/ethnicity.

METHODS

The present observational, prospective hospital-based case-control study. was conducted in the Department of Obstetrics and Gynaecology, SAIMS and PGI, Indore during the time May 2018 to December 2018.

50 knowns booked pregnant patients (case) with established thyroid disorder with more than 32 week of gestation and 50 matched euthyroid patient (control) who

attended the antenatal clinic regularly during the period were recruited for study. The study was started after obtaining ethical clearance from institute ethical review board.

Cases

50 known thyroid disease patients (subsequent cases)

Inclusion criteria

- Known pregnant patients with thyroid disorders and those having symptoms and signs suggestive of hypothyroidism and hyperthyroidism.

Booked patients following up regularly for antenatal check up and who delivered at SAIMS and PGI, Indore

Exclusion criteria

- Other medical disorders like pregnancy induced hypertension, diabetes.

Controls

50 euthyroid pregnant patients. Every patient's thyroid level should be checked attending the antenatal clinic in the study duration (50 patient) and fulfilling the inclusion and exclusion criteria was taken as a matched control.

Inclusion criteria

- No other medical disorder
- No obstetric risk factors
- Patients with a history of spontaneous abortion but with no identifiable or known cause

Exclusion criteria

H/o. LSCS for non-obstetric indication

Study procedure

Based on the inclusion and exclusion criteria, 50 patients in each group were selected from the Department of Obstetrics and Gynaecology, SAIMS and PGI, Indore.

The nature and purpose of the study was explained to the patients.

History, examination findings on antenatal visit, on admission and during the stay in hospital and investigations in chronological order were taken on the predesigned Performa by the Chief Investigator herself.

In the patients of thyroid disorder, besides the routine antenatal profile and ultra-sonography, thyroid function tests served as the guiding investigations in the

management of pregnancy. The T3, T4 and TSH levels were done on their first visit. According to the values, thyroxin dose was revised for hypothyroid patients and for hyperthyroid patient Later on, in the pregnancy, T3, T4 and TSH levels were done every 6-8 weeks or whenever required with respect to the signs and symptoms of the patient, fetal growth parameters and any dose revision.

In the euthyroid patients, besides the routine antenatal profile and ultra-sonography examination, T3, T4 and TSH level were done anytime between 16-20 weeks of gestation.

Whenever the patient was admitted to the hospital, either in labour or for any complication, she was managed appropriately.

The basic guidelines for management included maintaining euthyroid state of tile mother (in cases) and assuring a good maternal and fetal outcome.

After delivery the cord blood samples of neonate was sent for T3, T4, TSH level estimation and according to the initial values, babies were given thyroxine replacement therapy and followed-up later.

Statistical analysis

The statistical difference between the foetal outcome in the cases and controls were compared by Chi-square test.

RESULTS

The patients were divided into the following groups according to thyroid function test results:

Group 1: Euthyroid, defined as normal TSH (0.2–3.0 μ IU/l).

Group 2: Subclinical hypothyroid, defined as high TSH (>3.0 μ IU/l) in the presence of normal levels of Free T4 (0.8–2.0 ng/dl).

Group 3: Overt hypothyroid, defined as high TSH (>3.0 μ IU/l) with low Free T4 (<0.8 ng/dl).

Group 4: Subclinical hyperthyroid, defined as low serum TSH (<0.2 μ IU/l) concentration with normal Free T4 (0.8–2.0 ng/dl).

Group 5: Overt hyperthyroid, defined as with high Free T4 (>2.0 ng/dl) with decreased TSH (<0.2 μ IU/l).

Thyroid dysfunction is associated with adverse fetal outcomes in pregnancy. The data on hypothyroidism were more conclusive than in hyperthyroidism as the sample size in the hyperthyroidism group was small and the disease is comparatively infrequent. Women suffering from overt and subclinical hypothyroidism and hyperthyroidism are nulliparous in 72% cases as compared to 32% in euthyroid patient (Table 1).

Table 1: Relation of parity and thyroid disorder.

Parity	Euthyroid n=50, N (%)	Sub clinical hypothyroid n=35, N (%)	Overt hypothyroid n=12, N (%)	Subclinical hyperthyroid n=2, N (%)	Overt hyperthyroid n=1, N (%)
Nulliparous	16 (32)	25 (71.4)	9 (75)	01 (50)	01(100)
Primiparous	15 (30)	8 (22.85)	3 (25)	01 (50)	00
Multiparous	19 (38)	02 (5.71)	00	00	00

Table 2: Relation of age with thyroid disorder.

Age (year)	Euthyroid n=50, N (%)	Subclinical hypothyroid n=35, N (%)	Overt hypothyroid n=12, N (%)	Subclinical hyperthyroid n=2, N (%)	Overt hyperthyroid n=1, N (%)
Less than 20	10 (20)	02 (5.71)	00	00	00
21-25	17 (34)	09 (25.71)	01 (8.33)	01 (50)	00
26-30	15 (30)	13 (37.1)	7 (58.3)	01 (50)	01 (100)
More than 30	8 (16)	11 (31.4)	4 (33.4)	00	00

In present study noted that increased maternal age was associated with higher incidence of thyroid dysfunction. Median age of our cases 28.5 year as compared to Nidhi et al 22 which was 26.7 year. (Table 2). P=0.54 (the difference between the two groups is not statistically

significant) was found in Table 3. Also, it shows that normal vaginal delivery by spontaneous labour seen in 56% of euthyroid, 17.1% of subclinical hypothyroid, 16.7% of overt hypothyroid and 50% of subclinical hyperthyroid patient. 38% of altered thyroid profile

patient undergo induction of labour and 24% cases undergo caesarean section as compared to control (17%) (Table 3). P=0.04 (the difference between the two groups is statistically significant) found in table 4. It also shows adverse fetal outcome preterm birth in 33.4% of overt hypothyroid cases, 17.14% of subclinical hypothyroid cases as compared to 16% of euthyroid patient. In 58.33% of overt hypothyroid patient, 40% of subclinical hypothyroid patient have low birth weight baby as compared to 18% of euthyroid patient. Intrauterine

growth retardation found in 41.7% of overt hypothyroid patient baby which was statistically significant as compared to 4% of euthyroid patients' baby (Table 4). P=0.064 (the difference between the two groups is statistically significant) was found in table 5. It also shows 58.3% of overt hypothyroidism, 34.28% subclinical hypothyroid patient's baby undergo ICU admission as compared to 10% euthyroid patient. ICU admission not found in hyperthyroid patient's baby (Table 5).

Table 3: Mode of delivery.

Foetal outcome	Group 1 (euthyroid) n=50, N (%)	Group 2 (subclinical hypothyroid) n=35, N (%)	Group 3 (overt hypothyroid) n=12, N (%)	Group 4 (subclinical hyperthyroid) n=2, N (%)	Group 5 (overt hyperthyroid) n= 1, N (%)
Spontaneous labour	28 (56)	6 (17.1)	2 (16.7)	01 (50)	00
Induction of labour	07 (14)	15 (42.85)	2 (16.67)	01 (50)	01(100)
Caesarian section	9 (17)	8 (22.85)	4 (33)	00	00

Table 4: Foetal outcome.

Foetal outcome	Group 1 (euthyroid) n=50, N (%)	Group 2 (subclinical hypothyroid) n=35, N (%)	Group 3 (overt hypothyroid) n=12, n (%)	Group 4 (subclinical hyperthyroid) n=2, n (%)	Group 5 (overt hyperthyroid) n= 1, N (%)
Pre term birth	8 (16)	6(17.14)	4 (33.4)	00	00
Low birth weight	9(18)	14(40)	7(58.33)	01(50)	00
IUGR	2(4)	6(17.14)	5(41.7)	00	00
IUD	2(4)	4(11.4)	2(16.7)	00	00

Table 5: ICU admission.

Foetal outcome	Group 1 (euthyroid) n=50, N (%)	Group 2 (subclinical hypothyroid) n=35, N (%)	Group 3 (overt hypothyroid) n=12, N (%)	Group 4 (subclinical hyperthyroid) n=2, N (%)	Group 5 (overt hyperthyroid) n= 1, N (%)
ICU admission	5 (10)	6 (17.1)	5 (41.7)	00	00

DISCUSSION

This study at SAIMS and PGI, Indore (M.P.) was a prospective, observational, case-control study. In this study, the fetal outcome of 50 hypothyroid pregnant patients (subclinical hypothyroidism, overt hypothyroidism, Subclinical hyperthyroidism and overt hyperthyroidism) was studied in comparison to the 50 euthyroid pregnant patients who served as matched controls. All the patients included in the study were provided regular antenatal checkup. Routine investigations including ultra-sonography for fetal wellbeing and growth parameters were done. Iron and calcium supplementation was given to all patients. All hypothyroid patients were given optimum dose of thyroxine so as to ensure euthyroid state and subsequent

good fetal outcome.²³ Thyroid dysfunction is associated with adverse maternal and fetal outcomes in pregnancy. Thyroid hormone secretion physiological increases during pregnancy to meet the increase requirement of pregnant mother and foetus.

Women with marginally low thyroid function might not be able to meet this increase demand, leading to adverse consequences. Women on adequate replacement of thyroxine have good obstetrics outcome.²⁴ In the study of Tan et al no statistically differences in adequately treated thyroid patient and euthyroid patient.²⁵ Another study Albovich et al had shown same result that adequate treatment of thyroid disordered patient make it possible for pregnancy to be carried till term without added risk of complications.⁹

Maternal outcome

Women suffering from overt and subclinical hypothyroidism and hyperthyroidism are mainly nulliparous than Euthyroid patient, because most of the patients conceive after infertility treatment and also due to current trend of older women become pregnant. So, in present study, it is noted that overt hypothyroid and overt hyperthyroid women had higher maternal age as compared to women in the other groups.^{26,27} Median age 28.5 years comparable to Nidhi et al which was 26.7 year. In the study 50 thyroid disorder patient were studied among them vaginal delivery by spontaneous labour in different groups. 56 % of euthyroid, 17.1 % of subclinical hypothyroid, 16.7% of overt hypothyroid, 50 % of subclinical hyperthyroid and by induction of labour. 14% of euthyroid, 42.86% of subclinical hypothyroid, 16.67 % of overt hypothyroid, 50 % of subclinical hyperthyroid, 100% of overt hyperthyroidism cases. The rate of caesarean section was significantly higher in patients with overt hypothyroidism (33 vs. 17 % P=0.0031) as compared to the euthyroid controls. No significant increase was seen in the subclinical hypothyroid and hyperthyroid groups. So rate of vaginal delivery more 76% as compared to c-section 24%. This was comparable to Nidhi et al who had more vaginal delivery but in Dhara et al rate of c-section is more.²⁸

Perinatal outcome

Shows adverse fetal outcomes preterm birth in 33.3% of overt hypothyroid, 17.14% subclinical hypothyroid as compared to 16% of the euthyroid women. Preterm birth was found to be statistically significant (P = 0.02). Similar study by Negro et al found preterm delivery in altered thyroid profile patient as compared to euthyroid patient.

In the study mean birth weight in the group 1 was 2.61±0.45, in group 2 was 2.58±0.7, in group 3 was 2.2±0.8, in group 4 was 2.9±0.3, and in group 5 was 2.8±0.15. Mean birth weight in group 3 was significantly lower than that in Group 1 (P=0.0002). Mean birth weights in group 2, 4, and 5 were not statistically significant. In 58.33% of overt hypothyroidism and 40% of subclinical hypothyroid patient's baby have low birth weight (50vs. 26 %) as compared to the euthyroid women's baby (18%), found to be highly significant. In the study by Blazer et al birth weight was statistically smaller than control group.²⁹

Intrauterine growth retardation in 41.7% of overt hypothyroidism 17.14% of subclinical hypothyroid patient's baby is as compared to 4% of the euthyroid women, found to be highly significant (P=0.02).

In present study intrauterine death among overt hypothyroidism (16.6 vs. 4 %, P = 0.024) as compared to the euthyroid women, found to be highly significant. Which was same as found in study of Allen et al, but it

was not significant in subclinical hypothyroidism and hyperthyroidism as compared with euthyroid patient. 16.7% hypothyroid patient had history of still birth which was equivalent to study of Buckshee et al.

Allan et al. showed that TSH levels greater than 6 mU/liter were significantly associated with a higher frequency of stillbirth.³⁰ Benhadi et al found that high maternal TSH levels were associated with an increased risk of pregnancy loss. Because TSH is inversely related to hCG levels, women with low hCG levels are at a greater risk of child loss.³¹

Apgar score <7 at 1 min was seen in 37.5 % of overt hypothyroid as compared to 5.4 % of euthyroid neonates and was found to be statistically significant (P = 0.0088). I.C.U. admission in low Apgar score 41.7% of overt hypothyroidism, 17.14% of subclinical hypothyroid patient's baby, as compared to the 4% Of euthyroid women baby. It found to be highly significant (P= 0.064). In addition, maternal subclinical hypothyroidism increased the risk of fetal distress, which is in agreement with the study of Goel et al.³² who reported a higher incidence of fetal distress in pregnancies complicated by maternal hypothyroidism (subclinical hypothyroidism, euthyroid on replacement therapy, and overt hypothyroidism); it has been suggested that hypothyroidism may exert irreversible effects on the fetus and placenta in early pregnancy, which impair their subsequent ability to tolerate stress, thereby increasing the incidence of fetal distress in labor.³³ Fetal distress may impair infant developmental of the nervous system.³⁴ Although hyperthyroidism in pregnancy is uncommon, effects on both the mother and child are critical. However, in present study, no significant finding was seen as the sample size was small and the disease is comparatively infrequent.³⁵ The present study also shows that depression was associated with 25% hypothyroid mothers including both pre and post delivery period. Especially those patients who underwent LSCS as compared to control group had slow recovery and increased drowsiness and loss appetite and constipation. Therefore, the hypothyroidism seems to be the contributing factor for postpartum depression. Thyroxine dose increment was seen in 56% cases. The mean daily dose of thyroxine was found to be 120 mcg/ day in pregnancy. Thyroxine replacement was required in one baby born to the hypothyroid mother. There were main limitations in present study that TPO antibody levels were not examined in all the patients.

CONCLUSION

It is best to screen women early in the pregnancy for thyroid dysfunction because thyroid diseases satisfy most of the criteria for a disease to warrant population screening. Screening for thyroid dysfunction in a woman who is pregnant or wants to be pregnant is important because thyroid hormone status is directly related to fetal brain development.

ACKNOWLEDGMENTS

Authors would like to thank Dr. Suneel Singh Sengar for the support during study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Singh V, Natu N, Gupta AS. Comparison of maternal and perinatal outcome in pregnancy with altered thyroid profile and euthyroid patients: a prospective, observational and case control study in a tertiary care centre. *Int J Reprod Contracept Obstet Gynecol* 2019;8:1594-600.