

Postpartum Follow-up in Women Diagnosed with Subclinical Hypothyroidism during Pregnancy

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Abstract

Background: Management guidelines about the thyroid disease in pregnancy are silent about the postpartum course of new onset subclinical hypothyroidism (SCH). Hence, we analyzed the 2 years outcome of SCH diagnosed during pregnancy. **Materials and Methods:** We conducted this retrospective study using the medical records of patients with new onset SCH during pregnancy between 2010 and 2013 ($n = 718$). Patients who stopped their levothyroxine after delivery with a 2-year follow-up record were included. We excluded patients with known thyroid disorders and continuous use of drugs that affect the thyroid results. The patients were divided into two groups (Group 1 – euthyroid and Group 2 – hypothyroid) based on the final outcome after 2 years. The data were analyzed using appropriate statistical methods and a $P < 0.05$ was considered statically significant. **Results:** A total of 559 (77.8%) women stopped levothyroxine after delivery, and the final follow-up data were available for 467 patients only. At the end of 2 years, 384 (82.2%) remained euthyroid, and the remaining 83 (17.8%) developed hypothyroidism. SCH and overt hypothyroidism were seen in 22 and 61 patients, respectively. Group 2 patients had higher mean age (25.5 vs. 23.6 years), goiter (51 vs. 2%), initial thyroid stimulating hormone (7.9 vs. 5.1 $\mu\text{IU/mL}$), and thyroid antibody positivity (76 vs. 13%) ($P < 0.001$). **Conclusion:** The majority of patients with SCH during pregnancy remain euthyroid after delivery. Advanced age, goiter, positive family history, and thyroid autoimmunity increase the future risk of hypothyroidism in patients with SCH diagnosed during pregnancy.

Keywords: Autoimmunity, pregnancy, subclinical hypothyroidism, thyroid

INTRODUCTION

Subclinical hypothyroidism (SCH) and autoimmune thyroid disease (AITD) are associated with adverse pregnancy outcomes.^[1-3] SCH has also been shown to affect the long-term neuropsychological and intellectual development of the newborn.^[4] Increasing awareness about the thyroid disease and wide availability of thyroid hormone estimation led to increased number of women with SCH and AITD in pregnancy. Few reports exist from our country about the prevalence and the complications of SCH in pregnancy.^[5-7] The issue has been debated extensively in the last few years leading to the release of management guidelines from many international societies.^[8-10] Most of the guidelines recommend treatment with levothyroxine keeping the thyroid stimulating hormone (TSH) in the gestational age specific range. However, the guidelines are not very clear about the postpartum management of the patients diagnosed with the SCH during pregnancy. Pregnancy leads to an increase in the requirement of the thyroid hormone,

and the increasing requirement is not well defined during the postpartum period.

The natural course of the SCH in nonpregnant individuals has been identified clearly.^[11] One-third of the patients remain SCH, another third progress to overt hypothyroidism (OH) and the remaining third improve to have normal thyroid function. The diagnosis of the SCH in pregnancy is based on the trimester-specific cutoff values of the TSH.^[8] Similar to the nonpregnant individuals, the pregnant women with SCH may improve, remain with SCH or progress to hypothyroidism after delivery. Indian obstetric care is burdened with poor postpartum follow-up and early unplanned next pregnancy.^[12] In this scenario, it is important to identify the women, who are

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at a higher risk of developing hypothyroidism in subsequent pregnancy. This knowledge helps in planning the management strategy after pregnancy and prevents the adverse impact of the undetected thyroid dysfunction. Hence, we evaluated the course of new onset SCH diagnosed during pregnancy and the risk factors of progression to hypothyroidism.

MATERIALS AND METHODS

Study population

We conducted this retrospective study using the medical records in a tertiary care, teaching hospital. The records pertaining to the patients between January 2010 and June 2013, who attended the endocrinology clinic for the new onset SCH during pregnancy, were included. A total of 718 patients with a diagnosis of SCH during pregnancy were evaluated, and the study protocol with salient findings is shown in Figure 1. We excluded patients with known thyroid disease, past use of thyroid hormone therapy, amiodarone and use of any other drug that could affect the thyroid result. The patients were divided into two groups for the comparison as per the thyroid functional status at the end of the 2-year follow-up: Group 1 (normal thyroid function or euthyroidism) and Group 2 (subclinical or OH).

Study measures

Clinical data were collected from all the participant records, including demographic details such as family history of thyroid disorder, gestational age at the time of SCH, presence of the goiter, thyroid hormone requirement during pregnancy, and mode of delivery and peripartum complications. The decision to stop levothyroxine after the delivery was taken by the treating physician. We derived the data pertaining to the TSH (at the time of diagnosis, follow-up for the 2 years) and thyroid peroxidase (TPO) antibody status. The Institutional

Ethics Committee approved the study protocol for the data analysis. We did not take individual consent from the patients, as the data were derived from the records maintained in the department.

Definitions

SCH during pregnancy was defined as having normal free thyroxine (T4) with elevated TSH (more than 2.5 and 3 μ IU/ml in first and next trimesters, respectively).^[9] SCH after delivery was defined as elevated TSH (>5 μ IU/ml) with normal T4. OH was defined as elevated TSH coupled with low T4. Serial thyroid panel was estimated in the patients till the end of the follow-up period. Patients with normal TSH and T4 at the end of the follow-up were defined as euthyroid. A TPO antibody titer of more than 30 IU/L was considered as diagnostic of AITD.

Statistical analysis

Continuous variables data are presented as mean, standard deviation and categorical variables using the frequency and percentages. Unpaired *t*-test and Chi-square test were used to compare the data between the groups. We did not calculate the power of the study and sample size as our study was purely observational in nature. Univariate logistic regression analysis was done for assessing the risk of permanent hypothyroidism after delivery. A two-tailed $P < 0.05$ was considered statistically significant for all the tests. The statistical analysis and graph generation was done using the Graph Pad Prism Software, Version 6 (Graph Pad Software, San Deigo, CA, USA).

RESULTS

A total of 559 out of 718 (77.8%) women stopped levothyroxine after delivery. The final follow-up data were available for 467 patients only as shown in Figure 1. At the end of 2 years, 384 (82.2%) remained euthyroid (Group 1) and the remaining 83 (17.8%) developed hypothyroidism (Group 2). SCH and OH were seen in 22 and 61 patients, respectively. Out of the 61 patients who developed OH, 38 developed during the 1st year and the remaining 23 during the 2nd year of follow-up. The clinical and biochemical parameters between both groups are shown in Table 1. Briefly, Group 2 patients had higher mean age, goiter, initial TSH value, and thyroid antibody positivity ($P < 0.001$). The final dose of levothyroxine during the last trimester of pregnancy was significantly higher in hypothyroid women than in euthyroid women. Table 2 shows the findings of the univariate logistic regression analysis for the future risk of hypothyroidism.

DISCUSSION

Our study showed that the majority of women with SCH during pregnancy remain euthyroid at the end of 2-year follow-up. The rate of progression to OH depends on the underlying etiology, initial TSH level, TPO antibodies, and goiter.^[13] Wickham cohort survey showed that the risk of progression to OH is higher in individuals with high initial TSH-independent of the

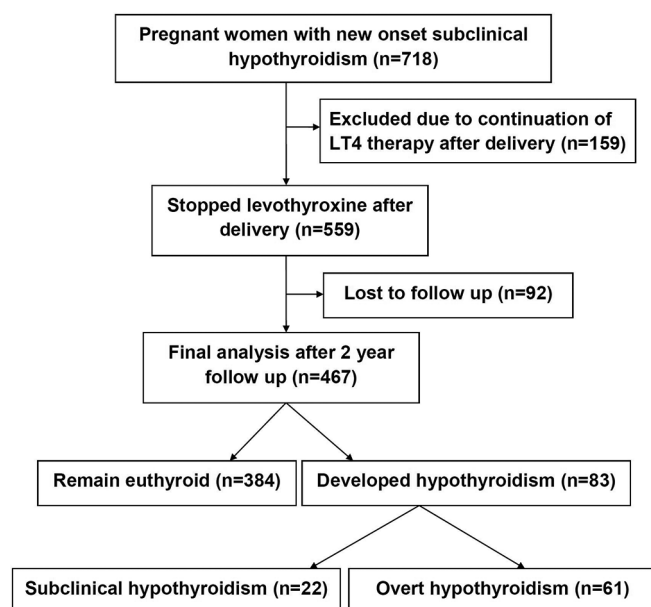


Figure 1: Flow diagram of the study

Table 1: Comparison between 2 groups regarding clinical and biochemical parameters

Feature	Units	Group 1 Euthyroid (n=384)	Group 2 Hypothyroid (n=83)	P
Age	Years	23.6 (1.9)*	25.5 (2.6)	<0.001
Positive family history	n (%)	6 (1.6)	8 (9.6)	<0.001
Palpable goiter	n (%)	6 (1.6)	42 (50.6)	<0.001
Initial TSH	μIU/ml	5.5 (1.1)	7.9 (1.2)	<0.001
Initial TSH				
<5 μIU/ml	n (%)	294 (76.6)	6 (7.2)	<0.001
Between 5 and 7.5 μIU/ml	n (%)	56 (14.6)	10 (12)	
>7.5 μIU/ml	n (%)	34 (8.9)	67 (80.7)	
TPO antibody				
Positive	n (%)	50 (13)	63 (75.9)	<0.001
Negative	n (%)	221 (57.6)	6 (7.2)	
Not known	n (%)	113 (29.4)	14 (16.9)	
Final LT4 dose	μg/day	41.2 (15.2)	79.8 (10.5)	<0.001

*Mean (SD). SD: Standard deviation, TSH: Thyroid stimulating hormone, TPO: Thyroid peroxidase

Table 2: Logistic regression model for the risk of development of hypothyroidism

Independent variable	OR	95% CI	P
Age	0.66	0.59-0.75	<0.0001
Initial TSH	0.24	0.18-0.32	<0.0001
Positive family history	0.15	0.05-0.44	<0.0001
Presence of goiter	0.02	0.01-0.04	<0.0001
Final LT4 dose	0.81	0.76-0.85	<0.0001
Positive TPO antibody	0.02	0.01-0.05	<0.0001

TSH: Thyroid stimulating hormone, TPO: Thyroid peroxidase, OR: Odds ratio, CI: Confidence interval

TPO antibody status.^[14] The natural course of the new onset SCH during pregnancy was evaluated by few authors.^[15-17] Haddow *et al.* showed that 64% of women developed OH over a decade of follow-up.^[15] The pregnant women in their study had a mean TSH of 13.2 μIU/ml. The reduced progression (18%) observed in our study could be explained by the short duration of follow-up and low value of TSH (7.9 μIU/ml). Our results are similar to that of a recent study with a 5-year follow-up duration that showed the development of OH in 25% of the patients.^[17]

Another important observation from our study is the predictive ability of higher initial TSH during pregnancy (81% of patients with initial TSH >7.5 μIU/ml develop hypothyroidism), for the future risk of hypothyroidism as shown in Table 1. A similar finding was observed in previous studies, where an elevated TSH (>5 μIU/ml) predicted the likelihood of hypothyroidism after delivery.^[16] Future management guidelines should consider the initial TSH value as a marker for recommending continuation of levothyroxine therapy after delivery. AITD was more in patients with hypothyroidism, and higher TPO positivity rates have been observed in Indian pregnant women.^[18] The predictive value of TPO antibodies for progression to OH is shown in several studies.^[5,14,19] Therefore, women with AITD in pregnancy are at a higher risk of future hypothyroidism.

The other finding observed in our study was a higher rate of palpable goiter in hypothyroid group than in euthyroid group. The presence of a goiter in pregnant women could be physiological or pathological with multiple risk factors.^[20] AITD frequently runs in the families and could be responsible for the persistence of a goiter after pregnancy.^[21] The higher levothyroxine requirement during the last trimester in hypothyroid women could be explained by the diminished thyroid reserve and the presence of other risk factors for hypothyroidism. The risk of hypothyroidism could be identified by the goiter, AITD, and higher thyroxine requirement.^[22] The strengths of our study include the seminal nature of the study with a sizeable number of participants. The limitations of our study include retrospective design, diagnosis of thyroid disease based on a single TSH and TPO value and lack of sonological evaluation of the goiter. We did not perform the multivariate analysis, due to the less number of hypothyroidism patients and missing TPO value in a significant proportion of patients. The failure of multivariate analysis and data being derived from a single center are the other limitations of our study.

CONCLUSION

The majority of patients with SCH during pregnancy remain euthyroid after delivery. Advanced age, goiter, positive family history, and thyroid autoimmunity increase the future risk of hypothyroidism in these patients. Large prospective studies with more number of patients are required to study the natural course of SCH detected during pregnancy.

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Conflicts of interest

There are no conflicts of interest.

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