SUBCLINICAL HYPOTHYROIDISM IN EARLY GESTATION: PREGNANCY OUTCOME IN TREATED AND UNTREATED WOMEN

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Manuscript Info

Abstract

Background: Thyroid disorders are among the most common endocrine disorders in pregnancy. Signs and symptoms of SCH are variable, often asymptomatic. Mostly SCH is a laboratory diagnosis; Risk factors include personal or family history of thyroid dysfunction, advanced maternal age, diabetes, other autoimmune disorders and morbid obesity.

Objective: To investigate the outcome of pregnancy in women detected to have subclinical hypothyroidism in early gestation and to evaluate whether treatment of subclinical hypothyroidism reduces the adverse pregnancy outcome.

Methods: A total of 200 subclinical hypothyroid pregnant women in their first trimester of pregnancy (TSH > 2.5-6mU/L) were included in the study. Out of these 100 women received treatment with thyroxine (group A) and 100 were left untreated and acted as controls (group B).

Results: The mean age of both the groups was 25 years. In obstetric score; most of the women were primigravida. Antenatal complications like GDM, PIH, small for gestational age and preterm delivery were observed almost equally. In the mode of delivery, 67 women in the treated group and 78 women in the control group delivered vaginally at term. Majority of newborns in both the groups had birth weight in the range of >2.5 to <3.5 kg.

Conclusion: In pregnant women with SCH (TSH > 2.5-6mU/L and normal T4 level), treatment with thyroxine does not have any association in reducing the incidence of preterm labour, gestational diabetes or hypertension. Neonatal outcome was normal in both the groups.
There are many studies which have reported adverse effects of SCH on pregnancy and neonatal outcome, these associations include pregnancy loss, preterm delivery, gestational diabetes, gestational hypertension, preeclampsia, placental abruption, premature rupture of membranes, intrauterine growth restriction, low birth weight, small for gestational age, low APGAR score and neonatal death\textsuperscript{5-10}. Similarly other studies however have not found any adverse outcomes associated with SCH\textsuperscript{11-13}.

**Causes:**
1. Iodine deficiency
2. Congenital
3. Postoperative or ablative changes
4. Viral thyroiditis
5. Autoimmune thyroiditis

**Diagnosis:**
1. Mostly SCH is a laboratory diagnosis
2. However when to suspect if
3. Personal or family history
4. Advanced maternal age
5. Diabetes or other autoimmune disorders
6. Morbid obesity

**Trimester specific range:**
1. 1\textsuperscript{st} trimester TSH 0.1-2.5 mIU/L
2. 2\textsuperscript{nd} trimester TSH 0.2-3 mIU/L
3. 3\textsuperscript{rd} trimester TSH 0.3-3 mIU/L

SCH can lead to:
1. Placental abruption
2. Preterm labour
3. Diabetes
4. Gestational hypertension
5. Neonatal complications like
6. Neurological deficits
7. Respiratory distress syndrome

Currently there is no evidence that identification and treatment of SCH during pregnancy improve these outcomes. No consensus has been reached about the need for universal thyroid screening and the treatment of subclinical hypothyroidism in pregnancy.

**Methodology:**
This prospective randomized study was conducted in Department of Obstetrics and Gynaecology, Government Medical College Srinagar. A total of 200 pregnant women having TSH value between 2.5-6 mIU/L were taken. Half of patients received treatment as (Group A) and another half were left untreated as controls (Group B).

**Inclusion criteria:**
1. All pregnant women who have subclinical hypothyroidism in 1\textsuperscript{st} trimester of pregnancy.
2. Singleton pregnancy.

**Exclusion criteria:**
1. Pregnant women with overt hypothyroidism.
2. Pregnant women with subclinical hypothyroidism having TSH>6mIU/L but <10mIU/L.
3. Pregnant women with medical complications like chronic hypertension, overt diabetes.
4. Multiple pregnancy.

The selected group received 25-50 mcg thyroxine daily. They were followed till delivery and the outcome compared in both groups.
Results:

Table 1: Maternal age.

| Age (years) | Group A | Group B |
|-------------|---------|---------|
| <20         | 9       | 16      |
| 21-30       | 72      | 66      |
| >30         | 19      | 18      |

From group A most of the patients (72) corresponds to age group 21-30 years and among group B most of the patients (66) corresponds to same age group.

Table 2: Obstetric Score.

| GPLA          | Group A | Group B |
|---------------|---------|---------|
| G1            | 49      | 55      |
| G2A1,G3A2     | 20      | 11      |
| G2P1L1 and above | 31      | 34      |

In the obstetric score, primigravida were highest in number from both the groups. There was a significant difference in the number of two groups regarding women with previous abortions (G2A1,G3A2) ($\chi^2$ =4.26, p<0.05). In our study multi gravida were also comparable.

Antenatal Complications:

Gestational Diabetes was found in 12 cases from group A and 14 controls from group B. Gestational hypertension was found in 7 cases from group A and 5 controls from group B. SGA /IUGR was found in 4 cases from both groups. Preterm deliveries were found in 6 cases from group A and 8 controls from group B. From above results we observed almost equal results in both groups.
In the mode of delivery 62 women from treated group and 70 women in the control group delivered vaginally at term and there was no significant difference ($\chi^2 = 0.49, p>0.05$). In the treated group 20 cases delivered by primary LSCS whereas among controls 8 women delivered by primary LSCS, there was significant difference in both groups ($\chi^2 = 5.82, p<0.05$). The number of repeat caesarean section and preterm vaginal delivery were comparable in the two groups.

Table 3: Gestational Age At Delivery.

| Gestational age (weeks) | Group A | Group B |
|------------------------|---------|---------|
| <34                    | 5       | 4       |
| >34 to <37             | 4       | 6       |
| >37                    | 91      | 90      |

Regarding the gestational age at delivery, 5 cases from group A and 4 controls from group B delivered less than 34 weeks whereas 4 cases from group A and 6 controls from group B delivered between 34 to 37 weeks. Majority of women delivered after 37 weeks and the numbers were 91 from group A and 90 from group B.

Table 4: Birth Weight At Delivery.

| Birth Weight (KG)  | Group A | Group B |
|--------------------|---------|---------|
| <2.5               | 18      | 19      |
| >2.5 TO <3.5       | 74      | 71      |
| >3.5               | 8       | 10      |

Majority of newborns in both groups had birth weight in the range of >2.5 to <3.5 kg. The mean birth weight in the treated group was 2.75 kg and in the control group was 2.84 kg and there was no significant difference ($p$ value $>0.05$).

Discussion:
TSH levels are generally lower throughout the pregnancy especially during the 1st trimester when HCG levels peak. Subclinical hypothyroidism is found to have a high risk for placental abruption, preterm labour, gestational hypertension, diabetes and neurodevelopmental delay in the baby. Multiple studies done earlier emphasized the treatment for SCH in early pregnancy. In the present study pregnant women with SCH and TSH level <6μ/l were selected and were divided into two groups. Group A received thyroxine and group B were given placebo. They were
evaluated for development of complications and was found that both the groups had almost equal number of complications. These results were similar to study by Cleary-Goldman et al done as part of FASTER trial.\textsuperscript{11}

However observations made by Casey BM and associates\textsuperscript{14} were different, they found significant increase in placental abruption, preterm labour and neonatal respiratory distress among patients who were not treated. The mean age of both the groups and the gestational age at delivery was comparable among both the groups in our study. In the obstetric score, significant number of women with previous abortion were from group A. Among the mode of delivery in the present study, statistically significant difference was found in the primary caesarean rate. There was no significant difference in the average birth weight of newborns in both the groups. Casey BM\textsuperscript{14} and associates found that although SCH has been associated with severe obstetric complications there has been no direct evidence that levothyroxine therapy reduces these risks. Similar observation was made in present study.

**Conclusion:**
In pregnant women with SCH (TSH> 2.5-6 mu/l and normal T4 level) treatment with thyroxine does not have any association in reducing the incidence of complications. Experts in 2011 opine that even if subclinical hypothyroidism is diagnosed insufficent evidence exists either for or against a recommendation for treatment with a low dose of thyroxine. So universal screening of all pregnant women for SCH is not recommended.

**References:**
1. Cooper DS. Subclinical hypothyroidism. N Engl J Med. 2001;345:260-65.
2. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, Nixon A, Pearce EN, Soldin OP, Sullivan S, Wiersinga W. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011; 21:1081-25.
3. 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(3):387-90.
4. Negro R, Stagnaro, Green A. Diagnosis and management of subclinical hypothyroidism in pregnancy. BMJ 2014; 349:g4929.
5. Casey BM, Dashe JS, Wells CE, McIntire DD, Byrd W, Leveno KJ, Cunningham FG. Subclinical hypothyroidism and pregnancy outcomes. ObstetGynecol2005; 105:239-45.
6. Su PY, Huang K, Hao JH, Xu YQ, Yan SQ, Li T, Xu YH, Tao FB. Maternal thyroid function in the first twenty weeks of pregnancy and subsequent fetal and infant development: a prospective population based cohort study in China.J ClinEndocrinolMetab2011; 96:3234-41.
7. Tudela CM, Casey BM, McIntire DD, Cunningham FG. Relationship of subclinical thyroid disease to the incidence of gestational diabetes. ObstetGynecol2012; 119:983-88.
8. Wang S, Teng WP, Li JX, Wang WW, Shan ZY. Effects of maternal subclinical hypothyroidism on obstetric outcomes during early pregnancy. J Endocrinol Invest2012; 35:322-25.
9. Feldthunen AD, Larsen J, Pedersen PL, Kristensen TT, Kventy J. Pregnancy induced alterations in mitochondrial function in euthyroid pregnant women and pregnant women with subclinical hypothyroidism: relation to adverse outcome. J ClinTranslEndocrinol2014; 1:e109364.
10. Wilson KL, Casey BM, McIntire DD, Halvorson LM, Cunningham FG. Subclinical thyroid disease and the incidence of hypertension in pregnancy. ObstetGynecol2012; 119:315-20.
11. Cleary–Goldman J, Malone FD, Lambert-Messerlian G,Sullivan L, Canick J, Porter TF, Luthy D, Gross S, Bianchi DW, D Alton ME. Maternal thyroid hypofunction and pregnancy outcome.ObstetGynecol2008; 112:85-92.
12. Mannisto T, Vaarasmaki M, Pouta A, Hartikainen AL, Ruokonen A, Surcel HM, Bloigu A, Jarvelin MR, Suvanto-Luukkonen E. Perinatal outcome of children born to mothers with thyroid dysfunction or antibodies: a prospective population based cohort study. J ClinEndocrinolMetab2009; 94:772-79.
13. 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 GynecolObstet2010; 281:215-20.
14. Casey BM, Thom EA, Peaceman AM, Varner MW, Sorokin Y, Hirtz DG et al. Treatment of subclinical hypothyroidism or hypothyroxinemia in pregnancy. N Engl J Med. 2017;376(9):815-25.